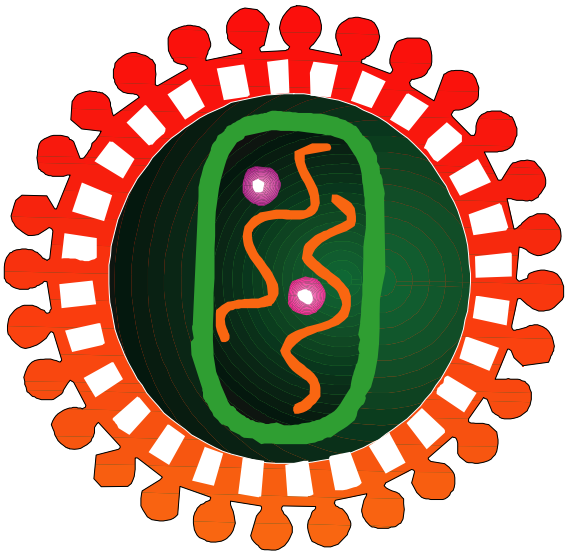
Centers for Disease Control and Prevention
Model Performance Evaluation Program

Human Immunodeficiency Virus Type 1 (HIV-1) Rapid Antibody Testing

Report of Results
for the Performance Evaluation Survey
Conducted during July 2003



U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention
Public Health Practice Program Office
Division of Laboratory Systems
Atlanta, Georgia 30341-3717

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

The production of this report was coordinated in CDC by:

Public Health Practice Program Office..... Suzanne M. Smith, M.D., M.P.H., M.P.A., Acting Director
Division of Laboratory Systems..... Robert Martin, M.P.H., Dr.P.H., Director

Laboratory Practice Evaluation and Genomics Branch.... Devery Howerton, Ph.D., Chief

The content was developed by:

Model Performance Evaluation Program (MPEP)..... Laurina O. Williams, Ph.D., M.P.H., Co-Manager
G. David Cross, M.S., Co-Manager

MPEP HIV-1 Rapid Testing Performance Evaluation..... Leigh Inge Vaughan, B.A.
HIV-1 Rapid Testing Project Coordinator

Inquires should be directed to the Model Performance Evaluation Program managers by calling (770) 488-8130 or (770) 488-8091.

Table 1 **Panel and Vial Designations, CDC Donor Numbers, CDC HIV Rapid Test Results, and Donor HIV Status**

Panel Letter	Vial Label	CDC Donor Number	CDC Interpretation of Test Result[1,2]	Donor HIV Status	Laboratory Interpretation[3] and/or Results	
					Test Result	Interpretation
A	A1	2	Positive (S)	Infected	_____	_____
	A2	3	Positive (W)	Infected	_____	_____
	A3	5	Negative	Uninfected	_____	_____
	A4	1	Positive (W)	Infected	_____	_____
	A5	5	Negative	Uninfected	_____	_____
	A6	1	Positive (W)	Infected	_____	_____
B	B1	2	Positive (S)	Infected	_____	_____
	B2	5	Negative	Uninfected	_____	_____
	B3	1	Positive (W)	Infected	_____	_____
	B4	5	Negative	Uninfected	_____	_____
	B5	1	Positive (W)	Infected	_____	_____
	B6	3	Positive (W)	Infected	_____	_____
C	C1	5	Negative	Uninfected	_____	_____
	C2	1	Positive (W)	Infected	_____	_____
	C3	3	Positive (W)	Infected	_____	_____
	C4	1	Positive (W)	Infected	_____	_____
	C5	2	Positive (S)	Infected	_____	_____
	C6	5	Negative	Uninfected	_____	_____
D	D1	1	Positive (W)	Infected	_____	_____
	D2	5	Negative	Uninfected	_____	_____
	D3	1	Positive (W)	Infected	_____	_____
	D4	2	Positive (S)	Infected	_____	_____
	D5	5	Negative	Uninfected	_____	_____
	D6	3	Positive (W)	Infected	_____	_____

1 Strong (S) and Weak (W) designations are based on qualitative observations of the colorimetric test results for reactive samples

2 The CDC result was obtained after pre-shipment testing for the presence of HIV-1 Antibody with all commercially available HIV Rapid Testing kits licensed by the Food and Drug Administration (FDA) and with selected FDA-licensed Enzyme Immunoassay (EIA) kits. The CDC result is consistent with the manufacturers' criteria for interpretation of results.

3 Laboratory Interpretation space (to be completed by participant laboratory) provided to facilitate comparison of participant laboratory result with CDC result.

HIV Rapid Testing Model Performance Evaluation Program Results

Introduction:

The plasma samples for the first challenge shipment of the HIV Rapid Testing Model Performance Evaluation Program (HIV-R MPEP) were shipped in July 2003. Six plasma samples including a strong HIV-antibody positive sample, an HIV-antibody negative sample, and two samples derived from seroconverters were sent to 225 testing sites within and outside of the United States. The response rate for the HIV-R MPEP was 82.7% (186/225). Of those who responded, 156 (83.9%) were from U.S. testing sites and 30 (16.1%) were from foreign testing sites. Twenty-four testing sites submitted multiple responses, indicating the use of from one to four different test kits, so that the total number of responses was 220.

Description of Challenge Samples:

All plasma samples were drawn from single donors. In some cases, a reactive serial bleed from a weak-positive donor was diluted with a nonreactive bleed from the same donor to achieve the desired antibody reactivity level. The resulting plasma was reactive by the Genetic Systems rLAV enzyme immunoassay (EIA) kit at a signal-to-cut off ratio of between 3 and 5. Western blot (WB) patterns for all samples were reactive by the APHL/CDC interpretative criteria. HIV-1 antibody-positive plasma samples were heat-inactivated at 56°C for 60 minutes. HIV antibody-negative samples were not heat treated and were negative for HIV-1 antigen using a FDA-approved monoclonal antibody based p24 antigen test. All donor samples were clarified prior to dispensing and tested to ensure they were free of bacterial contamination. The serostatus of all samples was confirmed by several FDA-approved EIA and WB test kits, the two FDA-approved Rapid HIV test kits, and by several other test kits currently in use. The negative sample and one of the seroconverter samples were included in the shipment in duplicate. The challenge samples in this first rapid test shipment were identical to those sent to participants in the HIV-antibody MPEP (HIV-Ab MPEP).

