An Evaluation of Proficiency Testing by Laboratories Performing HIV Antibody Immunoassays

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Background

Under the Clinical Laboratory Improvement Amendment (CLIA) regulations, laboratories performing non-waived HIV antibody testing are required to participate in a proficiency testing (PT) program. Currently, ten PT programs for HIV antibody are CLIA-approved and five of them are active. Some of the PT programs have recently expanded to include rapid testing, even though some of the rapid tests are CLIA-waived. We were interested in reviewing the data available from PT programs to determine 1) the proportion of laboratories using the various non-waived test kits, 2) whether any performance problems were discernable, and 3) how the laboratories performed that reported results using rapid test methods.

Methods

Two data sources were used for this evaluation. One source was the PT participant summary reports for surveys conducted during 2004 by selected CLIA-approved PT providers. The second source was the Centers for Medicare & Medicaid Services (CMS) databases that contain the CLIA laboratory demographics [Online Survey Certification and Reporting (OSCAR) database] and the PT performance database that contains scores for HIV antibody performance reported by the PT providers to CMS. We extracted performance data from these two sources and calculated the rates of unacceptable results.

Results

In 2004, a total of 2356 laboratories were enrolled in PT for HIV antibody according to CMS statistics. Of these, 82% were hospital (1529) and independent (395) laboratories. An analysis of CMS data available over the 10 year period 1994-2004 indicated that the rates of PT event failure ranged from 1% to 6% per year (failure is defined as a score of less than 80% correct results for a survey event and includes scores of 0% for failing to participate).

An evaluation of PT summary reports from the individual providers for surveys conducted during 2004, showed that

- the most common EIA test system used was the Abbott HIV-1/2 recombinant method,
- in the College of American Pathologists' surveys (the program with the largest enrollment), the majority of laboratories performing both the HIV-1 and HIV-1/2 EIA test methods (non-rapid) demonstrated error rates of less than 1%, and
- Performance using rapid tests showed a relatively high rate of invalid results (up to 22% in some surveys) with false-positive and false-negative rates ranging from 0 to 10%, varying by survey provider. These results with rapid testing are most likely due to the composition of the challenge samples, some of which were diluted serum (matrix effects).

CLIA-approved PT Programs for HIV Antibody Testing

1. Accutest, Inc.*
2. American Association of Bioanalysts (AAB)
3. American Association of Family Physicians (AAFP)*
4. American Proficiency Institute (API)
5. College of American Pathologists (CAP)
6. Medical Laboratory Evaluation (MLE)*
7. New Jersey Dept. of Health and Senior Services*
8. New York State Dept of Health
9. Puerto Rico Dept of Health*
10. Wisconsin State Laboratory of Hygiene

* Programs approved by CMS, but either inactive or limited participation.

Laboratories Enrolled in HIV Antibody PT Programs - 2004

Lab Type*	Number	Percent
Hospital	1529	65%
Independent	395	17%
Physician Office	70	3%
Blood bank	51	2%
Community clinic	37	2%
Ancillary test site	26	1%
All others	248	10%
Total	2356	

* Self-reported laboratory types; data extracted from CMS database (OSCAR); public health laboratories were not designated.

