



DEPARTMENT OF HEALTH AND HUMAN SERVICES

**Centers for Disease Control and Prevention
Model Performance Evaluation Program
Human Immunodeficiency Virus Type 1
(HIV-1) Antibody Testing**

**Report of Results
for the Performance Evaluation Survey
Conducted during January 2003**



**PUBLIC HEALTH PRACTICE PROGRAM OFFICE
DIVISION OF LABORATORY SYSTEMS
ATLANTA, GEORGIA**

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Department of Health and Human Services.

Report of the January 2003 Human Immunodeficiency Virus Type I (HIV-1)
Antibody Performance Evaluation Sample Testing Results Provided by Participant
Laboratories in the Model Performance Evaluation Program,
Centers for Disease Control and Prevention (CDC)

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Table of Contents

Introduction	5
Methods and Materials	5
Overall Summary of Results	8
EIA Results	10
WB Results	11
WB Results Interpretations	11
WB Interpretative Criteria	12
WB Band Patterns	13
IFA Results	14
IFA Intensity Patterns	15
“Other” Tests Performed	16
“Other” Results Interpretations	17
Quality Control Testing	18
Frequency of External QC Testing	18
Discussion of HIV Results	18
HIV Rapid Testing Questionnaire Results	20
Glossary of Terms	23

List of Tables

Table 1: Human Immunodeficiency Virus Type 1 (HIV-1) Antibody Testing for the January 2003 Shipment	6
Table 2: CDC Western Blot (WB) Testing Results for the January 2003 Shipment	7
Table 3: Results Summary.....	8
Table 4: Location of the laboratories that reported results for this shipment	9
Table 5: False-positive and false-negative EIA results, by kit manufacturer, reported by participant laboratories.....	11
Table 6: False-positive, false-negative, and indeterminate results for both positive and negative donor samples for Western blot test, by manufacturer	12
Table 7: Indeterminate and false-negative results reported, by participants, by manufacturer for immunofluorescent antibody tests	15
Table 8: "Other" test kits: False-positive, false-negative and indeterminate results	17
Table 9: Summary of External Quality Control Material Sources	18

List of Figures

Figure 1: Number of HIV-1 participants by laboratory type that reported EIA, WB, IFA, and "Other" results	8
Figure 2: The combination of HIV-1 antibody tests reported by participant laboratories	9
Figure 3: Percentages of laboratories using EIA test kits, by manufacturer	10
Figure 4: Percentages of WB test reagents, by manufacturer, used by participant laboratories ...	11
Figure 5: Western blot HIV-1 antibody patterns reported by participant laboratories	13
Figure 6: Percentage IFA test kits, by manufacturer, used by participant laboratories	14
Figure 7: Fluorescence intensity patterns of HIV-1 infected cells, for IFA results, reported by participant laboratories.....	15
Figure 8: Percentages of "Other" HIV-1 antibody test kits, by manufacturer, used by participants	16
Figure 9: Percentages of HIV-1 rapid test reagents, by manufacturer, used by participant laboratories	17
Figure 10: Type of laboratories performing HIV rapid testing	20
Figure 11: Type of HIV rapid testing kits used by U.S. and Non-U.S. laboratories	21
Figure 12: Specimen types used by U.S. and Non-U.S. laboratories*	22

**Analysis of the January 2003 Performance Evaluation
HIV-1 Antibody Testing Results
Reported by Laboratories Participating in the Model Performance Evaluation Program**

Introduction

This report analyzes results provided to the Centers for Disease Control and Prevention (CDC) by laboratories participating in the Model Performance Evaluation Program (MPEP) after they tested the human immunodeficiency virus type 1 (HIV-1) performance evaluation samples and completed a brief questionnaire concerning HIV rapid testing shipped to them in January 2003. Test results were reported by 743 (91.4%) and completed questionnaires were returned by 708 (87%) of the 813 enrolled laboratories.

Methods and Materials

Samples used in the MPEP surveys are undiluted, defibrinated plasma obtained from individual donors who are HIV-1-infected (positive) or HIV-1-uninfected (negative). The HIV-1 antibody-positive samples were heat treated at 56° C for 60 minutes to inactivate blood borne viruses including HIV-1, human T-lymphotropic virus types I and II (HTLV-I/II), and hepatitis B and C viruses. The HIV-1 antibody-negative samples were not heat treated. Before shipment, each donor sample was tested with the following:

- two HIV-1 enzyme immunoassay (EIA) kits,
- two HIV-1/HIV-2 EIA kits
- two rapid test (RT) kits, and
- supplemental tests;
 - two HIV-1 Western blot (WB) kits and
 - one HIV-1 indirect immunofluorescence assay (IFA).

In pre-shipment testing, the strong-positive HIV-1 donor sample (Donor 5) was repeatedly EIA reactive with all of the HIV-1 EIA and the HIV-1/HIV-2 EIA kits. It was also WB reactive with the two HIV-1 FDA-licensed WB kits. The negative donor sample (Donor 1) was repeatedly EIA non-reactive and demonstrated no bands with the FDA-licensed HIV-1 WB kits. Donor samples 3 and 4, obtained from individual donors recently infected with HIV-1, were positive for HIV-1 antibody and demonstrated EIA and WB reactivity with the FDA-licensed EIA, WB and RT kits used for pre-shipment testing. Testing information for sequential serum samples from Donors 3 and 4 demonstrated factors consistent with seroconversion such as a positive p24 antigen test, positive test for HIV-1 ribonucleic acid (RNA), rising HIV-1 antibody titers in all EIA tests, and WB reactivity changing from one donation to the next from nonreactive (no bands) to indeterminate or reactive.

Table 1 and Table 2 on pages 6 and 7, respectively, are provided for the participant laboratories to record and compare their results with the CDC MPEP results for survey samples.

Table 1: Human Immunodeficiency Virus Type 1 (HIV-1) Antibody Testing for the January 2003 Shipment

Panel Letter	Vial Label	CDC Donor Number ¹	CDC Test Result ²	Donor HIV Status	Laboratory Interpretation ³			
					EIA		WB	IFA
					Initial	Final		
A	A1	1	Negative	Uninfected	_____	_____	_____	_____
	A2	3	Positive	Infected	_____	_____	_____	_____
	A3	4	Positive	Infected	_____	_____	_____	_____
	A4	5	Positive	Infected	_____	_____	_____	_____
	A5	3	Positive	Infected	_____	_____	_____	_____
	A6	5	Positive	Infected	_____	_____	_____	_____
B	B1	3	Positive	Infected	_____	_____	_____	_____
	B2	1	Negative	Uninfected	_____	_____	_____	_____
	B3	5	Positive	Infected	_____	_____	_____	_____
	B4	3	Positive	Infected	_____	_____	_____	_____
	B5	4	Positive	Infected	_____	_____	_____	_____
	B6	5	Positive	Infected	_____	_____	_____	_____
C	C1	5	Positive	Infected	_____	_____	_____	_____
	C2	4	Positive	Infected	_____	_____	_____	_____
	C3	3	Positive	Infected	_____	_____	_____	_____
	C4	1	Negative	Uninfected	_____	_____	_____	_____
	C5	5	Positive	Infected	_____	_____	_____	_____
	C6	3	Positive	Infected	_____	_____	_____	_____
D	D1	4	Positive	Infected	_____	_____	_____	_____
	D2	3	Positive	Infected	_____	_____	_____	_____
	D3	1	Negative	Uninfected	_____	_____	_____	_____
	D4	5	Positive	Infected	_____	_____	_____	_____
	D5	5	Positive	Infected	_____	_____	_____	_____
	D6	3	Positive	Infected	_____	_____	_____	_____

1. Donor 2 was intentionally omitted.
2. The CDC result was obtained after composite testing with the commercially available HIV -1 and HIV -1/HIV -2 EIA, HIV -1 WB and IFA kits licensed by the Food and Drug Administration (FDA). The CDC WB interpretation is consistent with the manufacturer's criteria for interpretation of WB results.
3. Laboratory Interpretation space (to be completed by participant laboratory) provided to facilitate comparison of participant laboratory result with CDC result.