Summary of Findings:

1. Overall accuracy for detecting HIV antibody, defined as percentage of positive interpretations reported for all positive samples, was 93.4% (792/848). Overall accuracy for negative samples, defined as percentage of negative interpretations reported for negative samples, was 97.9% (414/423). Overall EIA accuracy for HIV-Ab positive and HIV-Ab negative samples in the HIV-antibody MPEP, receiving the same samples was 99.5% (2759/2772) and 99.1% (1358/1371), respectively.

2. Accuracy for both positive and negative samples was kit-dependent. Accuracy for detecting HIV-Ab in positive samples varied from 82.3% to 100% with various kit types. Accuracy for negative samples varied from 95.4% to 100%. Incorrect results for some kit types may have reflected matrix effects.

3. The overall accuracy for detecting HIV antibody on the weakest positive sample was 87.6% (range, 56.6% to 100% by test kit used), a finding that was worse than overall accuracy on positive samples for some test kits. (Test kits for which less than three interpretations were reported were included in the "other" category for this analysis.)

4. A total of 51.6% (112/217) of respondents reported normally running some type of external quality control (controls not included in the test kit) when performing HIV rapid tests. The responses generally seemed to be a reflection of the kit type used. However, 13.3% (14/105) of participants who reported using no external quality control used kits that did not include quality control samples within the kit.

Demographics:

A total of 186 different testing sites submitted results. These included 156 testing sites within the United States and 30 testing sites in other countries. Within the United States participation was spread throughout the states in no particular pattern. U.S. sites are depicted in Figure 1. A list of foreign countries submitting results is shown in Table 2. The types of testing site participants responding are depicted in Figure 2. Hospital testing sites predominated.

