CLIA-waived Rapid HIV Testing in the Public Health Sector

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The findings and conclusions in this presentation are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention

Need for Expanding HIV Testing

- 252,000 – 312,000 persons with undiagnosed HIV infection
- ~ 40,000 new HIV infections per year
- ~ 50% of all new sexually transmitted HIV infections are attributed to persons unaware of their infection
- ~ 33% of HIV-infected persons are diagnosed late in the course of their illness
- ARV therapy is of proven benefit clinically and in reducing perinatal HIV transmission
- CDC has supported the use of CLIA-waived rapid tests since 2003 to expand testing to reduce undiagnosed infections, late diagnoses, and perinatal transmission

Presentation Objectives

1. Review the performance of CLIA-waived rapid HIV tests
2. Characterize quality assurance practices and outcomes
3. Describe magnitude of CLIA-waived rapid HIV testing

OraQuick *Advance* HIV-1/2

FDA-approved claims for:

Sensitivity (HIV-1):

- Whole blood 99.6% *(98.5 - 99.9)*
- Oral fluid 99.3% *(98.4 - 99.7)*

Specificity (HIV-1):

- Whole blood 100% *(99.7-100)*
- Oral Fluid 99.8% *(99.6 – 99.9)*

CLIA-waived:

- Whole blood: Jan 2003
- Oral fluid: Jul 2004

Uni-Gold Recombigen

FDA-approved claims for:

Sensitivity:

Whole blood 100% *(99.5 - 100)*

Plasma/serum 100% *(99.5 -100)*

Specificity:

Whole blood 99.7% *(99.0-100)*

Plasma/serum 99.8% *(99.3 -100)*

CLIA-waived:

Whole blood: Nov 2004

Clearview HIV-1/2 Stat-Pak

FDA-approved claims for:

Sensitivity (HIV-1):

- Whole blood 99.7% *(98.9-100)*
- Plasma/serum 99.7% *(98.9-100)*

Specificity (HIV-1):

- Whole blood 99.9% *(99.6-100)*
- Plasma/serum 99.9% *(99.6-100)*

CLIA-waived:

- Whole blood: Nov 2006

Data Sources

1. Four CDC-sponsored studies, 2000-2005
2. Post-marketing surveillance, 2004-2005
3. Selected health departments, 2005-2006

Four CDC-sponsored Studies*

Objectives & Methods

- Evaluate performance of OraQuick in settings of likely use
- Performance compared with conventional EIA/WB algorithm
- Subjects included pregnant women at 18 hospitals, and HRH, IDU, and MSM at 41 community outreach sites, 3 HIV tests sites, and 2 STD clinics
- Tests administered by laboratorians, physicians, nurses, midwives, and HIV counselors
- Studies implemented between April 2000 and January 2005

*Delaney KP, et al. Performance of an oral fluid rapid HIV-1/2 test: experience from four CDC studies. *AIDS* 2006;20:1655-1660.

Sensitivity Results*

Rapid Test (Specimen)	Reference Positive	False Negative	Sensitivity
OraQuick (Whole blood)	327	1	99.7%
OraQuick (Oral fluid)	327	3	99.1%