Table 2: CDC Western Blot (WB) Testing Results for the January 2003 Shipment

Panel Letter	Vial Label	CDC Donor Number ¹	CDC Western Blot Test Results Specific WB Band Detected ²	WB Test Kit Manufacturer	CDC Interpretation ³
A	A1	1	No Bands	Both Manufacturers	Negative
	A2, A5	3	17, 24, 41, 51, 55, 66, 120, 160 18, 24, 31, 40, 55, 65, 160	Cambridge Biotech ⁴ Genetic Systems	Positive Positive
	A3	4	17, 24, 31, 41, 51, 55, 66, 120, 160 18, 24, 31, 40, 51, 55, 65, 160	Cambridge Biotech Genetic Systems	Positive Positive
	A4, A6	5	17, 24, 31, 41, 51, 55, 66, 120, 160 24, 31, 40, 51, 55, 65, 160	Cambridge Biotech Genetic Systems	Positive Positive
B	B1, B4	3	17, 24, 41, 51, 55, 66, 120, 160 18, 24, 31, 40, 55, 65, 160	Cambridge Biotech Genetic Systems	Positive Positive
	B2	1	No Bands	Both Manufacturers	Negative
	B3, B6	5	17, 24, 31, 41, 51, 55, 66, 120, 160 24, 31, 40, 51, 55, 65, 160	Cambridge Biotech Genetic Systems	Positive Positive
	B5	4	17, 24, 31, 41, 51, 55, 66, 120, 160 18, 24, 31, 40, 51, 55, 65, 160	Cambridge Biotech Genetic Systems	Positive Positive
C	C1, C5	5	17, 24, 31, 41, 51, 55, 66, 120, 160 24, 31, 40, 51, 55, 65, 160	Cambridge Biotech Genetic Systems	Positive Positive
	C2	4	17, 24, 31, 41, 51, 55, 66, 120, 160 18, 24, 31, 40, 51, 55, 65, 160	Cambridge Biotech Genetic Systems	Positive Positive
	C3, C6	3	17, 24, 41, 51, 55, 66, 120, 160 18, 24, 31, 40, 55, 65, 160	Cambridge Biotech Genetic Systems	Positive Positive
	C4	1	No Bands	Both Manufacturers	Negative
D	D1	4	17, 24, 31, 41, 51, 55, 66, 120, 160 18, 24, 31, 40, 51, 55, 65, 160	Cambridge Biotech Genetic Systems	Positive Positive
	D2, D6	3	17, 24, 41, 51, 55, 66, 120, 160 18, 24, 31, 40, 55, 65, 160	Cambridge Biotech Genetic Systems	Positive Positive
	D3	1	No Bands	Both Manufacturers	Negative
	D4, D5	5	17, 24, 31, 41, 51, 55, 66, 120, 160 24, 31, 40, 51, 55, 65, 160	Cambridge Biotech Genetic Systems	Positive Positive

1. Donor 2 was intentionally omitted.

2. Western blot (WB) result based on band intensity of $\geq 1+$ staining.

3. The CDC interpretation is consistent with the manufacturer's criteria for interpretation of WB results.

4. Cambridge Biotech/Calypte Biomedical

Overall Summary of Results

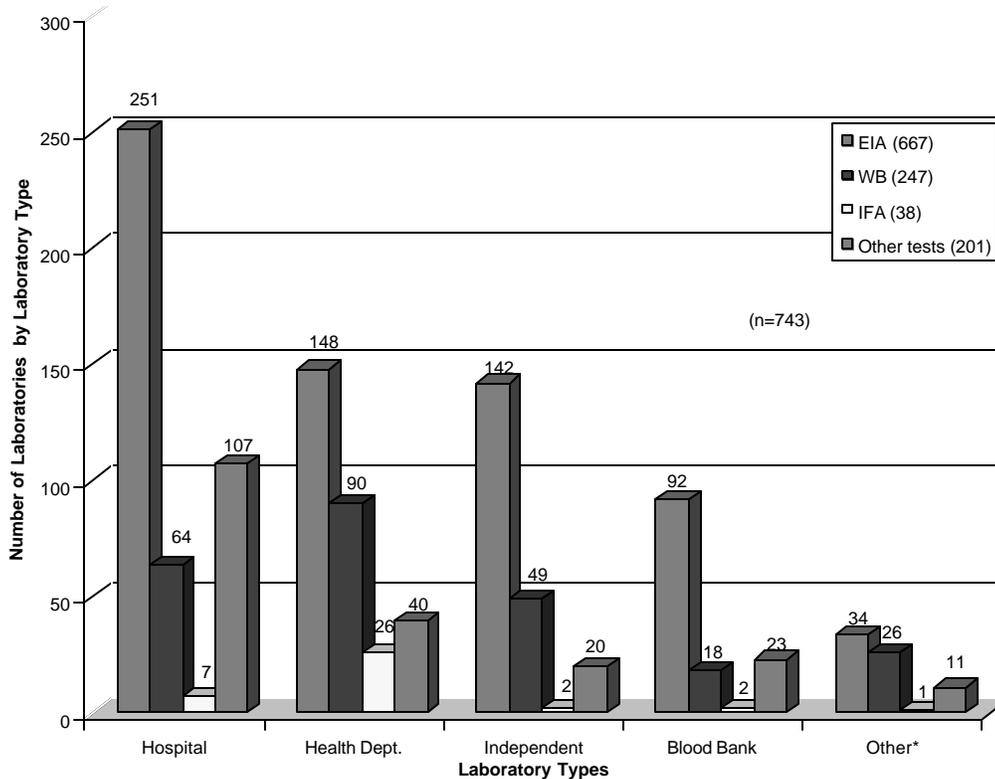
Table 3 below summarizes the results grouped by test type; EIA, WB, IFA, and "Other."

Method	Total # of laboratories	Total # of results	Positive Donors	Negative Donor	Overall Performance (TP+TN/total # result) ¹
			False-negative or indeterminate results	False-positive or indeterminate results	
EIA	667	4266	11/3560 (0.3%)	5/706 (0.7%)	99.6%
WB	247	1353	37/1232 (3.0%) ³	4/121 (3.3%) ⁴	99.7% ⁵
IFA	38	215	27/189 (14.3%)	None	95.8% ⁵
OTHER ²	201	1345	17/1133 (1.5%)	None	Not applicable

1. TP, true positives; TN, true negatives.
2. "Other" test methods refer to test types other than EIA, WB or IFA, such as line or strip assays, microparticle capture, chemiluminescence, etc.
3. All indeterminate.
4. One false-positive and 3 indeterminates.
5. When calculating overall performance, indeterminate interpretations are considered to be correct for HIV-1 antibody-positive donors, and incorrect for HIV-1 antibody-negative donors.

The types of laboratories reporting results are shown in Figure 1 (below). Each laboratory type is listed with the test methods used. Some laboratories reported using more than one method; therefore, the sum is greater than the total number of laboratories. The "n" value reflected in all figures refers to the number of laboratories, not the number of methods or tests kits used.

Figure 1: Number of HIV-1 participants by laboratory type that reported EIA, WB, IFA, and "Other" results



*Other laboratory types include university-associated research centers, university clinics, Federal government facilities, STD clinics, etc.