Figure 1: Number of HIV Rapid Testing Site Participants in the United States

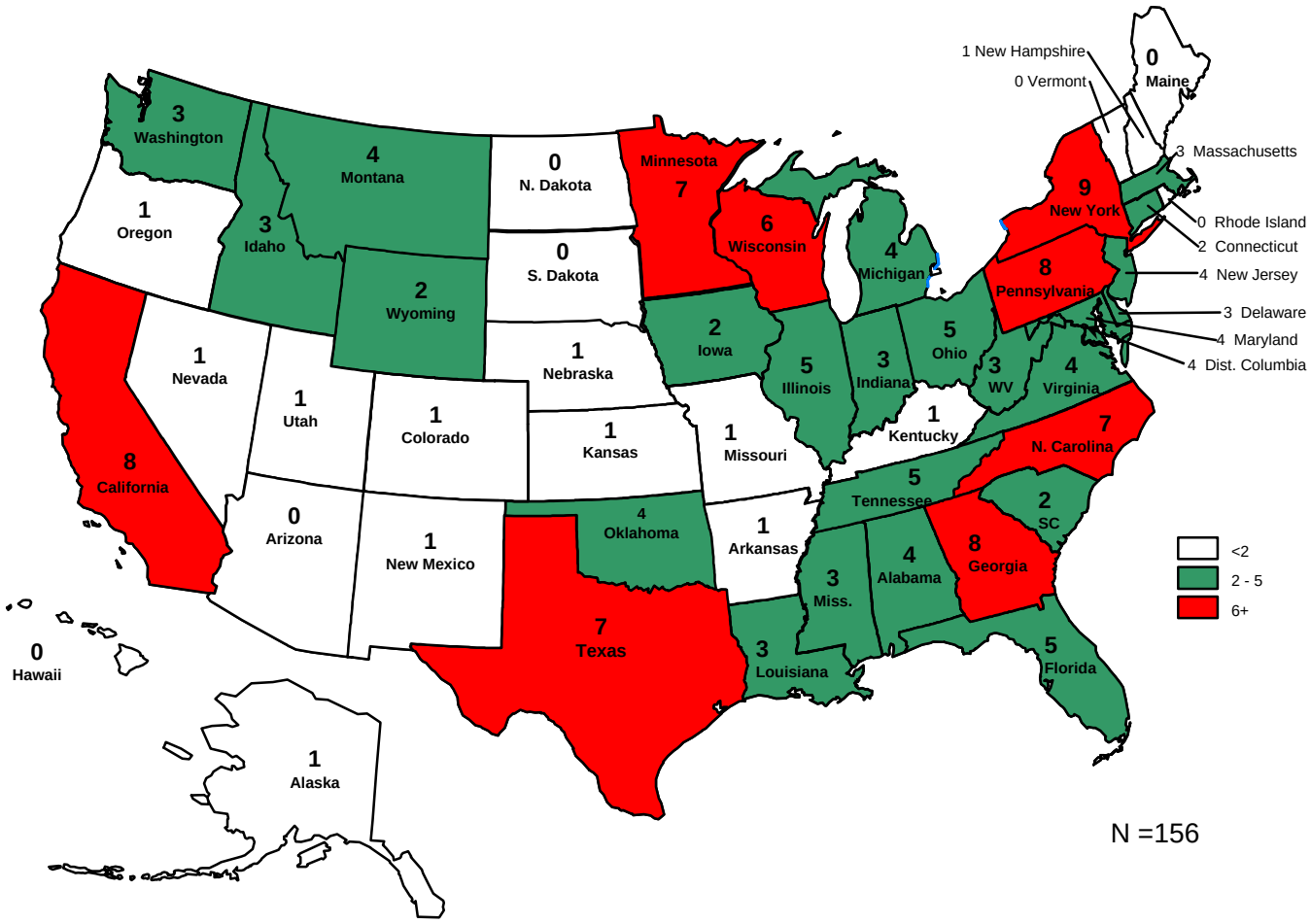
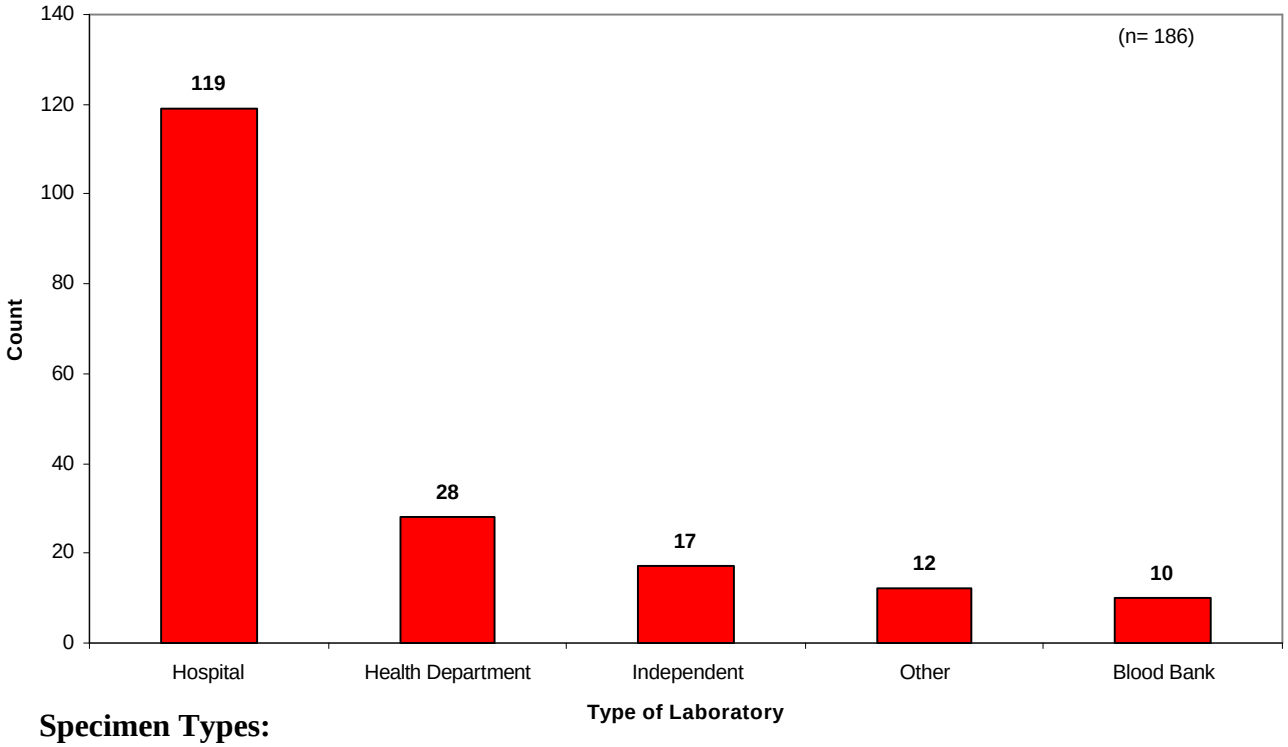


Table 2: Number of HIV Rapid Testing Participants in Countries outside the United States

n= 30

Country	Number	Country	Number
Australia	1	Philippines	2
Bahamas	1	Republic of Singapore	1
Belgium	1	Slovakia	1
Cote d'Ivoire	1	South Korea	1
Ghana	1	Sri Lanka	1
Honduras	1	Suriname	1
Hungary	1	Taiwan	2
India	2	Tanzania	1
Malaysia	1	Thailand	7
Nicaragua	1	Zimbabwe	1
Nigeria	1		

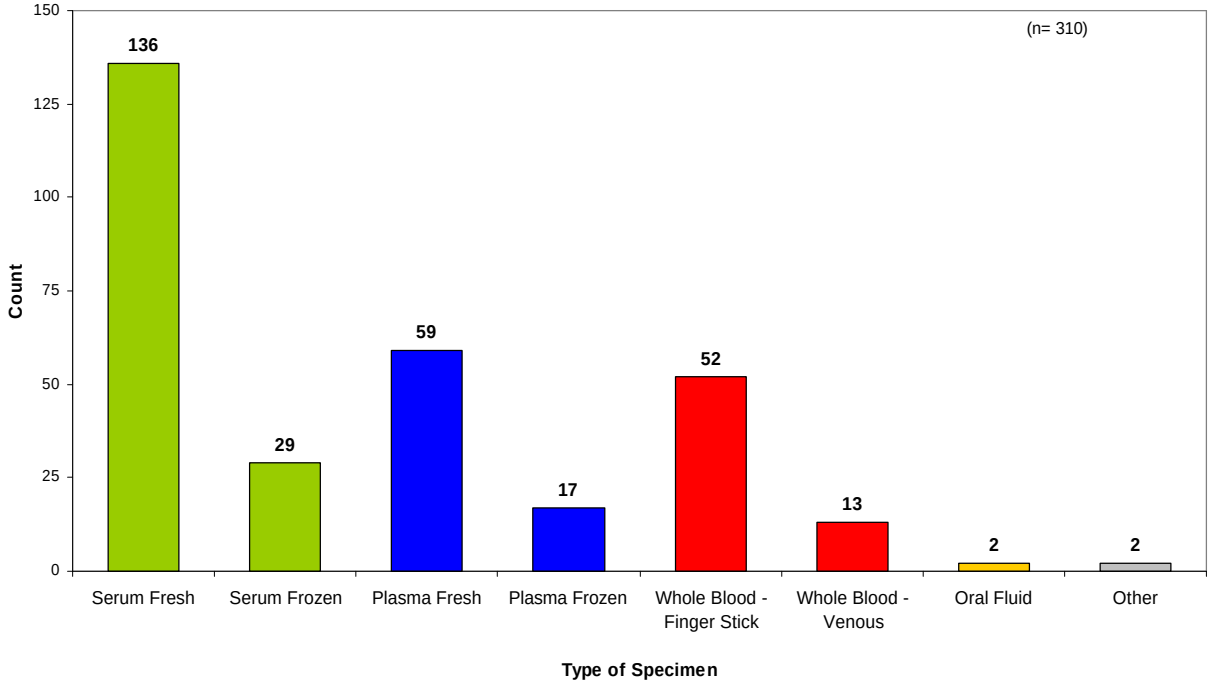
Figure 2: Type of Testing Site Participants



