Rapid HIV Testing: 2005 Update

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Associate Director for Laboratory Diagnostics
Division of HIV/AIDS Prevention
### Awareness of Serostatus among Persons with HIV, United States

<table>
<thead>
<tr>
<th>Category</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number HIV infected</td>
<td>850,000 - 950,000</td>
</tr>
<tr>
<td>Number unaware of their HIV infection</td>
<td>180,000 - 280,000</td>
</tr>
</tbody>
</table>
Advancing HIV Prevention: New Strategies for a Changing Epidemic

Four priorities:

1. Make voluntary HIV testing a routine part of medical care
2. Implement new models for diagnosing HIV infections outside medical settings
3. Prevent new infections by working with persons diagnosed with HIV and their partners
4. Further decrease perinatal HIV transmission

MMWR April 18, 2003
Four FDA-approved Rapid HIV Tests

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity (95% C.I.)</th>
<th>Specificity (95% C.I.)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>OraQuick Advance</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- whole blood</td>
<td>99.6 (98.5 - 99.9)</td>
<td>100 (99.7-100)</td>
</tr>
<tr>
<td>- oral fluid</td>
<td>99.3 (98.4 - 99.7)</td>
<td>99.8 (99.6 – 99.9)</td>
</tr>
<tr>
<td>- plasma</td>
<td>99.6 (98.5 - 99.9)</td>
<td>99.9 (99.6 – 99.9)</td>
</tr>
<tr>
<td><strong>Uni-Gold Recombigen</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- whole blood</td>
<td>100 (99.5 – 100)</td>
<td>99.7 (99.0 – 100)</td>
</tr>
<tr>
<td>- serum/plasma</td>
<td>100 (99.5 – 100)</td>
<td>99.8 (99.3 – 100)</td>
</tr>
</tbody>
</table>
# Four FDA-approved Rapid HIV Tests

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(95% C.I.)</td>
<td>(95% C.I.)</td>
</tr>
<tr>
<td><strong>Reveal G2</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- serum</td>
<td>99.8 (99.2 – 100)</td>
<td>99.1 (98.8 – 99.4)</td>
</tr>
<tr>
<td>- plasma</td>
<td>99.8 (99.0 – 100)</td>
<td>98.6 (98.4 – 98.8)</td>
</tr>
<tr>
<td><strong>Multispot</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- serum/plasma</td>
<td>100 (99.9 – 100)</td>
<td>99.9 (99.8 – 100)</td>
</tr>
<tr>
<td>- HIV-2</td>
<td>100 (99.7 – 100)</td>
<td></td>
</tr>
</tbody>
</table>
OraQuick Advance HIV-1/2

- CLIA-waived for finger stick, whole blood, oral fluid; moderate complexity with plasma
- Store at room temperature
- Screens for HIV-1 and 2
- Results in 20 minutes
Obtain finger stick specimen...
Insert loop into vial and stir
Collect oral fluid specimens by swabbing gums with test device.

Gloves optional; waste not biohazardous
Insert device; test develops in 20 minutes
Positive Negative
Reactive Control
Positive HIV-1/2
Positive
Negative

Read results in 20 – 40 minutes
Uni-Gold Recombigen

- CLIA-waived for finger stick, whole blood; moderate complexity with serum, plasma
- Store at room temperature
- Screens for HIV-1
- Results in 10 minutes
Add 1 drop specimen to well
Add 4 drops of wash solution
Read results in 10 - 12 minutes
Reveal G2

- CLIA moderate complexity with serum, plasma
- Reconstitute and refrigerate reagents
- Screens for HIV-1
- Perform test in 5 minutes
Centrifuge to obtain serum or plasma
Add buffer to reconstitute conjugate.
(Sufficient for 15 tests; Refrigerate to store)
Add 3 drops buffer to moisten membrane
Add one drop of serum or plasma, followed by 3 drops of buffer.
Add 4 drops of Colorimetric Detection Agent
Add 3 drops of buffer to wash
Reactive

Negative

Read results immediately
Multispot HIV-1/HIV-2

- CLIA moderate complexity with serum, plasma
- Refrigerate reagents
- Distinguishes HIV-1 from HIV-2
- Perform test in 15 minutes
Dilution of plasma or serum
Remove and discard pre-filter
Several timed reagent & wash steps
Peptide HIV-2
Recombinant HIV-1
Reactive Control
HIV-1 & HIV-2
Positive
Peptide HIV-2
Peptide HIV-1
Negative
Remember the tradeoffs…

- **Good News:** More HIV-positive people receive their test results.