Laboratories from 70 countries, and most of the regions of the world submitted results for this survey. (Table 4)

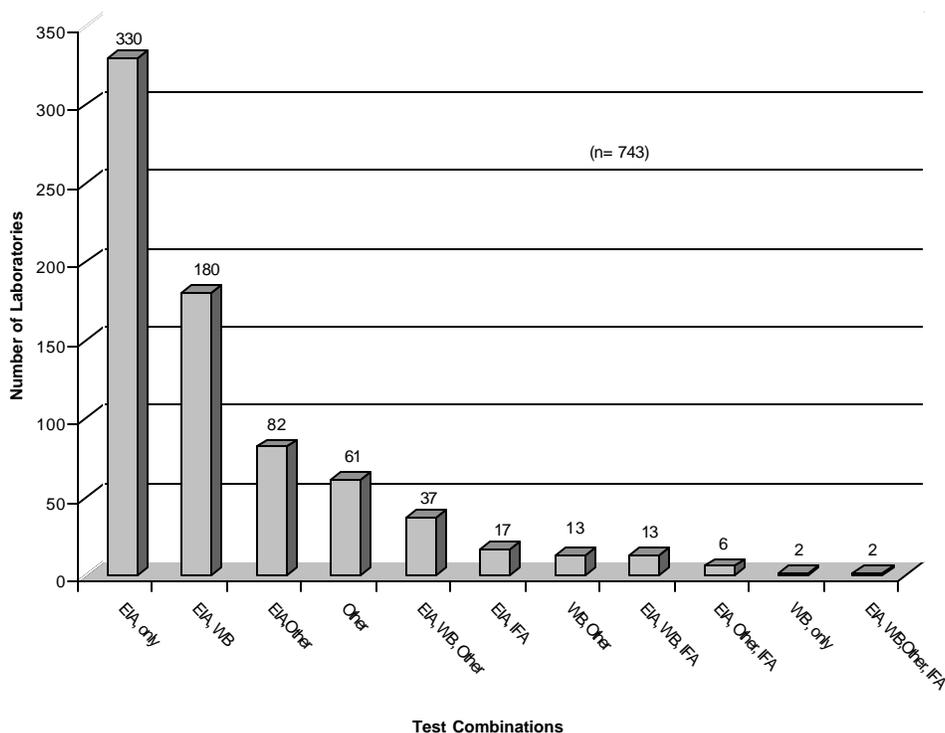
Table 4: Location of the laboratories that reported results for this shipment

Region	Number Of Laboratories (%)
US (including US territories)	600 (80.8%)
Africa	16 (2.2%)
Asia	36 (4.8%)
Australia	6 (0.8)
Canada	19 (2.6%)
Central America*	11 (1.5%)
Europe	29 (3.9%)
Middle East	7 (0.9%)
South America	19 (2.6%)
Total	743

*Includes Dominican Republic and St. Kitts/Nevis

The combinations of test methods used by the laboratories and the frequency of use are shown in Figure 2. Of the 743 laboratories reporting results, 330 (44.4%) performed only EIA, 210 (28.3%) performed EIA and a supplemental test, and two (0.3%) performed only a supplemental test. These numbers do not include the 201 (27.1%) laboratories that performed an AOther@test in addition to or instead of EIA, WB and IFA. The data for these AOther@tests are presented in Figure 8, page 16.

Figure 2: The combination of HIV-1 antibody tests reported by participant laboratories



The percentages of test kits used, listed by kit manufacturer, for the EIA, WB, and IFA are shown in Figures 3, 4, and 6, respectively. Some laboratories indicated using test kits for which there were no unique manufacturer codes provided in the report booklet. These responses have been grouped as "Other" manufacturer kits. Some AOther@EIA kits reported include, BioTest Anti-HIV Tetra Elisa (two laboratories), Bio-Chem Immunosystems Detect HIV (three laboratories), Abbott HIV-1/2 gO EIA (two laboratories), and Dade Behring Enzygnost HIV Integral (three laboratories). There were laboratories located outside the United States that used the Abbott AxSYM system or the Abbott PRISM analyzer that reported results as S/CO (sample/cutoff ratio). Since the S/CO data can not be entered correctly on the MPEP EIA result form, the data from laboratories using either AxSYM or PRISM systems are reported with AOther@tests in Figure 8, page 16.

The reports of false-negative and false-positive results for the HIV-1-positive and HIV-1-negative samples for the EIA, WB, and IFA methods, listed by kit manufacturer, are shown in Tables 5, 6 and 7, respectively.

EIA Results

Table 5, page 11, shows the five false-positive EIA interpretations reported for Donor 1. There were eleven false-negative interpretations reported by seven different laboratories for HIV-1 positive samples; five were reported for Donor 3 by laboratories using two different test kits. Three false-negative interpretations were reported for Donor 4 by laboratories using the same two test kits. There were also three false-negatives for Donor 5 reported by two laboratories using the same kit manufacturer.

Figure 3: Percentages of laboratories using EIA test kits, by manufacturer

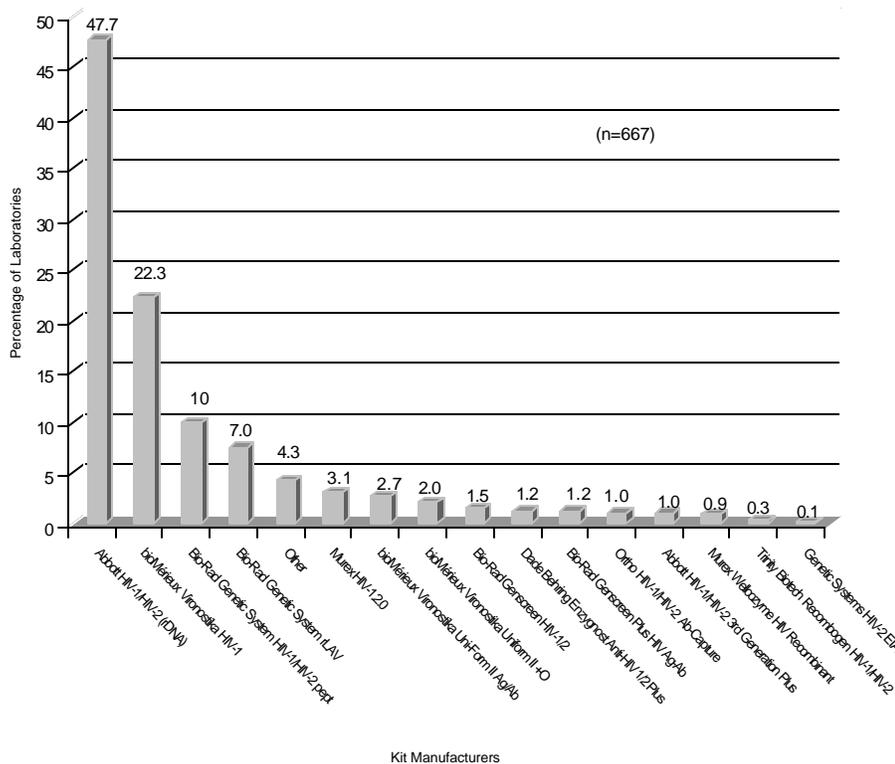


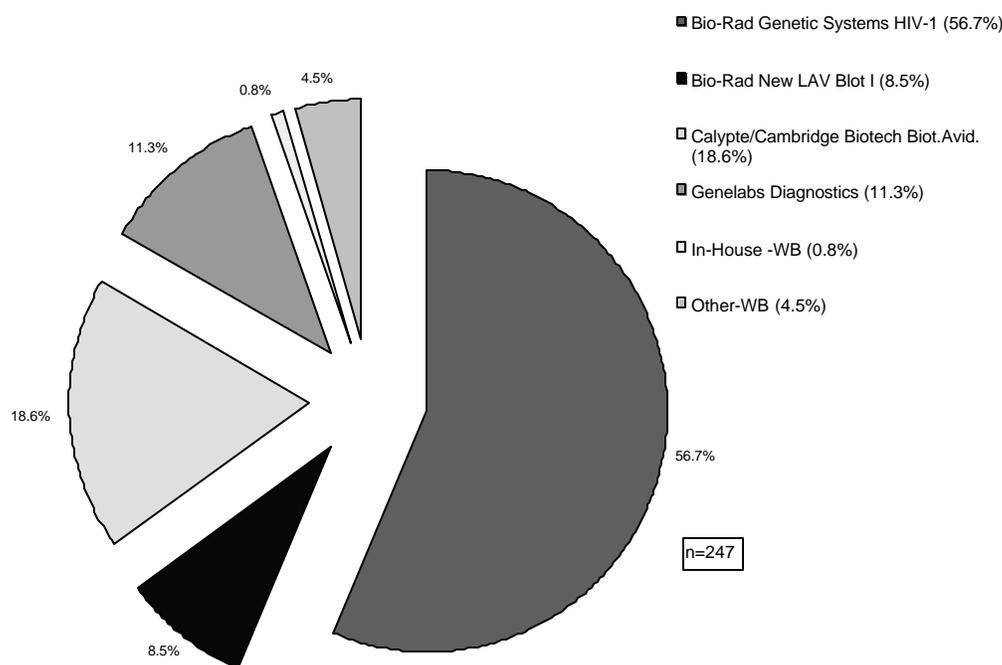
Table 5: False-positive and false-negative EIA results, by kit manufacturer, reported by participant laboratories