Specimen Types:

Most specimens typically used for HIV rapid testing were either serum or plasma, as shown in Figure 3. Testing sites could report using more than one specimen type. Testing sites that used the whole-blood finger stick specimens typically used the OraQuick Rapid HIV-1 Antibody Test testing method. Two U.S. labs reported using oral fluid specimens with the OraQuick test.

Figure 3: Specimen Types used by Participants



Kit types:

The predominant kit types used were OraQuick Rapid HIV-1 Ab (31.8%; 69/217), MedMira Reveal Rapid HIV (25.3%; 55/217) and Abbott/Murex SUDS (19.8%; 43/217) as shown in Figure 4. The SUDS test is no longer on the market. U.S. laboratories typically used FDA-approved kit types (97.6%; 166/170). Kit usage by lab type is shown in Figure 5.

Figure 4: Kit Types used by Participants

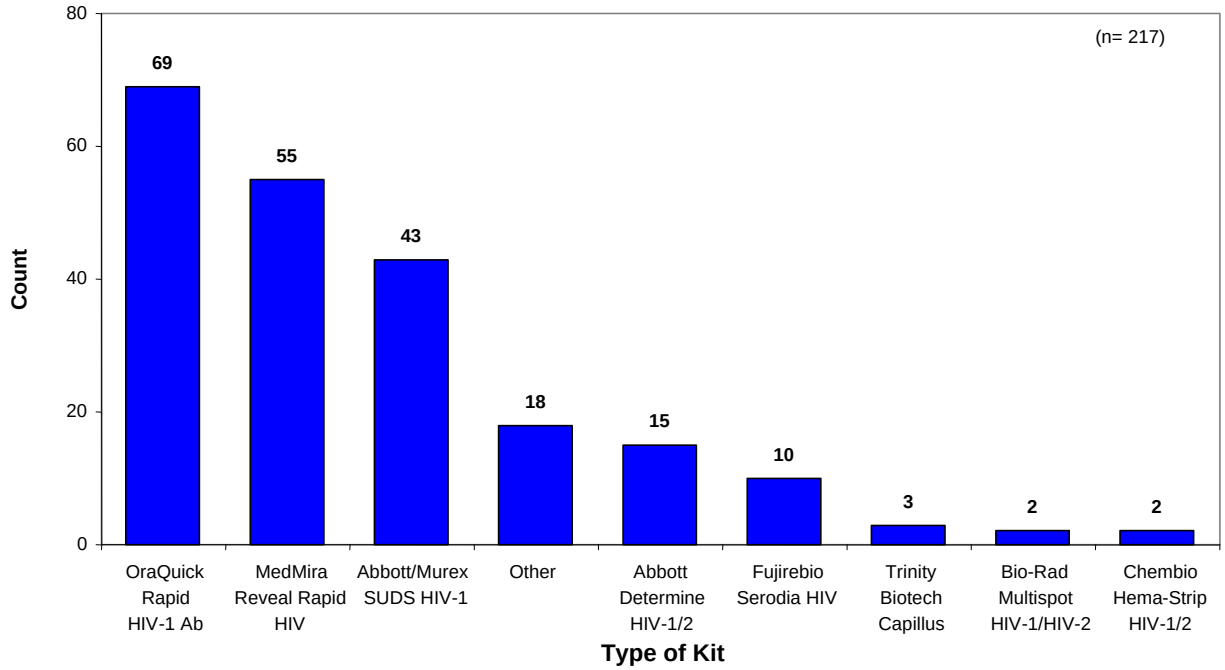
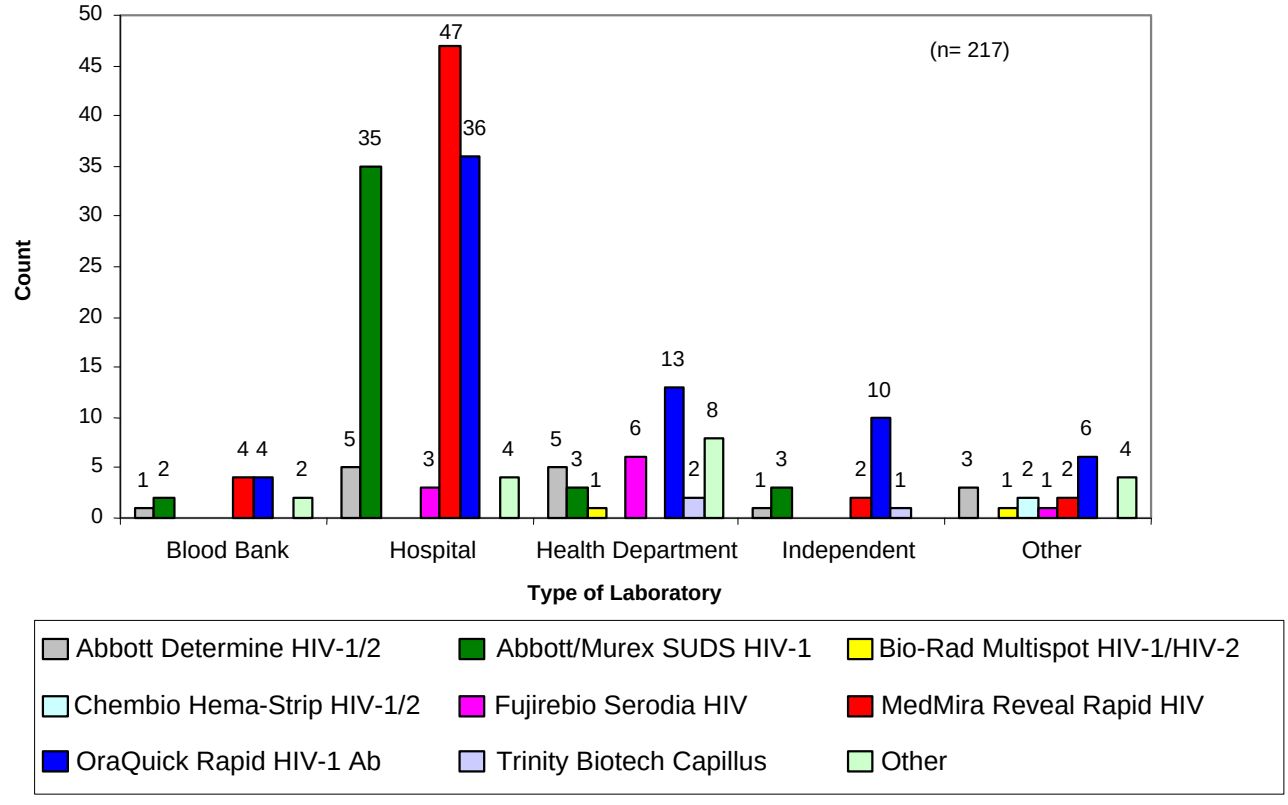