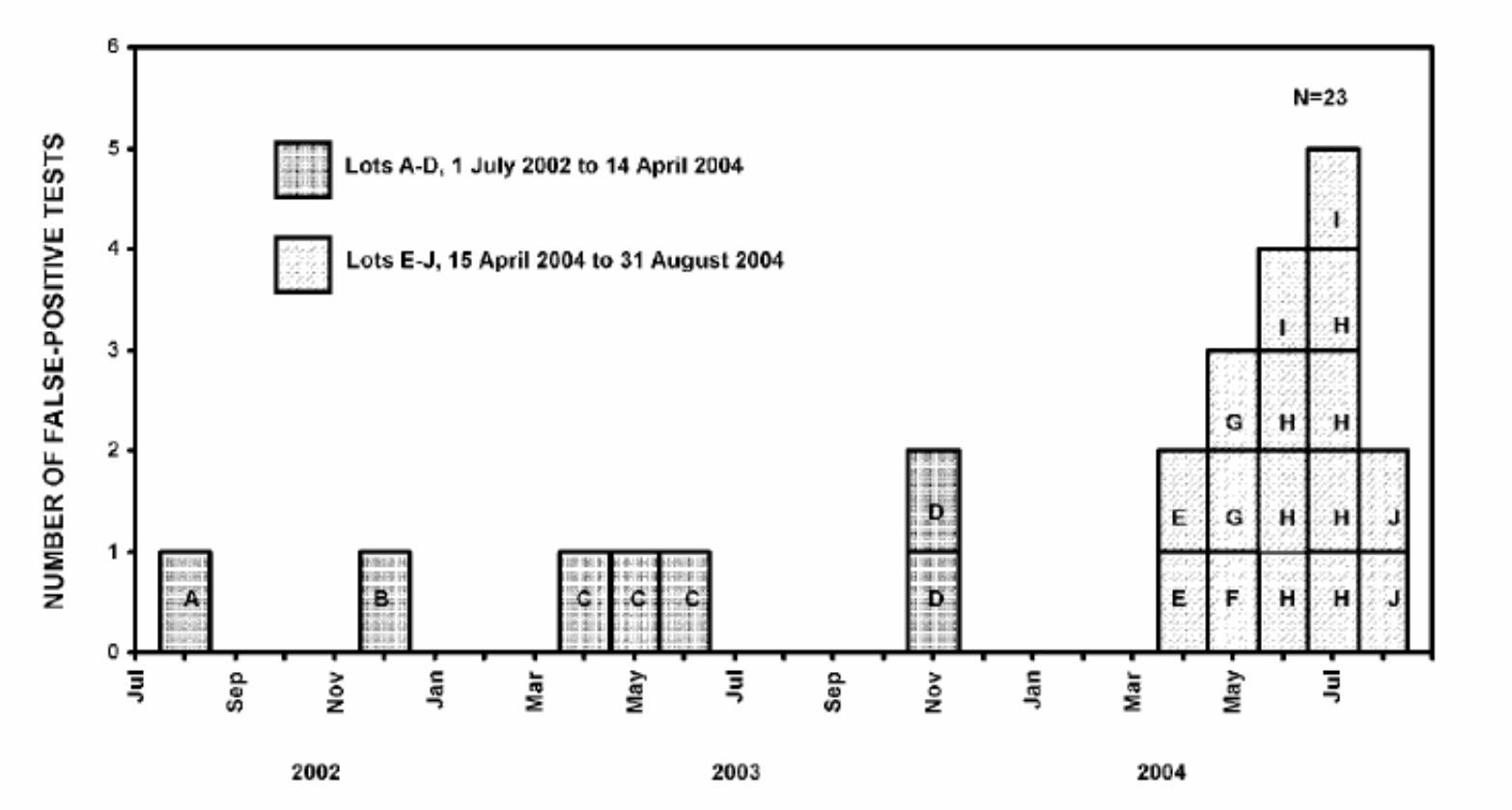
*Delaney KP, et al. Performance of an oral fluid rapid HIV-1/2 test: experience from four CDC studies. *AIDS* 2006;20:1655-1660.

Specificity Results*

Rapid Test (Specimen)	Reference Negative	False Positive	Specificity
OraQuick (Whole blood)	12,010	12	99.9%
OraQuick (Oral fluid)	12,010	54	99.6%
Conventional EIA	12,010	35	99.7%

*Delaney KP, et al. Performance of an oral fluid rapid HIV-1/2 test: experience from four CDC studies. *AIDS* 2006;20:1655-1660.

False Positive OraQuick Oral Fluid Results, University of Minnesota*



*Jafa K, et al. Investigation of false positive results with an oral fluid rapid HIV-1/2 antibody test. PLos one 2007;1:1-6.

Observed Specificity University of Minnesota*

Time Period	Reference Negative	False Positive	Specificity
Jul 2002 – Apr 2004	2,017	7	99.7%
Apr 2004 – Aug 2004	388	16	95.9%
Jul 2002 – Aug 2004	2405	23	99.0%

*Jafa K, et al. Investigation of false positive results with an oral fluid rapid HIV-1/2 antibody test. PLos one 2007;1:1-6.

Investigation & Incidence Study*

Investigation

- 16 false-positive results from unexpired devices from 6 lots
- All lots produced and shipped within specifications
- Each lot used at other sites without excess false-positive results
- All temperatures recorded in device storage and test logs were within manufacturer's specifications
- Devices had very faint, gray, or shadowy test lines
- Four operators interpreted the results
- Operator practices observed in accordance with PI
- Only significant factor: age $\geq$ 37 years

Incidence study, Feb-May 2005, 9 cities in 3 states*

- 2,268 tests, no false-positive results (specificity 100%)
- Case-control study could not proceed

*Jafa K, et al. Investigation of false positive results with an oral fluid rapid HIV-1/2 antibody test. PLos one 2007;1:1-6.