Enzyme Immunoassay (EIA)			
<u>Manufacturer</u>	<u>Total # of Results</u>	<u>False-positive</u>	<u>False-negative</u>
Abbott HIV-1/HIV-2 (rDNA)	1900	4	5
bioMérieux Vironostika HIV-1	894	1	6
Total	2794	5	11

WB Results

Of the 743 laboratories reporting test results in this survey, 247 (33.2%) performed WB testing. Six U.S. laboratories reported WB testing results on the plasma performance evaluation samples using the OraSure HIV WB test which is FDA approved only for oral fluids. All six laboratories were Health Department laboratories.

Figure 4: Percentages of WB test reagents, by manufacturer, used by participant laboratories



WB Results Interpretations

One false-positive and three indeterminate WB interpretations were reported by four different laboratories for the HIV-1 uninfected donor sample (Donor 1), using two different commercially manufactured WB kits and one in-house kit. Normally, Western blot tests are not performed on specimens that are non-reactive by other test methods.

Table 6: False-positive, false-negative, and indeterminate results for both positive and negative donor samples for Western blot test, by manufacturer

Manufacturer	Western Blot (WB)				
	Total # of Results	Negative Donor		Positive Donors	
		False-positive	Indeterminate	False-negative	Indeterminate
Bio-Rad Genetic Systems HIV-1	769	0	2	0	26
Bio-Rad New LAV Blot I	113	0	1	0	4
Calypse/Cambridge Biotech (Biotin)	248	0	0	0	4
In House	11	1	0	0	0
Other*	59	0	0	0	3
Total	1200	1	3	0	37

*There are no manufacturers' codes in the report booklet for these manufacturers.

There were a total of 40 indeterminate and one false-positive WB results reported;

Donor 1 (HIV-1 negative)

- 3 indeterminates
- 1 false-positive

Donor 4 (HIV-1 infected seroconverter)

- 7 indeterminates

Donor 3 (HIV-1 infected seroconverter)

- 27 indeterminates

Donor 5 (HIV-1, strong positive)

- 3 indeterminates

The indeterminates were reported by 28 laboratories using four different kits. (see Table 6, above)

WB Interpretative Criteria

Of the 247 laboratories reporting WB test results, 231 indicated which WB criteria they used to interpret their WB tests. Most used the Association of Public Health Laboratories/Centers for Disease Control and Prevention (APHL/CDC) WB interpretive criteria;

- 194 (84.0%) APHL/CDC
- 17 (7.4%) stated "other" (Red Cross, Manufacturers' insert, Australian National Reference Laboratory, etc.)
- 18 (7.8%) World Health Organization, and
- 2 (0.9%) Consortium for Retrovirus Serology Standardization.

The WB interpretive guidelines published by the two FDA-licensed WB kit manufacturers are identical to the APHL/CDC HIV-1 WB interpretive criteria. According to these interpretive criteria, a positive test result is defined by the presence of any two of the following bands: p24, gp41, and gp120/160. (Distinguishing the gp120 band from the gp160 band is often very difficult. These two glycoproteins can be considered as one reactant for purposes of interpreting WB test results.) Nine U.S. laboratories indicated they were using interpretive criteria different from those recommended by the kit manufacturer as licensed by the FDA:

- 2 used Consortium for Retrovirus Serology Standardization criteria,
- 3 used "other" criteria, and
- 4 used World Health Organization criteria.

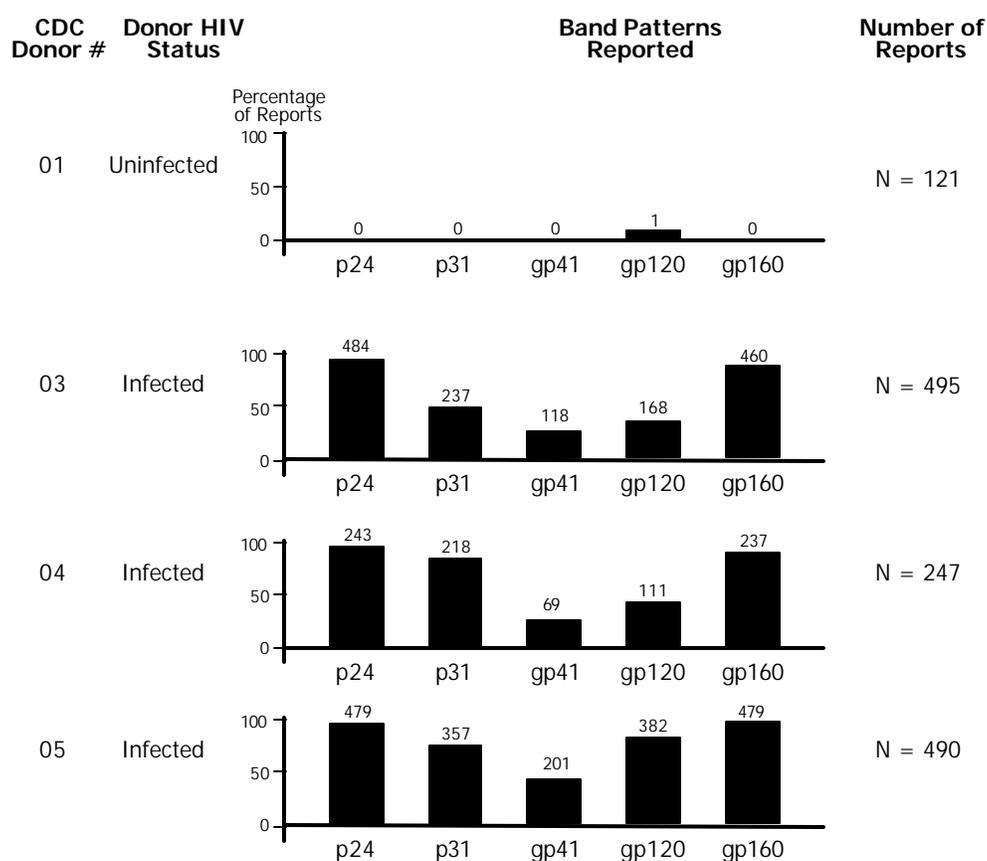
WB Band Patterns

The WB bands for the donor samples in this survey, as determined in pre-shipment testing with two FDA-licensed WB test kits, are shown in Table 2, page 7. Only bands scoring greater than or equal to 1+ intensity are listed in Table 2.

The protein band patterns for the major viral proteins, as reported by participant laboratories for each donor sample, are shown in Figure 5. The frequency of a reported band is listed above the column. The number of WB reports received for the donor sample is indicated in the far right column. This figure does not include WB bands reported as “W” or “weak,” indicating intensity less than that of the designated band of the weak positive control provided in the WB kit, nor does it include bands of greater than 1+ intensity reported for p15, p17, p51, p55, or p66.