- **Bad News:** Some people will receive a false-positive result before confirmatory testing.
Interpreting Rapid Test Results

For a laboratory test:

**Sensitivity:** Probability $test = \text{positive}$ if $patient = \text{positive}$

**Specificity:** Probability $test = \text{negative}$ if $patient = \text{negative}$

**Predictive value:**

Probability $patient = \text{positive}$ if $test = \text{positive}$

Probability $patient = \text{negative}$ if $test = \text{negative}$
Example: Test 1,000 persons
Test Specificity = 99.6%  (4/1000)

HIV prevalence = 10%

True positive: 100  False positive: 4

Positive predictive value: 100/104 = 96%
Example: Test 1,000 persons

Test Specificity = 99.6% \( (4/1000) \)

HIV prevalence = 10%

True positive: 100  
False positive: 4  
Positive predictive value: \( \frac{100}{104} = 96\% \)

HIV prevalence = 0.4%

True positive: 4  
False positive: 4  
Positive predictive value: \( \frac{4}{8} = 50\% \)
Positive Predictive Value of a Single Test Depends on Specificity & Varies with Prevalence

<table>
<thead>
<tr>
<th>HIV Prevalence</th>
<th>OraQuick</th>
<th>Reveal</th>
<th>Uni-Gold</th>
<th>Single EIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>10%</td>
<td>99%</td>
<td>92%</td>
<td>97%</td>
<td>98%</td>
</tr>
<tr>
<td>5%</td>
<td>98%</td>
<td>85%</td>
<td>95%</td>
<td>96%</td>
</tr>
<tr>
<td>2%</td>
<td>95%</td>
<td>69%</td>
<td>87%</td>
<td>91%</td>
</tr>
<tr>
<td>1%</td>
<td>91%</td>
<td>53%</td>
<td>77%</td>
<td>83%</td>
</tr>
<tr>
<td>0.5%</td>
<td>83%</td>
<td>36%</td>
<td>63%</td>
<td>71%</td>
</tr>
<tr>
<td>0.3%</td>
<td>75%</td>
<td>25%</td>
<td>50%</td>
<td>60%</td>
</tr>
<tr>
<td>0.1%</td>
<td>50%</td>
<td>10%</td>
<td>25%</td>
<td>33%</td>
</tr>
<tr>
<td>Test Specificity</td>
<td>99.9%</td>
<td>99.1%</td>
<td>99.7%</td>
<td>99.8%</td>
</tr>
</tbody>
</table>
Routine HIV Screening for Emergency Department Patients

- OraQuick testing since October 2002
  - 60% accept HIV testing
  - 98% receive test results
  - 2.5% new HIV positive
  - 80% entered HIV care

- 4 new demonstration projects (Wisconsin, Massachusetts, Los Angeles, New York)
Characteristics
Rapid Test Positive Patients

N=82

No previous test  47 (57%)
Risk Factors
MSM        29 (34%)
IDU         8 (10%)
Sex Partner IDU  3 ( 4%)
No identified risk  42 (51%)
### HIV Screening in Acute Care Settings

<table>
<thead>
<tr>
<th>Location</th>
<th>New HIV+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cook County ED, Chicago</td>
<td>2.5%</td>
</tr>
<tr>
<td>Grady ED, Atlanta</td>
<td>2.7%</td>
</tr>
<tr>
<td>Johns Hopkins ED, Baltimore</td>
<td>3.2%</td>
</tr>
<tr>
<td>Massachusetts (4 hospitals)</td>
<td>2.0%</td>
</tr>
</tbody>
</table>

*HIV testing sites* 1.2%
HIV Screening with OraQuick in Labor and Delivery: the MIRIAD Study

- Testing of pregnant women in labor for whom no HIV test results are available; 12 hospitals in 5 cities: Atlanta, Chicago, Miami, New Orleans, New York

- To date
  - 4894 women screened
  - 34 (0.7%) new HIV infections identified
  - 4 false positive OraQuick tests, no false negatives
  - 11 false-positive EIAs: 5 p24 only, 6 WB negative

- Positive Predictive value: OraQuick 90%; EIA 76%

Bulterys et al, JAMA July 2004
Point-of-care testing: median 45 min
  – (range 30 min – 2.5 hours)

Same test in Laboratory: median 3.5 hours
  – (range 94 min – 16 hours)