Data Sources

1. Four CDC-sponsored studies, 2000-2005
2. Post-marketing surveillance, 2004-2005
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Post-marketing Surveillance, 2004-2005*

Objectives

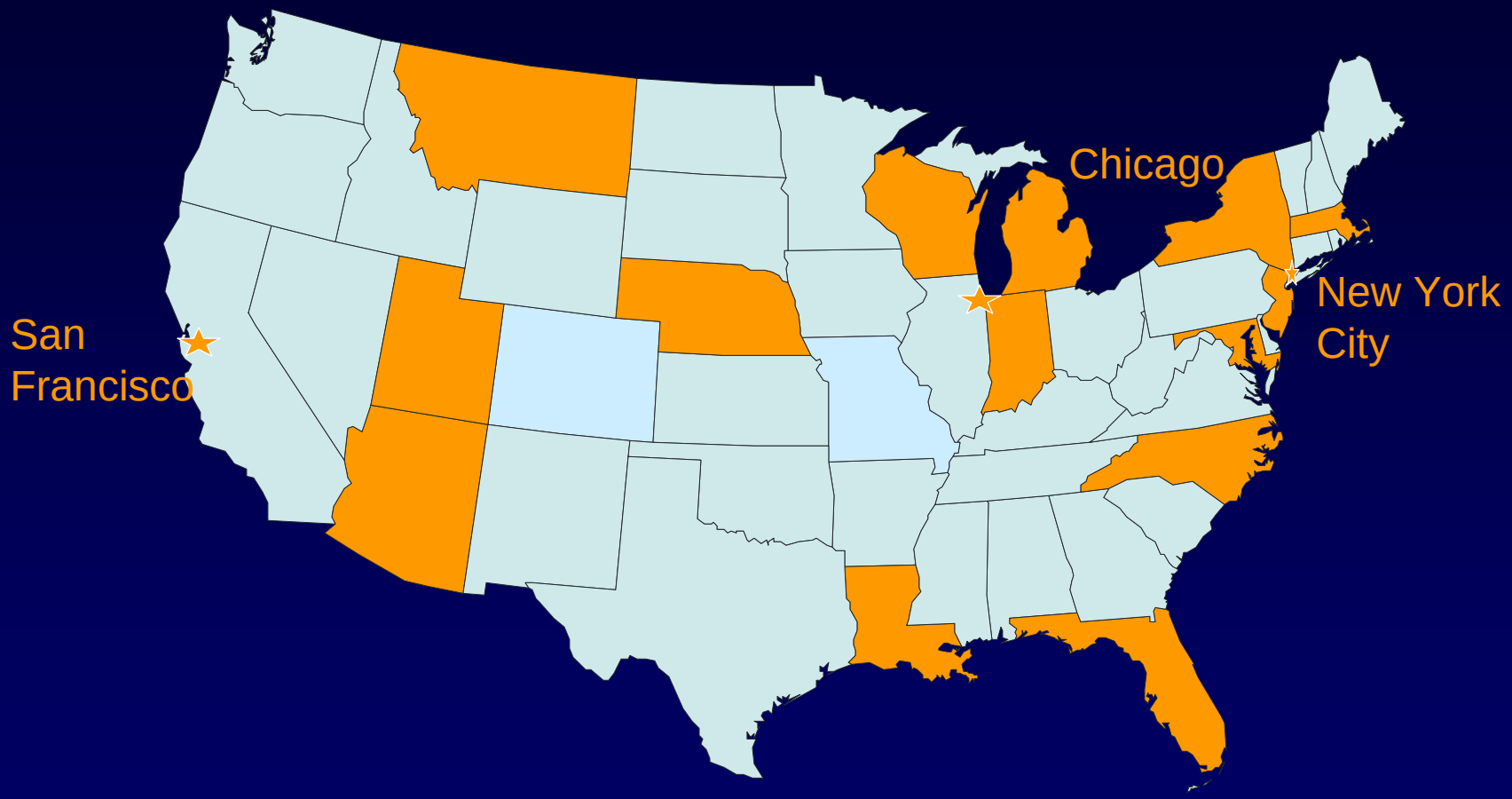
- Evaluate use and performance of OraQuick
- Characterize quality assurance practices and outcomes

Methods

- 17 participating health departments, 368 sites, Aug 2004 – June 2005
- Predominately CTS, STD, outreach, and correctional settings
- Tests administered by counselors and lab techs
- Preliminary positive results subject to WB/IFA confirmation, clients with discordant test results were counseled to re-test.
- Active surveillance of all discordant test results
- False positive results based on initial or repeat WB/IFA confirmation

*Wesolowski LG, et al. Post-marketing surveillance of OraQuick whole blood and oral fluid rapid HIV testing. *AIDS* 2006;20:1661-1666.