Note that 121 WB results were reported for Donor 1, the HIV-1 antibody-negative donor, although most laboratories do not normally include WB testing of EIA non-reactive donor samples in their routine algorithm for HIV antibody testing. Three laboratories reported indeterminate interpretations for WB for Donor 1. Two of the three laboratories reported non-reactive EIA results. One laboratory reported non-reactive EIA and no WB protein bands, yet interpreted the WB test as reactive for Donor 1.

Figure 5: Western blot HIV-1 antibody patterns reported by participant laboratories



For the HIV-1 antibody strong-positive sample (Donor 5) and the seroconversion samples (Donor 3 and Donor 4), most laboratories had no difficulty in detecting antibodies to gag (p24), pol (p31), and env (gp41, gp120, gp160) antigens. There were 12 indeterminate interpretations reported however, even though the band patterns and band intensity appeared to fit the reported criteria for reactive results.

IFA Results

Figure 6 shows the percentages of laboratories using the various IFA test reagents.

For the 189 IFA interpretations reported for the HIV-1-positive samples there were;

Donor 3 (HIV-1 positive seroconverter)

- 10 indeterminates
- 6 false-negatives

Donor 5 (HIV-1 strong positive)

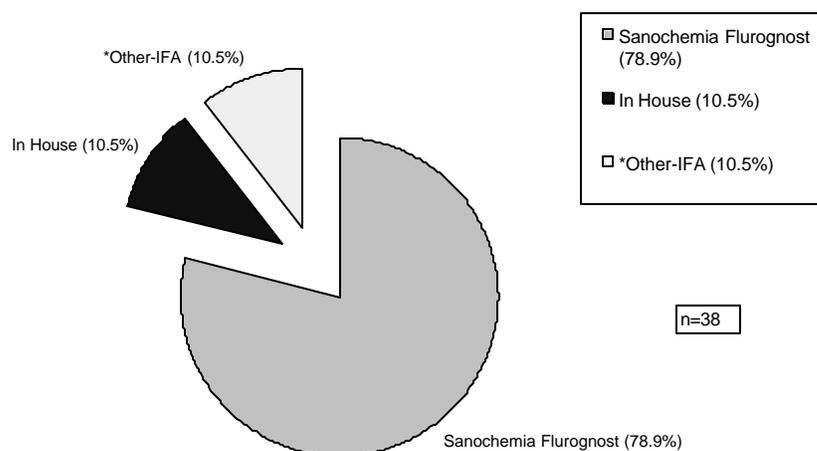
- 5 indeterminates

Donor 4 (HIV-1 positive seroconverter)

- 3 indeterminates
- 3 false-negatives

The 18 indeterminates were reported by 6 different laboratories, while the 9 false-negative results were reported by 4 laboratories. Four laboratories reported indeterminate results for Donor 5, the strongly reactive donor. Table 7, on page 15, shows the number of false-negative and indeterminate results by manufacturer.

Figure 6: Percentage IFA test kits, by manufacturer, used by participant laboratories



*Other-IFA: Manufacturers for which there are not codes in the result booklet.

Table 7: Indeterminate and false-negative results reported, by participants, by manufacturer for immunofluorescent antibody tests

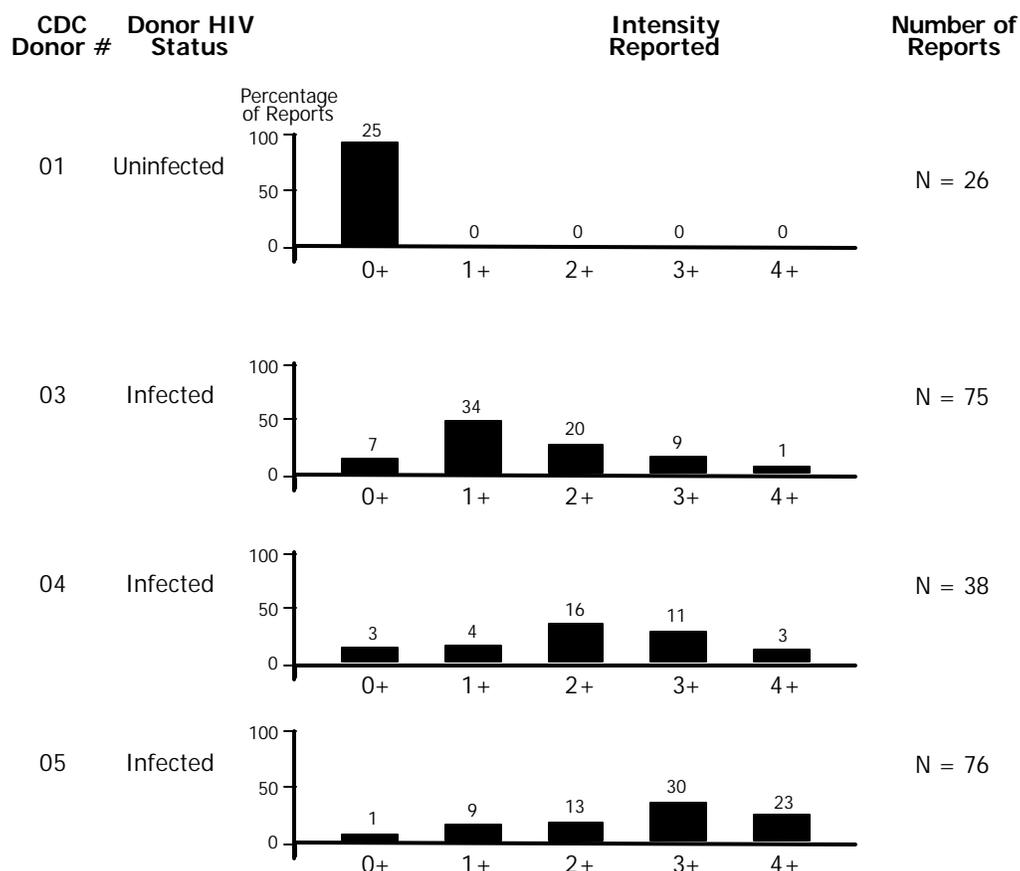
Manufacturer	IFA Antibody		
	Total # of results	Indeterminate	False-negative
In House	23	5	2
Other*	24	3	0
Sanochemia Fluorognost	168	10	7
Total	215	18	9

Note: No false-positive results were reported.

IFA Intensity Patterns

The IFA intensity patterns for HIV-1 infected cells, as reported by participating laboratories, are shown in Figure 7. The frequency of reports of fluorescence intensity for each donor is listed in the far right column. A scoring of fluorescence intensity is not required for interpretation of seroreactivity with the FDA-licensed Sanochemia (formerly know as Waldheim) Fluorognost HIV-1 IFA kit; therefore, some laboratories provided interpretations, but did not score fluorescent intensity. Data from these laboratories were not included in Figure 7. No fluorescence was reported for one of the 26 negative Donor 1 samples; four of the 75 IFA Donor 3 samples; and one of the 38 IFA Donor 4 samples.