Summary of Rapid HIV PT Results - 2004

Program/Date/ Samples	Mnf. Kit	Total Results	False Pos	Ind/Invalid	False Neg	% FP	% FN	% Ind.
AAB								
Jan-04 (Serum)	MedMira	170	1/68	2/170	10/102	1.5%	9.8%	1.2%
*Saline Diluted	OraQuick	333	2/121	43/333	0	1.7%	0.0%	12.9%
Apr-04 (Serum)	MedMira	155	0	3/155	0	0.0%	0.0%	1.9%
*Saline Diluted	OraQuick	398	0	62/398	0	0.0%	0.0%	15.6%
Oct-04 (Serum)	MedMira	155	0	7/155	5/93	0.0%	5.4%	4.5%
*Saline Diluted	OraQuick	359	3/137	79/359	2/222	2.2%	0.9%	22.0%
	Trinity	35	0	3/35	0	0.0%	0.0%	8.6%
API								
Mar-04 (Serum)	MedMira	139	2/55	0	1/84	3.6%	1.2%	0.0%
	OraQuick	314	9/188	0	0	4.8%	0.0%	0.0%
Jun-04 (Serum)	MedMira	167	0	0	0	0.0%	0.0%	0.0%
	OraQuick	369	11/215	0	0	5.1%	0.0%	0.0%
	Trinity	20	0	0	0	0.0%	0.0%	0.0%
Oct-04 (Serum)	MedMira	204	0	0	1/123	0.0%	0.8%	0.0%
	OraQuick	335	0	0	0	0.0%	0.0%	0.0%
	Trinity	55	0	0	0	0.0%	0.0%	0.0%
CAP RHIV								
Feb-04 (Plasma)	MedMira	2429	1/1457	0	2/972	0.1%	0.2%	0.0%
	OraQuick	530	0	0	0	0.0%	0.0%	0.0%
May-04 (Plasma)	MedMira	2764	8/1658	0	3/1106	0.5%	0.3%	0.0%
	OraQuick	575	5/345	0	0	1.4%	0.0%	0.0%
Sep-04 (Plasma)	MedMira	2569	1/1545	0	4/1024	0.1%	0.4%	0.0%
	OraQuick	653	3/392	0	3/261	0.8%	1.1%	0.0%
	Abbott	10	0	0	0	0.0%	0.0%	0.0%
	Trinity	115	0	0	0	0.0%	0.0%	0.0%
CAP RHIVW								
May-04 (Plasma)	OraQuick	586	2/293	0	1/293	0.7%	0.3%	0.0%
Sep-04 (Plasma)	OraQuick	618	0	0	0	0.0%	0.0%	0.0%
	Trinity	28	0	0	0	0.0%	0.0%	0.0%
NY State								
Jan-04 (Serum)	MedMira	165	0	0	0	0.0%	0.0%	0.0%
	OraQuick	305	0	0	0	0.0%	0.0%	0.0%
May-04 (Serum)	MedMira	170	0	0	0	0.0%	0.0%	0.0%
	OraQuick	320	0	0	0	0.0%	0.0%	0.0%
Sep-04 (Serum)	MedMira	170	0	0	0	0.0%	0.0%	0.0%
	OraQuick	355	0	0	0	0.0%	0.0%	0.0%
Wisconsin								
Jan-04 (Plasma)	MedMira	880	6/351	0	6/529	1.7%	1.1%	0.0%
	OraQuick	275	1/110	0	1/165	0.9%	0.6%	0.0%

Highlights of 2004 PT Results for Rapid HIV

- Six PT programs were available for rapid HIV testing.
- One program provided saline diluted serum challenge samples, resulting in a high rate of invalid results.
- Other programs provided serum or plasma samples with no invalid results, but some false-positive (FP) and false-negative (FN) results.
- The CAP offers a program specifically for waived rapid testing.

Summary of CAP* 2004 PT Survey Results For Anti-HIV EIA (Viral Marker Program)

	Total Results	FP	FN	%FP	%FN
Anti-HIV-1 EIA					
Rapid	3991	101/2660	27/1331	3.8%	2.0%
Recombinant	954	0	1/317	0.0%	0.3%
Synthetic	150	0	1/50	0.0%	2.0%
Viral Lysate	2132	2/1414	0	0.1%	0.0%
Anti- HIV-1/2 EIA					
Rapid	165	1/111	0	0.9%	0.0%
Recombinant	12224	12/8142	10/4082	0.1%	0.2%
Synthetic	1869	2/1242	3/627	0.2%	0.5%
Viral Lysate	590	0	0	0.0%	0.0%
Anti-HIV- 2 EIA					
Viral Lysate	273	0	14/73	0.0%	19.2%

* College of American Pathologists; CAP is the largest PT provider for anti -HIV testing

Summary of 2004 CAP Survey Results For Anti-HIV-1 EIA by Kit Type

Manufacturer	Anti-HIV-1 Kit Types*	Total Results	FP	FN	%FP	%FN
Abbott	Rapid	283	12/189	1/94	6.3%	1.1%
	Recombinant	67	0	0	0.0%	0.0%
	Viral Lysate	15	0	0	0.0%	0.0%
Biomerieux	Rapid	50	1/34	0	2.9%	0.0%
	Recombinant	80	0	0	0.0%	0.0%
	Synthetic Based	15	0	0	0.0%	0.0%
	Viral Lysate	1793	2/1191	0	0.2%	0.0%
Bio-Rad/Genetic Systems	Rapid	5	0	0	0.1%	0.0%
	Recombinant	659	0	1/220	0.0%	0.5%
	Viral Lysate	135	0	0	0.0%	0.0%
	Synthetic Based	5	0	0	0.0%	0.0%
Calypte/Campbridge	Rapid	10	0	0	0.0%	0.0%
Diamedix	Viral Lystate	5	0	0	0.0%	0.0%
Lab Prepared/In-House	Recombinant	10	0	0	0.0%	0.0%
Murex Diagnostics	Rapid	239	2/154	2/85	1.3%	2.4%
	Synthetic Based	5	0	0	0.0%	0.0%
Orasure Technologies	Rapid	2407	81/1611	1/796	5.0%	0.1%
Organics	Recombinant	20	0	0	0.0%	0.0%
Sanofi Diag Pasteur	Recombinant	69	0	0	0.0%	0.0%
	Viral Lystate	10	0	0	0.0%	0.0%

* CAP summary reports did not designate test kits by name.