Project Areas*



*Wesolowski LG, et al. Post-marketing surveillance of OraQuick whole blood and oral fluid rapid HIV testing. *AIDS* 2006;20:1661-1666.

Post-marketing Surveillance, 2004-2005*

Test and specimen type	No. of Tests	HIV + Median % (range)	Estimated Specificity Median % (range)	PPV Median % (range)
OQ whole blood	135,724	0.8 (0.1-2.6)	99.98 (99.73-100)	99.2 (66.7-100)
OQ oral fluid	26,066	1.0 (0.0-4.0)	99.89 (99.44-100)	90.0 (50.0-100)

Discordant test results

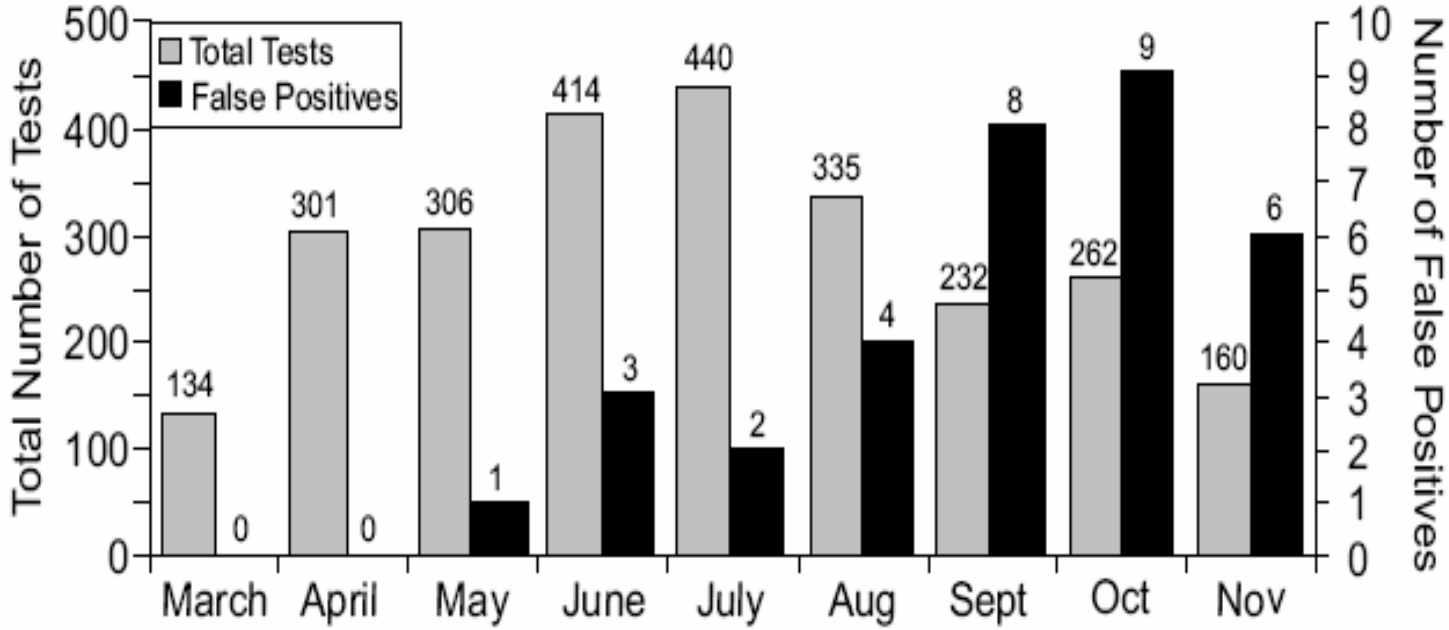
- Of 124 initially discordant test results: 17 (14%) true positive

Receipt of test results

- 94% of non-reactive rapid test results provided
- 95% of reactive rapid test results provided
  - 75% of confirmed results provided

*Wesolowski LG, et al. Post-marketing surveillance of OraQuick whole blood and oral fluid rapid HIV testing. *AIDS* 2006;20:1661-1666.