Figure 7: Fluorescence intensity patterns of HIV-1 infected cells, for IFA results, reported by participant laboratories

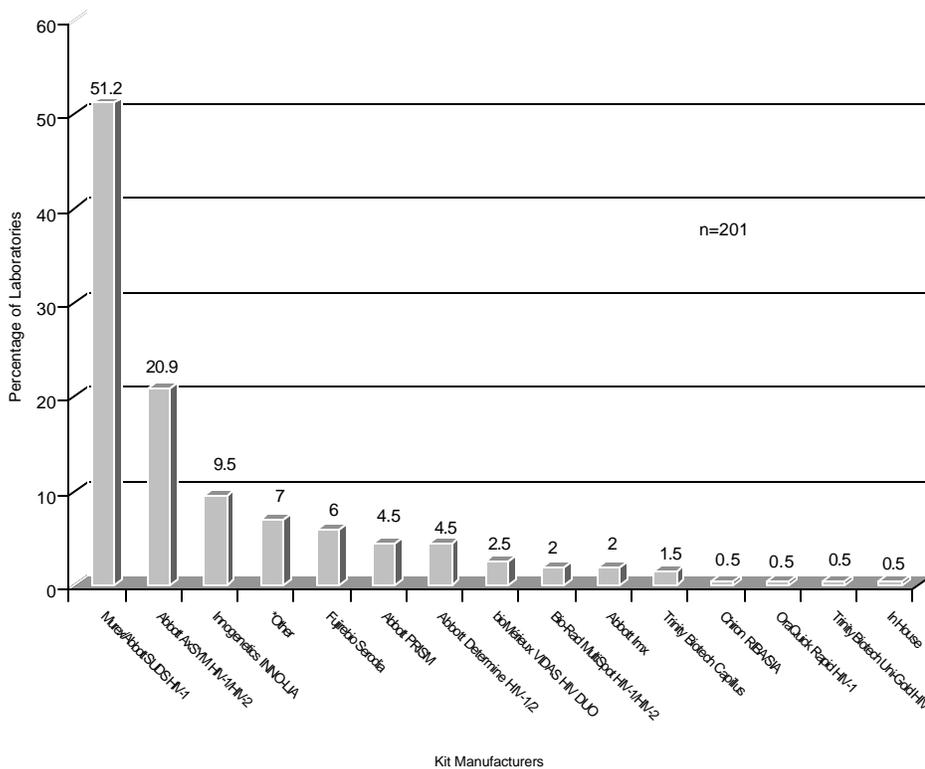


“Other” Tests Performed

Figure 8 shows manufacturers of "Other" types of tests and percentages of use by the reporting laboratories.

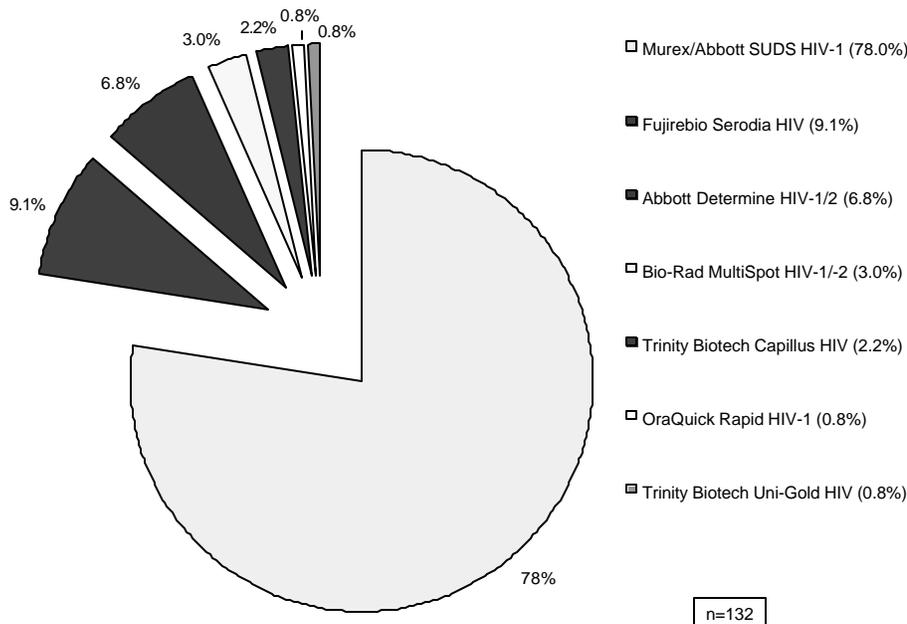
The procedures used by 132 (65.7%) of 201 laboratories that reported using “Other” tests can be described as “rapid tests” (see Figure 9, page 17). The results of “Line” or “Strip Immunoassay” tests such as Qualitative Immunoblot (1), HIV 1+2 Immunodot Test (1), and Organics LTD HIV 1 & 2 BiSpot (1) are not included in this figure. Also, note that all laboratories using the Abbott AxSYM (42 laboratories) or PRISM (9 laboratories) systems reported their results on the AOther@test type result form, since these tests are based on microparticle capture and chemiluminescence measurement and differ from the traditional microtiter-format EIA tests.

Figure 8: Percentages of "Other" HIV-1 antibody test kits, by manufacturer, used by participants



*Other: tests for which there are no manufacturers' codes listed in the result booklet.

Figure 9: Percentages of HIV-1 Rapid Test reagents, by manufacturer, used by participant laboratories



“Other” Results Interpretations

Among the 212 final interpretations reported for the HIV-1-negative sample (Donor 1) tested by laboratories using these **Other** procedures, there were no false-positive and no indeterminate interpretations reported. (Table 8, below)

Table 8: "Other" test kits: False-positive, false-negative and indeterminate results

Manufacturer	Total # Results	HIV-1 Negative Donor		HIV-1 Positive Donors	
		False-positive	Indeterminate	False-negative	Indeterminate
Innogenetics INNO-LIA	107	0	0	0	1
Murex/Abbott SUDS HIV -1	616	0	0	1	0
OraQuick Rapid HIV -1	6	0	0	0	2
Other*	87	0	0	0	7
Trinity Biotech Capillus	17	0	0	6	0
Total	833	0	0	7	10

* Other: There were no manufacturers' codes in the result booklet for these manufacturers.

Among the 1133 interpretations reported for the HIV-1-positive samples tested by procedures other than EIA, WB, or IFA, there were seven (0.6%) false-negative and ten (0.9%) indeterminate interpretations, as shown in Table 7. The results, by donor, are as follows:

Donor 3 (seroconverter)

- 4 false-negatives
- 6 indeterminates

Donor 4 (seroconverter)

- 2 false-negatives
- 2 indeterminates

Donor 5 (strong positive)

- 1 false-negative
- 2 indeterminates

Quality Control Testing

Table 9 describes the external quality control (QC) practices of most of the participating laboratories. Positive and negative samples included in manufactured kits are internal kit control material used to validate the test run, calculate test run cut-off values, and may not validate the analytic testing process, which may include testing problems such as faulty pipettors, inadequate incubation conditions, or sensitivity of the test kits.

Table 9: Summary of External Quality Control Material Sources

Test Type (Total # of Laboratories) ¹	Number of Laboratories (%) Reporting External QC	Source of External Quality Control Materials		
		In-House	Commercial	Both
EIA ² (648)	505 (77.9%)	156 (30.9%)	319 (63.2%)	27 (5.3%)
WB ² (237)	101 (42.6%)	56 (55.4%)	41 (40.6%)	2 (2.0%)
IFA (38)	14 (36.8%)	9 (64.3%)	4 (28.6%)	1 (7.1%)
Other (176)	61 (34.7%)	30 (49.2%)	29 (47.5%)	2 (3.3%)

1. Not all laboratories completed the QC section of the result booklet
2. For EIA three laboratories did not report the source of their external QC material. For WB, two laboratories did not report the source of their external QC material.

Frequency of External QC Testing

For the laboratories reporting using external QC material:

- EIA: Most laboratories ran QC with each set/run of plates or each EIA plate and indicated the use of weakly-positive and/or negative serum/plasma controls.
- WB: Most laboratories ran weakly-positive serum/plasma and indicated running QC with each set/run of WB strips.
- IFA: Less than half of the laboratories reported using external controls, and only 14.3% of those laboratories reported using controls with each run.
- “Other”: Of the 61 laboratories that reported external QC, 33 (54.1%) indicated using weakly-positive controls and 11 (18.0%) indicated using strong positive controls with each set/run.

Discussion of HIV Results

This program provides challenging samples with which participant laboratories perform HIV-1 antibody testing. Most participants performed well in testing the HIV-1 donor samples in this shipment (see Table 3, page 8):

For the negative Donor, false-positive rates were:

- EIA, 0.7%,
- WB, 3.3% (indeterminate results are considered to be incorrect),
- IFA, none and
- “Other” test, none.