Figure 5: Kit Type by Lab Type



Performance:

The overall accuracy for HIV-antibody positive samples was 93.4%, but ranged from 82.3% to 100%. The accuracy by kit type was lowest for sites using the MedMira Reveal Rapid HIV test (82.3%; 177/215 determinations). This could have been partially due to matrix effects. Accuracy for positive samples was 100% for sites using several of the kit types, although in some cases numbers for individual kit types were low. The overall accuracy for the OraQuick Rapid HIV test was 98.5%. Table 3 shows the accuracy of HIV rapid tests by kit type. The overall accuracy of sites using HIV rapid tests for positive samples for all methods was 93.4% (82.3% - 100%). The overall accuracy reported for sites using EIA and testing the same set of positive and negative samples was 99.5% (2759/2772) and 99.1% (1358/1371), respectively.

Table 3: Accuracy for all samples

Kit Type	OraQuick Rapid HIV-1 Ab (401/407)	MedMira Reveal Rapid HIV (280/323)	Abbott/Murex SUDS HIV-1 (240/252)	Other Kit Type, Specified (102/105)	Abbott Determine HIV-1/2 (90/90)	Fujirebio Serodia HIV (60/60)	Bio-Rad Multispot HIV-1/HIV-2 (12/12)	Chembio Hema-Strip HIV-1/2 (12/12)	Trinity Biotech Capillus (9/10)	Total (1206/1271)
No. of Determinations	407	323	252	105	90	60	12	12	10	1271
Correct Positive Results	267	177	158	67	60	40	8	8	7	93.40% (792/848)
False Negative Results	4	37	8	3					1	53
Positive Indeterminates		1	2							3
Correct Negative Results	134	103	82	35	30	20	4	4	2	97.87% (414/423)
False Positive Results	2	5	1							8
Negative Indeterminates			1							1
Accuracy	98.53%	86.69%	95.24%	97.14%	100.00%	100.00%	100.00%	100.00%	90.00%	94.89% (1206/1271)

The overall accuracy for the weakest positive donor (Donor 3) was 87.6% as shown in Table 4. (Test kits for which less than 3 interpretations were reported were included in the other category for this analysis.)