Excess False-positive OF Test Results, 1 San Francisco Test Site*



	March	April	May	June	July	Aug	Sept	Oct	Nov
True Positives	0	5	5	5	5	8	4	8	2
Prevalence	0%	1.7%	1.6%	1.2%	1.1%	2.4%	1.7%	3.1%	1.3%
Specificity	100%	100%	99.7%	99.3%	99.5%	98.8%	96.5%	96.5%	96.3%
PPV	n/a	100%	83.3%	62.5%	71.4%	66.7%	33.3%	47.1%	25.0%

*Wesolowski LG, et al. Post-marketing surveillance of OraQuick whole blood and oral fluid rapid HIV testing. *AIDS* 2006;20:1661-1666.

Investigation*

Findings

- 33 false-positive results from unexpired devices from 4 lots
- Each lot used at 11 other SF sites without excess false-positive results
- 29 (88%) devices had very faint, gray, or shadowy test lines
- Seven operators interpreted the results confirmed by ≥1 other operators
- Operator practices observed in accordance with PI with exception of OF collection (some recommended swabbing gum line ≥ 1 time)
- Operators re-trained in October; 13 (39%) false positive results occurred after re-training
- Of 163 external controls, two were invalid; 161 yielded concordant results
- All temperatures recorded in device storage and test logs were within manufacturer's specifications

*Wesolowski LG, et al. Post-marketing surveillance of OraQuick whole blood and oral fluid rapid HIV testing. *AIDS* 2006;20:1661-1666.

Data Sources

1. Four CDC-sponsored studies, 2000-2005
2. Post-marketing surveillance, 2004-2005
3. Selected health departments, 2005-2006

New York State Anonymous Counseling & Testing Program 2005*

Rapid Test (specimen type)	Reference Negative	False Positive	Specificity
OraQuick (whole blood)	13,473	7	99.9%
OraQuick (oral fluid)	10,077	29	99.7%

*San Antonio-Gaddy M. CDC Presentation, Jan 10, 2007.

New York State Anonymous Counseling & Testing Program 2006*

Rapid Test (specimen type)	Reference Negative	False Positive	Specificity
OraQuick (whole blood)	3,725	0	100%
OraQuick (oral fluid)	1,838	5	99.7%
Uni-Gold (whole blood)	16,540	17	99.9%

*San Antonio-Gaddy M. CDC Presentation, Jan 10, 2007.

Presentation Objectives

1. Review the performance of CLIA-waived rapid HIV tests
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Post-marketing Surveillance, 2004-2005*

Methods (Practices)

- Administered survey to rapid test program managers:
  - Training requirements
  - Quality assurance monitoring
  - Operator competency assessment
- Limitation: all assessments were made at the program level

Post-marketing Surveillance, 2004-2005*

Methods (Practices)

- Administered survey to rapid test program managers:
  - Training requirements
  - Quality assurance monitoring
  - Operator competency assessment
- Limitation: all assessments were made at the program level

Methods (Outcomes)

- From Jan 2005 – Jun 2005, provided monthly forms and conducted active surveillance of invalid tests, external quality control runs, and temperature violations

Quality Assurance Practices*

Required Training: Median (range)

- 6 (3-16) hrs for operating rapid tests
- 6 (1-40) hrs for counseling rapid-test clients
- 40 (20-80) total hrs for HIV test and counseling “certification”

Training Methods

- 4 (24%) internet or video
- 10 (59%) one-on-one training at rapid test site
- 15 (88%) state, city, or county developed training course
- 2 (12%) CDC rapid test training course
- 6 (35%) other
- 17 (100%) assessed competency in test performance and interpretation of all three types of results

Quality Assurance Practices

Post-training Monitoring

- 15 (88%) visited all test sites during PMS-2 to establish/evaluate QA
- 10 (59%) conducted onsite QA monitoring at least every six months

*Question: Which of the following activities were performed by HD staff **for all** sites during PMS-2? These QA activities may have been conducted on or off site.

Quality Assurance Practices

Post-training Monitoring

- 15 (88%) visited all test sites during PMS-2 to establish/evaluate QA
- 10 (59%) conducted onsite QA monitoring at least every six months
- 16 (94%) reviewed external QC test procedures*
- 16 (94%) examined test logs*
- 12 (71%) examined temperature logs*
- 8 (47%) observed operators collect specimens*
- 9 (53%) observed operators interpret results*
- 10 (59%) observed how test results were explained to clients*
- 15 (88%) reviewed procedures to address invalid and discordant test results*

*Question: Which of the following activities were performed by HD staff **for all** sites during PMS-2? These QA activities may have been conducted on or off site.

Quality Assurance Practices*

Internal Competency Assessment

- 10 (59%) conducted at least annual assessments after training
  - 4 used placards with OraQuick test results
  - 4 used blinded external control specimens
  - 2 used samples sent from health department lab

External Competency Assessment

- 13 (76%) enrolled in external assessment program
  - 10 (59%) MPEP
  - 3 (18%) CAP

*Survey of rapid test coordinators from 17 state and local health departments, post-marketing surveillance, 2004-2005.