MMWR 52:36, Sept 16, 2003
OraQuick Outreach Testing for High-risk Persons: El Paso

- On-site testing at community sites:
  Old Plantation night club and mobile van
- Individual counseling and testing
- El Paso Gay Community Center and Centro de Salud Familiar la Fe
OraQuick Fingerstick Results:
N = 1275

- Preliminary positive 18 (1.4%)
- True positives 17 (1.3%)
- False Positives 1 (0.07%)
- Specificity 1256/1257 (99.9%)
- Positive Predictive Value 17/18 (94%)
- All clients received their test results
OraQuick Outreach to High-risk Persons of Color

- On-site testing at sites throughout the community
- Group pretest counseling.
- Individual testing and post-test counseling.

*Patrick Keenan MD*
*University of Minnesota Medical School*
*Department of Family Practice and Community Health*
Outreach Testing Sites

- Chemical Dependency Programs
- Homeless shelters
- Sex worker support program
- Drop-in center for gay youth
- Teen clinic
- Gay bars

- Sex offender groups
- “Johns” programs
- Half-way houses
- Health fairs
- Strip club workers
- African-born groups
- Drug court support groups
OraQuick Fingerstick Results:
N = 1021

- Preliminary positive: 5 (0.5%)
- True positives: 4 (0.4%)
- False Positives: 1 (0.1%)
- Sensitivity: 4/4 (100%)
- Specificity: 1016/1017 (99.9%)
- Positive Predictive Value: 4/5 (80%)
Results

- 99.7% of clients received their test results and post-test counseling.

- The average time between fingerstick and learning test result was 28 minutes.
CDC’s OraQuick Procurement & Distribution

527,775 test kits shipped in 2003 and 2004
- 137 health depts and CBOs in 36 states

Utilization September 2003 – September 2004:
- 173,003 persons tested
- 2,741 (1.6%) HIV positive
- 17,266 devices used for training
- 25,926 devices use to run external controls
Changes in HIV Testing at Same Sites After Rapid Testing Introduced

<table>
<thead>
<tr>
<th>State</th>
<th>2002 EIA</th>
<th>2003 EIA</th>
<th>2002 Rapid Test</th>
<th>2003 Rapid Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Utah</td>
<td>666</td>
<td>932</td>
<td>666</td>
<td>932</td>
</tr>
<tr>
<td>Maryland</td>
<td>786</td>
<td>1002</td>
<td>786</td>
<td>1002</td>
</tr>
<tr>
<td>New York State</td>
<td>3839</td>
<td>5222</td>
<td>3839</td>
<td>5222</td>
</tr>
<tr>
<td>Wisconsin</td>
<td>1929</td>
<td>1359</td>
<td>1929</td>
<td>1359</td>
</tr>
</tbody>
</table>
Changes in Positive Tests at Same Sites After Rapid Testing Introduced

- **Utah**: 02 03
- **Maryland**: 02 03
- **New York State**: 02 03
- **Wisconsin**: 02 03

**Legend**:
- EIA
- Rapid Test
## Results of Confirmatory Testing

<table>
<thead>
<tr>
<th>Initial specimen</th>
<th>Confirmatory test</th>
<th>Follow-up specimen</th>
<th>Supplemental test</th>
</tr>
</thead>
<tbody>
<tr>
<td>EIA*</td>
<td>EIA†</td>
<td>EIA</td>
<td>Supplemental test</td>
</tr>
<tr>
<td>ND†</td>
<td>IFA</td>
<td>neg§</td>
<td>IFA†</td>
</tr>
<tr>
<td>neg</td>
<td>—</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>neg</td>
<td>WB‡‡,§§</td>
<td>Indeterm†‡</td>
<td>ND</td>
</tr>
<tr>
<td>neg</td>
<td>WB§§</td>
<td>pos</td>
<td>ND</td>
</tr>
<tr>
<td>neg</td>
<td>WB§§</td>
<td>pos</td>
<td>ND</td>
</tr>
<tr>
<td>pos</td>
<td>IFA</td>
<td>indeterm</td>
<td>pos</td>
</tr>
<tr>
<td>pos</td>
<td>WB</td>
<td>indeterm</td>
<td>pos</td>
</tr>
<tr>
<td>pos</td>
<td>WB</td>
<td>indeterm</td>
<td>ND</td>
</tr>
<tr>
<td>pos</td>
<td>WB</td>
<td>indeterm</td>
<td>pos</td>
</tr>
<tr>
<td>neg</td>
<td>WB</td>
<td>neg</td>
<td>ND</td>
</tr>
<tr>
<td>neg</td>
<td>WB</td>
<td>indeterm</td>
<td>ND</td>
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<tr>
<td>neg</td>
<td>WB</td>
<td>neg</td>
<td>neg</td>
</tr>
<tr>
<td>neg</td>
<td>WB</td>
<td>neg</td>
<td>neg</td>
</tr>
</tbody>
</table>
### Results of Confirmatory Testing