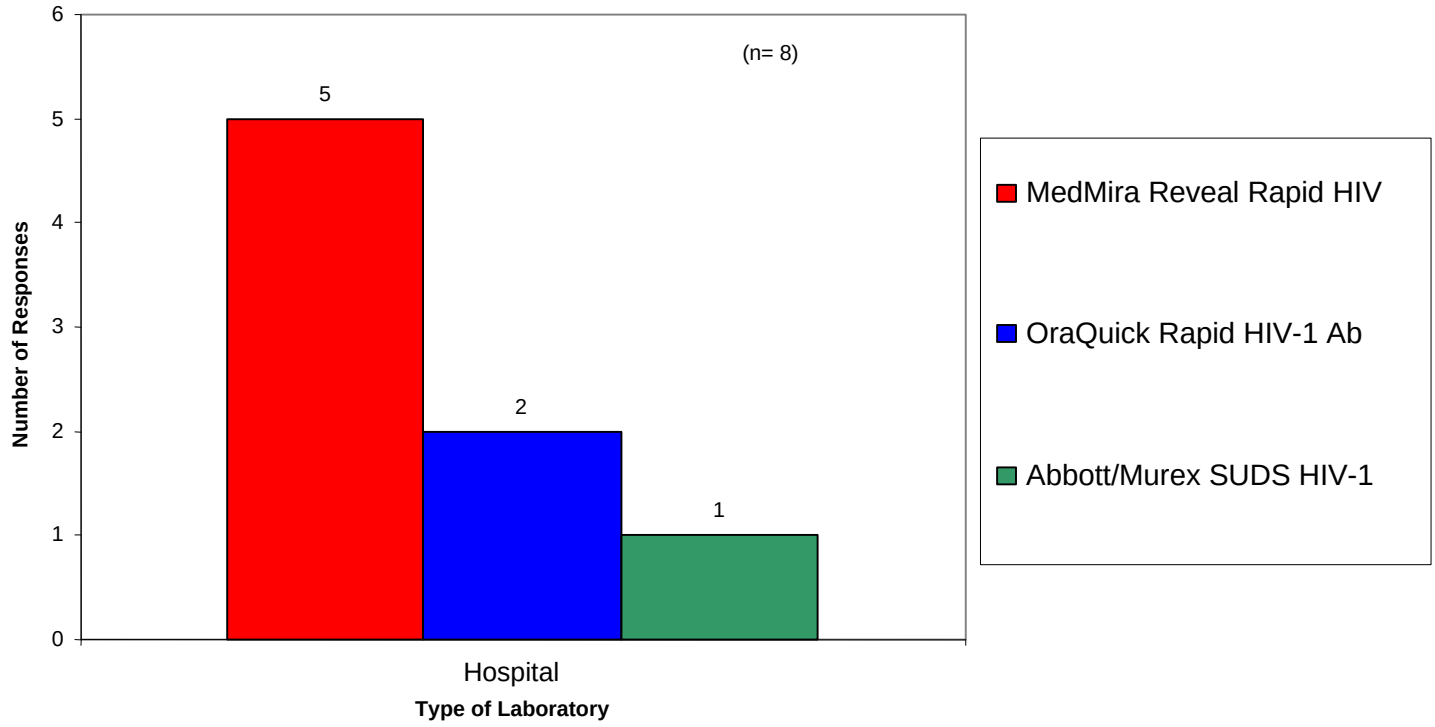
Table 4: Accuracy for weakest positive sample, Donor 3

Kit Type	OraQuick Rapid HIV-1 Ab (66/67)	MedMira Reveal Rapid HIV (30/53)	Abbott/Murex SUDS HIV-1 (42/42)	Other Kit Type, Specified (21/23)	Abbott Determine HIV-1/2 (15/15)	Fujirebio Serodia HIV (10/10)	Total (184/210)
No. of Determinations	67	53	42	23	15	10	210
Correct Positive Results	66	30	42	21	15	10	184
False Negative Results	1	22		2			25
Positive Indeterminates		1					1
Accuracy	98.51%	56.60%	100.00%	91.30%	100.00%	100.00%	87.62%

For Donor 3, the accuracy for sites using the MedMira Reveal test was 56.6%. The accuracy for sites using the OraQuick test for this donor was 98.5%. Accuracy could have been compromised due to matrix effects, as previously stated.

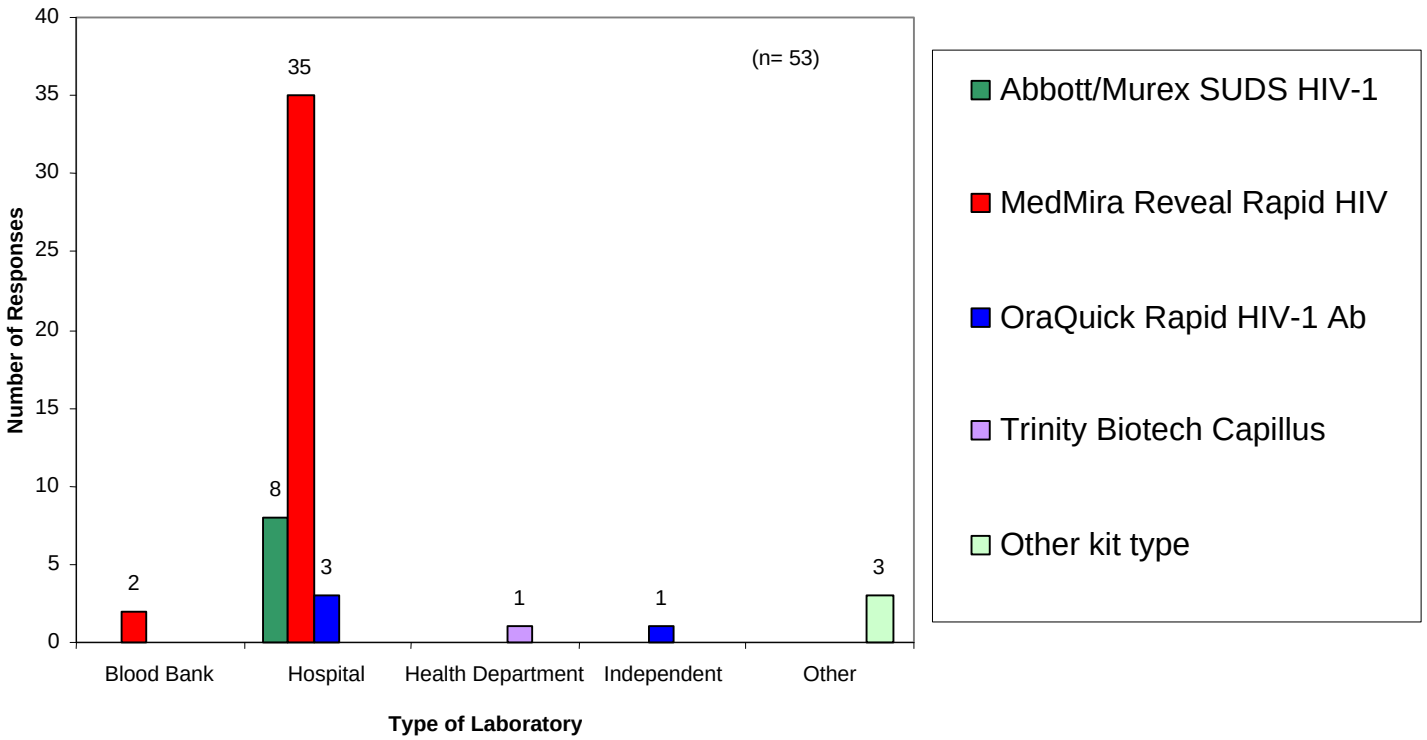
All 8 of the false positive results were reported by hospital testing sites (Figure 6) using FDA- approved test kits.