Quality Assurance Outcomes

Jan-Jun 2005: 86,749 Rapid Tests*

- 20 (0.02%) invalid test results (no control line or red background in results window)
- 9,217 external control runs ~ 10 persons tested/external quality control run (5/17 HDs recommended running daily controls)
- 4 external controls reported as “invalid” (3 health departments)
- 31 (0.06%) site-days where ≥ 1clients tested when temperature was out of spec (3 health departments)
- 161 (0.32%) site-days where tests stored when temperature was out of spec (5 health departments)

*308 reporting sites; representing ~ 49,896 site-days (308*162) during 6-month reporting period

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Data Sources

1. Rapid Test Distribution Program, 2003-2006
2. Rapid Test Assessment Report, NASTAD, 2005-2006
3. Selected Health Departments, 2005-2006

Rapid HIV Test Distribution Program

Objectives & Methods

- Implemented to help scale up rapid test programs in support of Advancing HIV Prevention initiative
- 2003-2005: distributed tests to state and local health departments, medical centers, and CBOs
  - Quarterly reports submitted on use of devices
- 2006-2007: distributed tests to state and local health departments in proportion to AIDS morbidity
  - Counseling and testing data sets will be submitted

MMWR
Morbidity and Mortality Weekly Report
Weekly June 23, 2006 / Vol. 55 / No. 24

National HIV Testing Day — June 27, 2006

June 27 is National HIV Testing Day. Initiated in 1995 by the National Association of People with AIDS, National HIV Testing Day serves to increase awareness of HIV/AIDS and to encourage all persons in the United States to get tested for human immunodeficiency virus (HIV). Locations of HIV test sites by postal code are available at National HIV Testing Resources at http://www.hivtest.org/index.htm.

Persons who know they have HIV infection often can receive antiretroviral treatment at an early stage of disease, when more treatment options are available. Knowing HIV status also has the potential to reduce transmission. Persons who learn they are infected with HIV usually take steps to reduce their risk for transmitting the virus (*1*).

In 2003, CDC began its Advancing HIV Prevention initiative (*2*), which aims to increase the prevalence of persons who know their HIV status by making HIV testing more available and by encouraging more people to take advantage of the tests. *MMWR* will publish CDC's revised *Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings* later this year.

References

1. Marks G, Crepaz N, Senterfitt JW, Janssen RS. Meta-analysis of high-risk sexual behavior in persons aware and unaware they are infected with HIV in the United States: implications for HIV prevention programs. J Acquir Immune Defic Syndr 2005;39:446–53.
2. CDC. Advancing HIV prevention: new strategies for a changing epidemic—United States, 2003. MMWR 2003;52:329–32.

Rapid HIV Test Distribution — United States, 2003–2005

At the end of 2003, an estimated 1 million persons in the United States were living with human immunodeficiency virus (HIV) infection, including those with acquired immunodeficiency syndrome (AIDS); approximately one fourth of these persons had not had their infections diagnosed (*1*). In 2003, CDC implemented a new initiative, Advancing HIV Prevention (AHP) (*2*), focused, in part, on reducing the prevalence of undiagnosed HIV infection by expanding HIV testing (*2*) and taking advantage of rapid HIV tests that enable persons to receive results within 30 minutes, instead of the 2 weeks typically associated with conventional tests (*3*). In support of AHP strategies, during September 2003–December 2005, CDC purchased and distributed rapid HIV tests to expand testing and assess the feasibility of using rapid tests in new environments (e.g., outreach settings or emergency departments). This report summarizes the results of this rapid HIV-test distribution program (RTDP), in which CDC distributed tests to 230 organizations in the United States and identified 4,650 (1.2%) HIV infections among 372,960 rapid tests administered. The results suggest that RTDP helped scale up rapid HIV-testing programs in the United States and enabled diagnosis of HIV in persons who might not have had their infections diagnosed otherwise.