For the positive Donors, false-negative/indeterminate rates were:

- EIA, 0.3%, false-negative,
- WB, 3.0% indeterminate,
- IFA, 14.3% indeterminate, and
- “Other”, 1.5% indeterminate.

All laboratories participating in the MPEP should be aware of several points:

- Six laboratories reported WB testing results using the OraSure HIV WB test. This test is FDA approved only for oral fluid. All of the MPEP samples are defibrinated plasma.
- For Western blot testing:
 - Several laboratories performed WB testing on Donor 1, even though the sample tested negative by EIA. This appears to be a deviation from the accepted algorithm for HIV testing.
 - There was a 100% increase in the number of indeterminate results reported, from 20 in the July 2002 shipment to 40 in this shipment.
 - Of the 40 indeterminate results, 28 (70%) were from laboratories using Bio-Rad Genetic Systems HIV-1, and 5 (12.5%) from laboratories using Bio-Rad New LAV Blot.
 - Nine of these laboratories reported indeterminate results, even though the band patterns and intensity appeared to fit their reported criteria for positive results.
 - Nine U.S. laboratories used interpretive criteria different from that recommended by the kit manufacturer as licensed by the FDA.
- There was an increase in the number of indeterminate results reported for IFA, from 13/138 (9.4%) in the June 2002 shipment, to 27/189 (14.3%) in this shipment.
- There was a slight increase in the number of laboratories performing rapid testing, from 62.7% to 66.7%; however,
 - one laboratory reported using OraQuick Rapid HIV-1 Rapid HIV. This laboratory reported 2 indeterminate results, and
 - three laboratories reported using Trinity Biotech Capillus. Two of the three reported six false negative results.

Adequate training is essential in the performance of all laboratory testing. The results of this survey for Western blot results, IFA and rapid test, may point to the need for greater understanding of test methods and procedures.

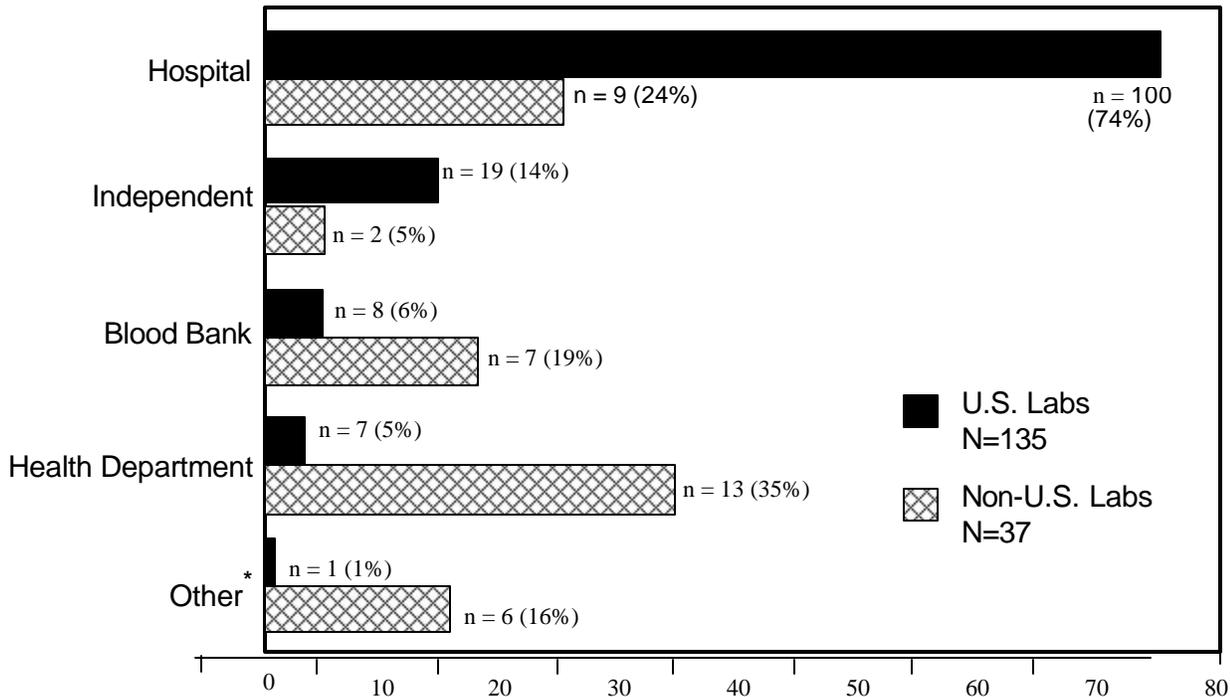
HIV Rapid Testing Questionnaire Results

To support our mission of improving public health and preventing disease through continuously improving laboratory practices, the CDC MPEP will offer a performance evaluation program for HIV Rapid Testing (HIV-R MPEP), beginning July 2003. This new program is especially targeted to probe performance and practice issues unique to HIV rapid testing. The program will provide laboratory aggregate results and information for all known HIV rapid tests, including but not limited to those approved by the FDA.

To collect preliminary information needed for designing the HIV Rapid Testing MPEP, we included a brief questionnaire as part of the January 2003 HIV sample survey. A total of 708/813 (87%) MPEP participants answered the questionnaire. Of those who answered, 215/708 (30%) reported they are either presently using HIV rapid tests or intend to begin offering HIV rapid tests within two years. The results of this survey, presented below, reflect responses of those laboratories enrolled at the time of the survey and may not be representative of all HIV rapid testing currently being performed.

Figure 10 shows the profile of laboratory type designations for U.S. and non-U.S. facilities currently performing HIV rapid testing.

Figure 10: Type of laboratories performing HIV Rapid testing



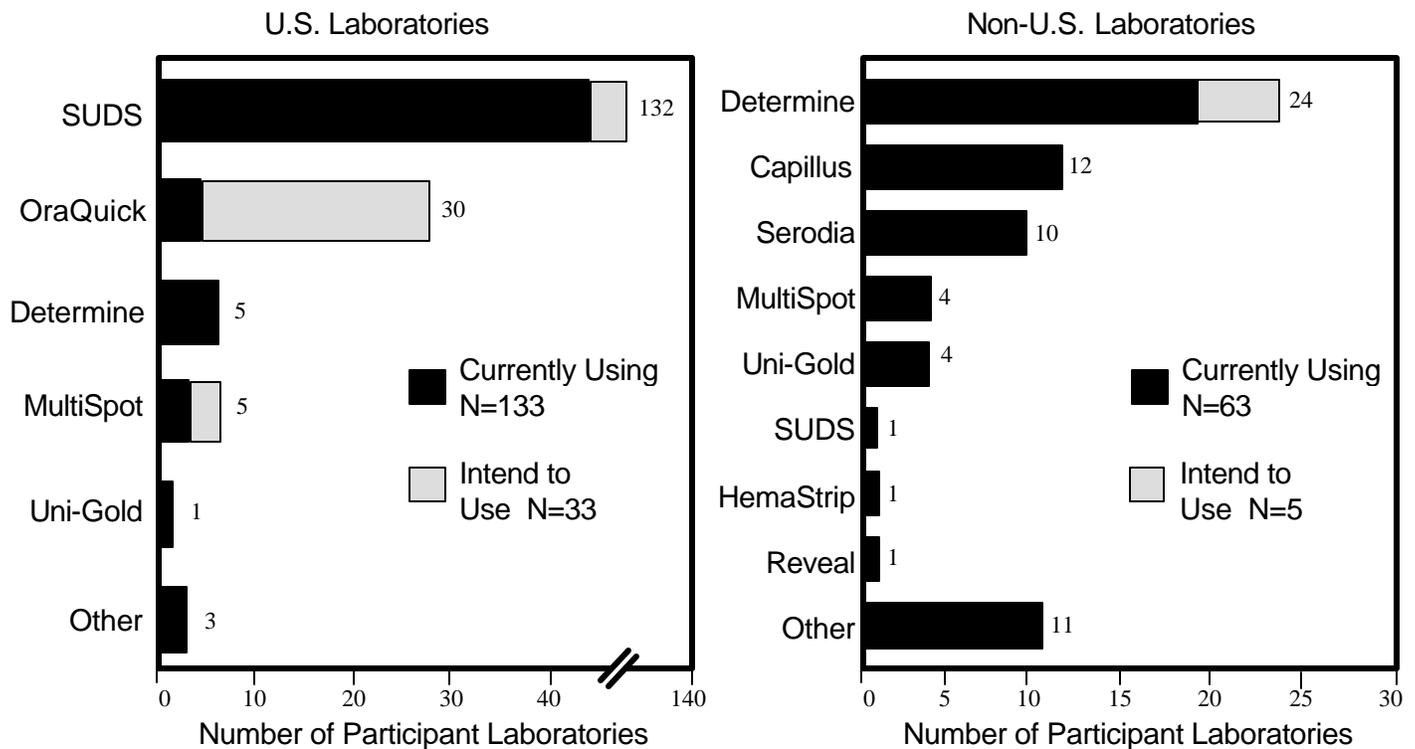
Percentage of U.S. and non-U.S. Laboratories Currently Performing HIV Rapid Testing