Figure 6: False Positive Results by Type of Laboratory and Type of Test Kit



False negative results are shown in Figure 7.

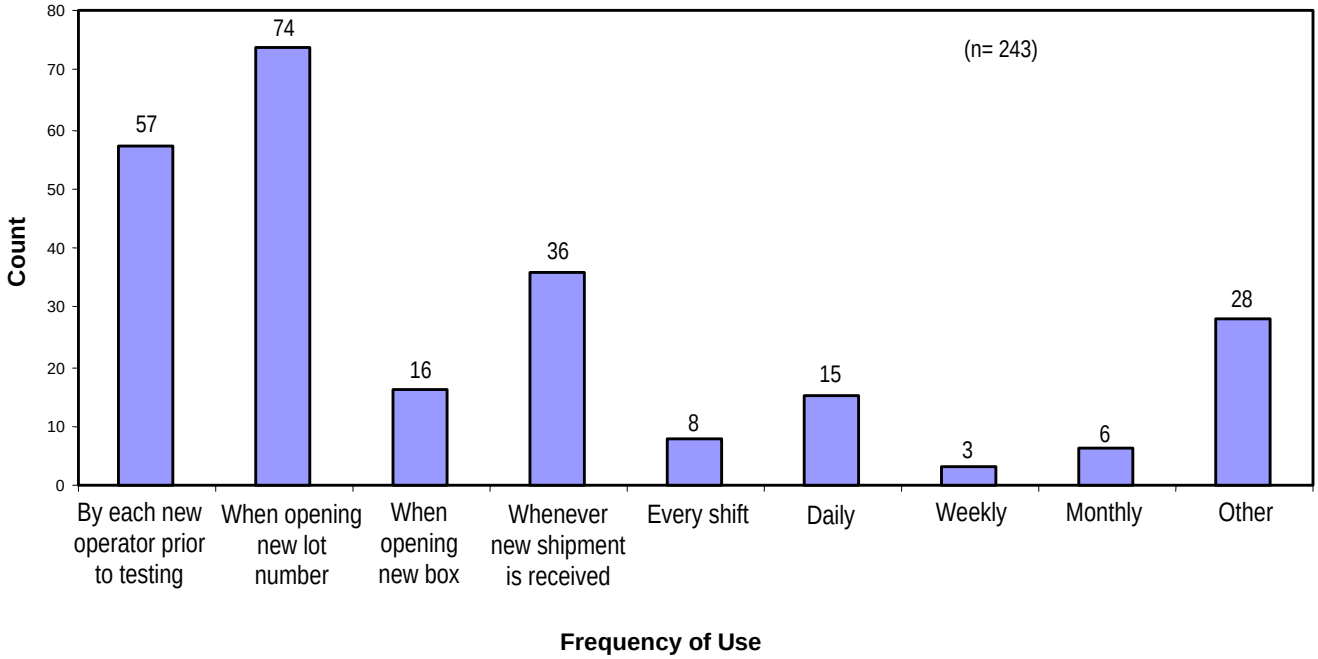
Figure 7: False Negative Results by Type of Laboratory and Type of Test Kit



Quality control:

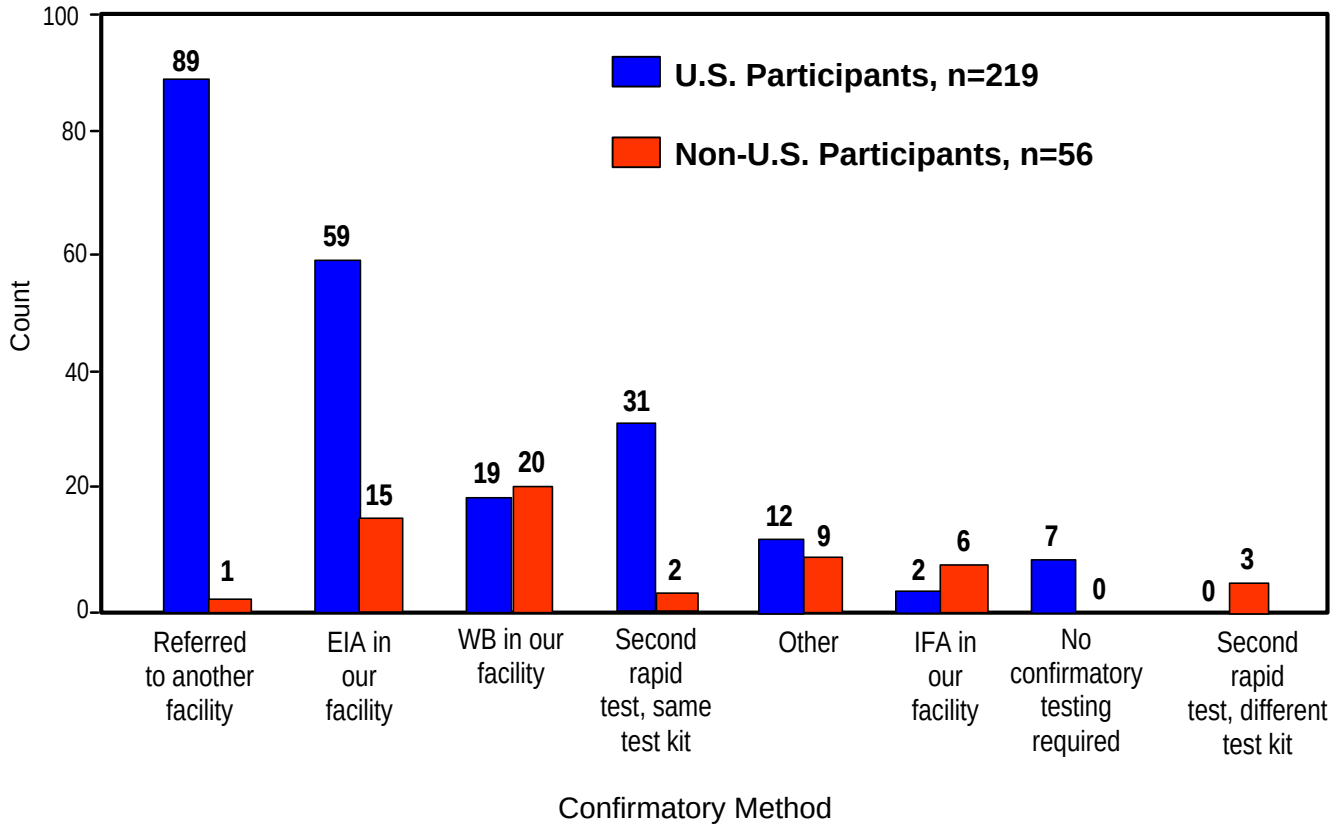
Testing sites were asked if they used external quality control, i.e., controls not included in the test kit, when performing HIV rapid tests. (Testing sites reporting the use of multiple kit types answered the question separately for each kit type.) About half (51.6%; 112/217) of the responses indicated the use of external quality control. The sources of the external controls tended to be controls obtained from the same manufacturer (130/174) or in-house controls (33/174). The frequency of use of external quality control materials is shown in Figure 8. Testing sites could provide more than one answer.