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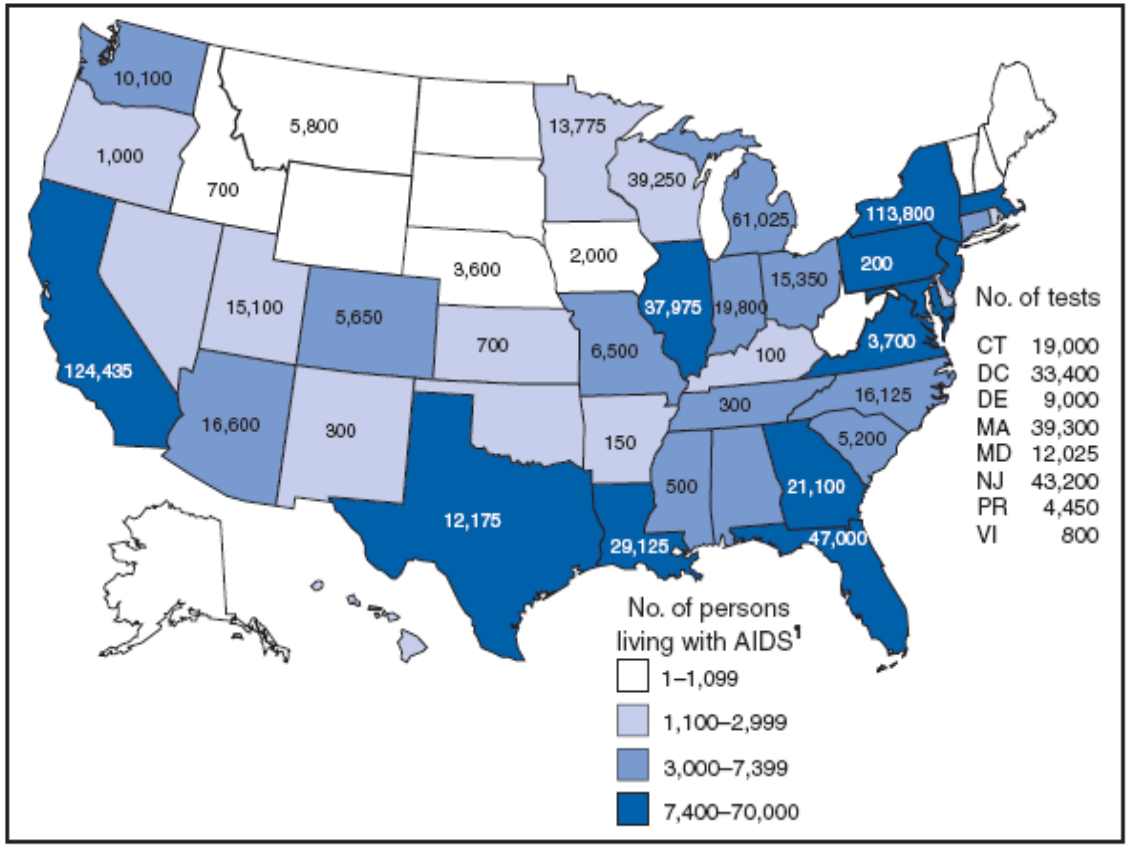
DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION

RTDP 2003-2005

- 790,310 devices distributed
- 121 state/local health depts
- 101 medical centers/CBOs
- 8 correctional facilities
- 230 organizations submitted reports (606,951 devices)
- 372,960 devices used
- 4,650 (1.2%) preliminary positive test results confirmed HIV positive
- 79% of confirmed results given to clients

Rapid Test Distribution Program

FIGURE. Number of rapid HIV* tests distributed by CDC during September 2003–December 2005 and estimated number of persons† living with AIDS§ at the end of 2004, by state/territory — United States



*Human immunodeficiency virus.
†Aged ≥13 years.
§Acquired immunodeficiency syndrome.
¶CDC. HIV/AIDS surveillance report, 2004. Vol. 16. Atlanta, GA: US Department of Health and Human Services, CDC; 2005:22. Available at http://www.cdc.gov/hiv/stats/2004surveillancereport.pdf.

Devices Distributed

- 37 States, DC, Puerto Rico and US Virgin Islands
- Primarily to moderate and high morbidity areas.
- RTDP July 2006 – June 2007:
  - 211,800 OraQuick devices
  - 59% distributed through Dec 2006

Data Sources

1. Rapid Test Distribution Program, 2003-2006
2. Rapid Test Assessment Report, NASTAD, 2005-2006
3. Selected Health Departments, 2005-2006

Rapid HIV Testing Assessment*

Objectives & Methods

- Evaluate procurement and use of rapid tests
- Questionnaires sent to 65 directly funded health department AIDS program directors and prevention managers
- Survey completed August 2006
- 43 (66%) respondents
  - 39 state health departments
  - 3 city health departments
  - 1 territorial health department

*NASTAD Rapid HIV Testing Assessment Report: www.nastad.org

Support Rapid HIV Test Programs*

Participating Health Departments (n=43)