*Other laboratory types include University-associated research centers, University clinics, Federal government facilities and STD clinics.

In this survey, hospitals comprise the majority of U.S. sites currently performing HIV rapid testing (74%). Among non-U.S. sites, the proportions of various laboratory types are more evenly distributed, e.g. Hospital (24%), Blood Bank (19%), Health Department (35%), and “Other” (16%).

Figure 11 shows the breakdown of kit types used, by numbers of U.S. and non-U.S. laboratories. Note: Since initiating the survey questionnaire we have learned that the distribution of the Abbott/Murex SUDS HIV rapid test was discontinued in May 2003. This market change will likely impact the relative proportions of types of HIV rapid test kits used. CDC HIV-R MPEP will continue to track the future trends in HIV rapid test usage.

Figure 11: Type of HIV Rapid testing kits used by U.S. and Non-U.S. laboratories



*Notes: Participants may have used more than one kit.

HIV Rapid Testing Kits include the:

Trinity Biotech Capillus™ HIV-1/HIV-2, Abbott Determine™ HIV-1/2, Chembio Diagnostic Hema.Strip HIV-1/2™, Biorad Laboratories MultiSpot® HIV-1/HIV-2, OraSure Technologies/Abbott OraQuick® Rapid HIV-1 Antibody Test, Medmira Laboratories Reveal™ Rapid HIV-1 Antibody Test, Fujirebio Diagnostics Inc. Serodia® HIV – 1/2, Abbott/Murex Single Use Diagnostic System (SUDS) HIV-1 Test, and the Trinity Biotech Uni-Gold™ HIV test.

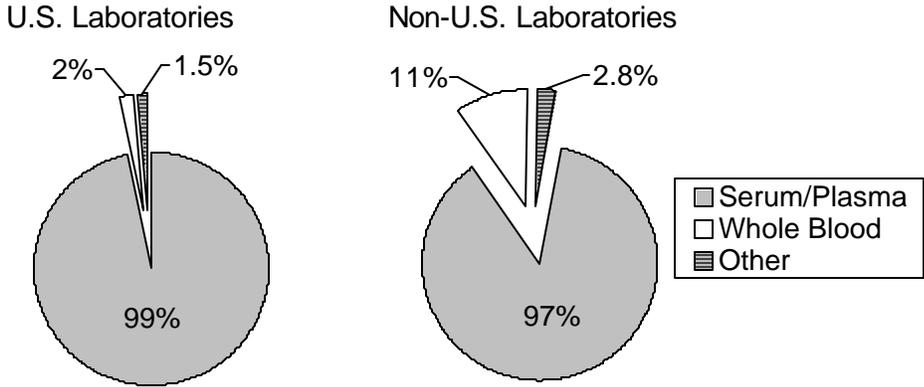
For those U.S. testing sites currently using HIV rapid test kits, the top three kits are SUDS (n=124; 93.2%), Determine (n=5; 3.8%), and OraQuick (n= 4; 3.0%). For those domestic laboratories intending to use HIV rapid test kits, the top three are OraQuick (n=26; 78.8%), SUDS (n= 8; 24.0%), and Multispot (n=3; 9.0%). These calculations are based on the number of domestic laboratories that currently use, or intend to use, kits and who also answered the question regarding kit type; N=133 and N=33, respectively.

Please note that as of this writing, OraQuick® Rapid HIV-1 Antibody Test, Single Use Diagnostic System (SUDS) HIV-1 Test, and Reveal™ Rapid HIV-1 Antibody Test are the only kits approved by the FDA for use in the U.S.

Based on the number of these laboratories that answered the question regarding kit type (N=37), the top three HIV rapid testing kits currently being used by non-U.S. laboratories are Determine (n=19, 51.4%), Capillus (n=12, 32.4%), and Serodia (n=10, 27.0%).

Figure 12 illustrates the relative proportions of specimen types used by U.S. and Non-U.S. sites, respectively. In most cases, the specimen type is dictated by the specific HIV rapid test used; however, some kits allow a choice of specimen type. It should be noted that laboratories had the option of listing multiple specimen types.

Figure 12: Specimen types used by U.S. and Non-U.S. laboratories*



*Note: Participants may have used more than one specimen type.

Nineteen of the 135 domestic laboratories (14%) that currently use HIV rapid testing kits reported that no confirmatory testing was performed in their laboratory, nor did they indicate that they referred specimens to another laboratory for confirmation. If specimens determined initially reactive by HIV rapid tests are not being confirmed by additional testing, this is of concern. The breakdown of laboratory types for these 19 facilities is as follows:

- 13 Hospital
- 4 Independent
- 1 Blood Bank
- 1 Health Department

In summary, the results from this HIV Rapid Testing Questionnaire provided data describing the types of laboratories, HIV Rapid Testing kits, and specimens used for participating U.S. and Non-U.S. laboratories. The analysis of information regarding the confirmatory practices for U.S. laboratories introduces the possibility that not all laboratories using HIV rapid test kits have procedures in place for confirming initial results. The reasons for this are unclear. The HIV-R MPEP will continue to track trends in laboratory practices and usage of HIV rapid tests. An expanded laboratory practices questionnaire will be sent to all participating laboratories with the first HIV-R MPEP sample shipment in July 2003.

Glossary of Terms

EIA: Enzyme immunoassay, sometimes referred to as ELISA, is a commonly used screening test to detect antibodies to HIV and other viruses and some bacteria.

Evaluation: A process for determining how well health systems, either public or private, deliver or improve services and for demonstrating the results of resource investments.

False-negative: A negative test result for a sample, that is actually positive

False-positive: A positive test result for a sample, that is actually negative.

HIV test: More correctly referred to as an HIV antibody test, this test detects antibodies to HIV, rather than detecting the virus itself.

Indeterminate test result: A possible result for IFA, WB or “Other” test that might represent a recent HIV infection.

Oral fluid test: A test using oral mucosal transudate, a serous fluid. To differentiate this fluid from saliva, an absorbent material is left in the mouth for several minutes. In an HIV-infected person, oral mucosal transudate is likely to contain HIV antibodies.

Positive test: For HIV, a specimen that is reactive on an initial EIA test, repeatedly reactive on a second EIA run on the same specimen, and confirmed positive on Western blot or other supplemental test indicating that the specimen donor is infected with HIV.

Rapid HIV test: A test to detect antibodies to HIV that can be collected and processed providing results within a short interval of time (e.g., approximately 10-60 minutes).

Seroconversion: Initial development of detectable antibodies specific to a particular antigen; the change of a serologic test result from negative to positive as a result of antibodies induced by the introduction of antigens or microorganisms into the host.

Western blot: A laboratory test that detects antibodies specific for components of the HIV virus. It is chiefly used to confirm the presence of HIV antibodies in specimens found repeatedly reactive using the EIA test.