**5 patients:**
- Initial EIA or confirmatory test negative
- Some labs did only EIA
- HIV-positive on follow-up specimen

<table>
<thead>
<tr>
<th>OraQuick</th>
<th>Initial specimen</th>
<th>Confirmatory test</th>
<th>Follow-up specimen</th>
<th>Supplemental test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reactive</td>
<td>ND†</td>
<td>IFA</td>
<td>neg§</td>
<td>neg</td>
</tr>
<tr>
<td>Reactive</td>
<td>neg</td>
<td>—</td>
<td>ND</td>
<td>IFA II</td>
</tr>
<tr>
<td>Reactive</td>
<td>neg</td>
<td>WB+++§§</td>
<td>Indeterm+++</td>
<td>pos**</td>
</tr>
<tr>
<td>Reactive</td>
<td>neg</td>
<td>WB§§</td>
<td>pos</td>
<td>ND</td>
</tr>
<tr>
<td>Reactive</td>
<td>neg</td>
<td>WB§§</td>
<td>pos</td>
<td>ND</td>
</tr>
</tbody>
</table>
### Results of Confirmatory Testing

**4 patients:**
- Initial confirmatory test indeterminate
- Early infection, evolving Western blot
- HIV-positive on follow-up specimen

<table>
<thead>
<tr>
<th>OraQuick</th>
<th>EIA*</th>
<th>Initial specimen</th>
<th>Confirmatory test</th>
<th>Follow-up specimen</th>
<th>EIA</th>
<th>Supplemental test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reactive</td>
<td>pos</td>
<td>pos</td>
<td>IFA</td>
<td>indeterm</td>
<td>pos</td>
<td>WB</td>
</tr>
<tr>
<td>Reactive</td>
<td>pos</td>
<td>pos</td>
<td>WB</td>
<td>indeterm</td>
<td>pos</td>
<td>WB</td>
</tr>
<tr>
<td>Reactive</td>
<td>pos</td>
<td>pos</td>
<td>WB</td>
<td>indeterm</td>
<td>ND</td>
<td>Viral load</td>
</tr>
<tr>
<td>Reactive</td>
<td>pos</td>
<td>pos</td>
<td>WB</td>
<td>indeterm</td>
<td>pos</td>
<td>WB</td>
</tr>
</tbody>
</table>
Results of Confirmatory Testing

4 patients:

• Initial and follow-up tests negative
• False-positive OraQuick rapid test
### Results of Confirmatory Testing

8 patients:
- Unsuccessful follow-up
- HIV status unconfirmed

<table>
<thead>
<tr>
<th>OraQuick</th>
<th>Initial specimen</th>
<th>Follow-up specimen</th>
<th>Supplemental test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EIA*</td>
<td>Confirmatory test</td>
<td>EIA</td>
</tr>
<tr>
<td>Reactive</td>
<td>pos</td>
<td>WB</td>
<td></td>
</tr>
<tr>
<td>Reactive</td>
<td>neg</td>
<td>WB</td>
<td>indetern</td>
</tr>
<tr>
<td>Reactive</td>
<td>neg</td>
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<td>Reactive</td>
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<td>WB</td>
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<td>Reactive</td>
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<td>WB</td>
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</tr>
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<td>neg</td>
<td>WB</td>
<td>neg</td>
</tr>
<tr>
<td>Reactive</td>
<td>neg</td>
<td>WB</td>
<td>neg</td>
</tr>
</tbody>
</table>

*Note: EIA stands for Enzyme-Linked Immunosorbent Assay.*
Confirmatory Testing

- Confirmatory test essential (not just EIA!)

- For Western blot:
  - Venipuncture for whole blood
  - Oral fluid specimen

- Follow-up testing of persons with negative or indeterminate Western blot results after 4 weeks
Additional Resources

General and technical information (updated frequently):

www.cdc.gov/hiv/rapid_testing