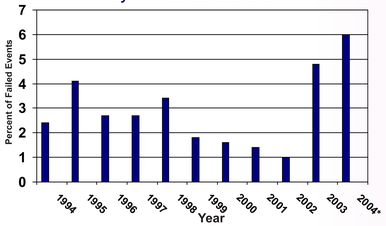
Summary of 2004 CAP Survey Results for Anti-HIV-1/2 EIA by Kit Type

Manufacturer	Anti-HIV-1/2 EIA Kit Types	Total Results	FP	FN	%FP	%FN
Abbott	Rapid	110	0	0	0.0%	0.0%
	Recombinant	11275	12/7507	10/3768	0.2%	0.3%
	Synthetic	45	0	0	0.0%	0.0%
	Viral Lysate	585	0	0	0.0%	0.0%
Abbott AXSYM	Recombinant	530	0	0	0.0%	0.0%
	Synthetic	5	0	0	0.0%	0.0%
Behring Diagnostics	Recombinant	45	0	0	0.0%	0.0%
Biomeriuex	Recombinant	35	0	0	0.0%	0.0%
	Synthetic	35	0	0	0.0%	0.0%
Bio-Rad/Genetic Systems	Rapid	10	0	0	0.0%	0.0%
	Recombinant	180	0	0	0.0%	0.0%
	Synthetic	1600	1/1061	2/539	0.1%	0.4%
	Viral Lysate	5	0	0	0.0%	0.0%
Diasorin	Synthetic	30	0	0	0.0%	0.0%
	Recombinant	5	0	0	0.0%	0.0%
Murex Diagnostics	Synthetic	20	0	0	0.0%	0.0%
	Recombinant	5	1/3	0	33.3%	0.0%
Orasure Technologies	Rapid	15	1/10	0	10.0%	0.0%
Organics	Recombinant	10	0	0	0.0%	0.0%
Ortho	Recombinant	55	0	0	0.0%	0.0%
	Synthetic	10	0	0	0.0%	0.0%
	Rapid	5	0	0	0.0%	0.0%
Roche	Recombinant	35	0	0	0.0%	0.0%
Sanofi Diag Pasteur	Recombinant	25	0	0	0.0%	0.0%
	Synthetic	49	0	0	0.0%	0.0%

Highlights of 2004 CAP Viral Marker Program Results for Anti-HIV EIA Testing

- Based on the number of total results, the most popular EIA test was the Abbott recombinant anti-HIV-1/2.
- Some rapid test users participated in the 2004 CAP Viral Marker survey.
- Compared with the solid phase EIAs, laboratories using rapid tests reported a higher rate of FP and FN results.
- Some of these erroneous results with rapid tests may have been due to matrix effects.

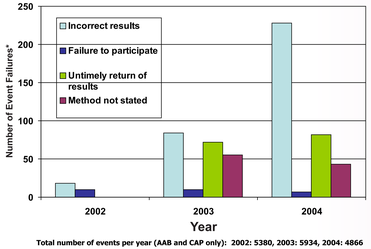
PT Failure Rates for Anti-HIV Testing Reported By PT Providers to CMS



* Failure is defined as scoring less than 80% in one survey event (this includes scores of 0% for failing to participate or sending results after the cut off date); each event includes 5 challenges and there are 3 events per year per laboratory; total number of events per year ranged from 4654 in 1994 to a maximum of 7828 in 2003.

* 2004 data not yet finalized

Reasons for Anti-HIV PT Failures Reported by AAB and CAP to CMS: Comparison of 2002 - 2004



Total number of events per year (AAB and CAP only): 2002: 5380, 2003: 5934, 2004: 4866

*Failure is defined as a score of less than 80% (with 5 challenges/survey, failure = score of 0%-60%)

Conclusions

Proficiency testing results provide a data source for evaluating trends in the use of various commercially available test kits and laboratory performance over time. A review of the 2004 PT program summary reports and performance score data submitted to CMS from 1994-2004 reveals changes that reflect:

- the introduction of new technology, such as rapid testing,
- the use of manipulated (e.g., diluted) samples that do not behave the same way in all test kits, and
- an increase in failures in 2003 and 2004 due to submission of incorrect results, as well as administrative errors such as untimely results reporting and failure to identify the test method.

As immunoassay technology changes, PT providers need to be aware that challenge samples acceptable for one type of method may not be acceptable for others (matrix effects). PT providers should resolve these issues to differentiate between poor performance and problems due to the PT samples. Also, laboratories need to be aware that submitting results late or providing incomplete information can result in PT failure.

Resources for Further Information

1. CLSI*. Using Proficiency Testing to Improve the Clinical Laboratory; Approved Guideline, CLSI document GP27-A. CLSI, 940 West Valley Road, Suite 1400, Wayne, PA 19807-1898, 2002.
2. CLSI. Evaluation of Matrix Effects; Approved Guideline-Second Edition, CLSI document EP14-A2. CLSI, 940 West Valley Road, Suite 1400, Wayne, PA 19807-1898, 2005.

*CLSI is the Clinical and Laboratory Standards Institute, formerly NCCLS.