- 35 (81%) supported a rapid testing program
- 8 did not currently support a program
  - 6 (75%) insufficient resources
  - 2 (25%) statutory or regulatory barriers
  - 4 (50%) will implement program in next 12 months
- 39 (91%) will support program in next 12 months
  - 39 (100%) will continue to use conventional testing
- Settings
  - Outreach (81%), HIV test sites (72%), CBOs (70%)
  - Labor & delivery (26%), Hospital EDs (19%)

*NASTAD Rapid HIV Testing Assessment Report: www.nastad.org

Projected Purchases, 2006*

Quantity of Tests	OraQuick N (%)	Uni-Gold N (%)	Total N
≤1,000	2 (6%)	5 (45%)	7
1,001 – 10,000	17 (55%)	5 (45%)	22
10,001 – 25,000	7 (23%)	1 (9%)	8
25,001 – 50,000	4 (13%)	0	4
50,001 – 75,000	1 (3%)	0	1
Total	31	11[1]	NA

[1] 4 Health departments plan to use Uni-Gold exclusively

*Reported by 35 health departments that currently implement rapid testing. NASTAD Rapid HIV Testing Assessment Report: www.nastad.org

Volume of Rapid and Conventional Testing*

Year	Rapid Tests N (%)	Conventional Tests N (%)	Total Tests N
2005	445,063 (25%)	1,358,644 (75%)	1,803,707
2006[1]	613,850 (33%)	1,236,382 (67%)	1,850,232

[1]Pojected

- Projected 37.9% increase in rapid testing
- Projected 9.0% decrease in conventional testing
- Projected 2.6% increase in total testing

*Reported by 39 health departments intending to implement rapid testing in the next 12 months. NASTAD Rapid HIV Testing Assessment Report: www.nastad.org

Data Sources

1. Rapid Test Distribution Program, 2003-2006
2. Rapid Test Assessment Report, NASTAD, 2005-2006
3. Selected Health Departments, 2005-2006

NYSDOH ACT Program
Number of Tests, by Year and Test Type*

Year	Rapid OraQuick	Rapid Uni-Gold	Conventional Oral Fluid	Conventional Serum	Total Tests
2003	6,581	0	10,261	2,434	19,471
2004	20,297	0	462	126	20,990
2005	23,657	0	144	48	23,944
2006[1]	3,460	16,540	0	0	20,000

[1]2006 Data is incomplete

- NYSDOH policy is for counselors to offer all testing options to all clients. Conventional testing was available in 2006.

*San Antonio-Gaddy M. CDC Presentation, Jan 10, 2007.

Florida Department of Health
Number of Tests, by Year and Test Type*

Year	Rapid OraQuick	Rapid Uni-Gold	Conventional Oral Fluid	Conventional Serum	Total Tests
2003	3,790	0	78,378	219,519	301,687
2004	23,926	0	63,293	208,383	295,602
2005	34,780	0	54,745	200,020	289,545
2006[1]	47,000	0	49,460	192,668	289,128

[1]Pojected

- Projected 37% decrease in conventional oral fluid testing 2003 through 2006
- Projected 12% decrease in conventional serum testing, 2003 through 2006

*Marlene LaLota, Florida Department of Health, personal communication, 02/08/2007.

Conclusions

CLIA-waived Rapid HIV Tests

- Provided by most health departments; use has increased remarkably
- Stored and used in accordance with the manufacturer's guidelines, including use on external quality controls
- Accurate, safe, and simple to use
- Enabled nearly all clients to receive their results
- Helped to expand testing, enabling HIV diagnoses of persons who might not have had their infections diagnosed otherwise

Conclusions

CLIA-waived Rapid HIV Tests

- Despite high specificity, positive predictive value can be low in some settings
- Clusters of excess false-positive test results have occurred and may continue to occur
- Many persons with preliminary positive test results do not return to the clinic to receive their confirmed results
- Need to evaluate the feasibility and performance of a POC rapid test algorithm to improve accuracy of results and linkage to care

Research Needs

Rapid Test Algorithm Study

- Collaborators: Departments of Health, San Francisco and Los Angeles
- Status: Protocol under development
- Expected start date: Spring, 2007
- Sites: multiple rapid test sites in SF and LA
- Methods:
  - Intervention sites: screen with OraQuick on oral fluid, if reactive, repeat in series with Uni-Gold and Stat-Pak
  - All clients with reactive OQ results undergo conventional WB/IFA confirmation
  - All clients with discordant WB/IFA results are followed
  - Evaluate % who use health-care from intervention and control sites

Questions