Figure 8: Frequency of Use of External Quality Control



Confirmatory testing:
The types of confirmatory testing reported by laboratories varied as shown in Figure 9. (Testing sites could answer by indicating more than one confirmatory test.) Many participants (32.4%; 61/188) reported either sending the reactive (or preliminary positive) specimens to another facility, or performing EIA in combination with other tests (39.4%; 74/188). Several participants (19.1%; 36/188) reported using a second rapid test for confirmatory testing. Of these, 15 (7.9%) reported using a second rapid test with no other type of confirmatory testing. Seven participants reported that no confirmatory testing was required prior to reporting a positive result. The circumstances surrounding the use of HIV rapid tests without confirmatory testing are unclear. The question may have been misinterpreted or ambiguous, however, most answers were reasonable.

Figure 9: Types of Confirmatory Testing Reported by Testing Sites



Conclusions and Discussion:

This report describes the results of the first HIV-R MPEP shipment. It represents a collection of data on HIV rapid tests done in the field by a variety of testing sites using different test kits on four plasma samples. Overall, HIV testing sites performed well in analyzing the challenge samples. However, accuracy was variable depending on the type of test kit used. Incorrect results, particularly false negative results, may have been affected by sample matrix effects with certain test kits. However, more false positive results were also reported by sites using some of those same test kits. Matrix effects would not necessarily explain this observation.

Test sites using the new OraQuick rapid test performed relatively well, but overall results were less accurate than overall composite results reported by laboratories testing the same plasma samples with EIA tests in the HIV-Ab MPEP program (98.5%, and 99.4%, respectively). (1)

Our survey included a question regarding confirmatory testing. The intent was to measure whether or not the testing sites require that confirmatory testing be done on preliminary positive (or reactive) samples before reporting a final "positive" result. The question could have been ambiguous to some respondents. However, most participants answered the question reasonably indicating a variety of confirmatory testing patterns. U.S. participants are reminded that HIV rapid tests are screening tests and reactive results are considered to be "preliminary positives" that must be confirmed by either a Western blot or IFA test. (2)

Testing sites should follow appropriate guidelines with respect to performing HIV rapid tests and reporting results. (2,3) Attention to recognized guidelines and good testing practices is crucial to patient safety and to the delivery of accurate test results. For example, the CDC has published quality assurance guidelines for testing using the OraQuick rapid test. (2) These guidelines stress that a testing site must have an adequate quality assurance (QA) program in place before offering OraQuick testing. The guidelines address recommendations for a comprehensive QA program including the organization and specifics of the QA program itself--testing personnel, process control, documents and records, and troubleshooting. The guidelines include recommendations regarding test verification to ensure that the test kits work as expected in a given testing environment, i.e. provide accurate results for a referenced panel of non-reactive, weakly reactive, and reactive specimens. It is also recommended that testing sites verify that the test kits are accurately detecting HIV-1 antibodies in positive and negative samples on a periodic basis by participating in an external quality control program, such as MPEP. Further, the guidelines address the logistics for providing confirmatory testing for preliminary positive (reactive) results. (2) Similar guidelines should be followed for other HIV rapid tests performed in U.S. sites.

References:

1. CDC MPEP. Human Immunodeficiency Virus Type 1 (HIV-1) Antibody Testing: Report of Results for the Performance Evaluation Survey, July 2003. http://www.phppo.cdc.gov/mpep/pdf/hiv/0307hiva.pdf

2. Quality Assurance Guidelines for Testing Using the OraQuick Rapid HIV-1 Antibody Test. Centers for Disease Control and Prevention, U.S. Department of Health and Human Services. 2003. http://www.cdc.gov/hiv/rapid_testing/materials/QA-Guide.htm

3. CDC. CDC revised guidelines for HIV counseling, testing, and referral. MMWR Recommendations and Reports. 2001; RR-19:50.