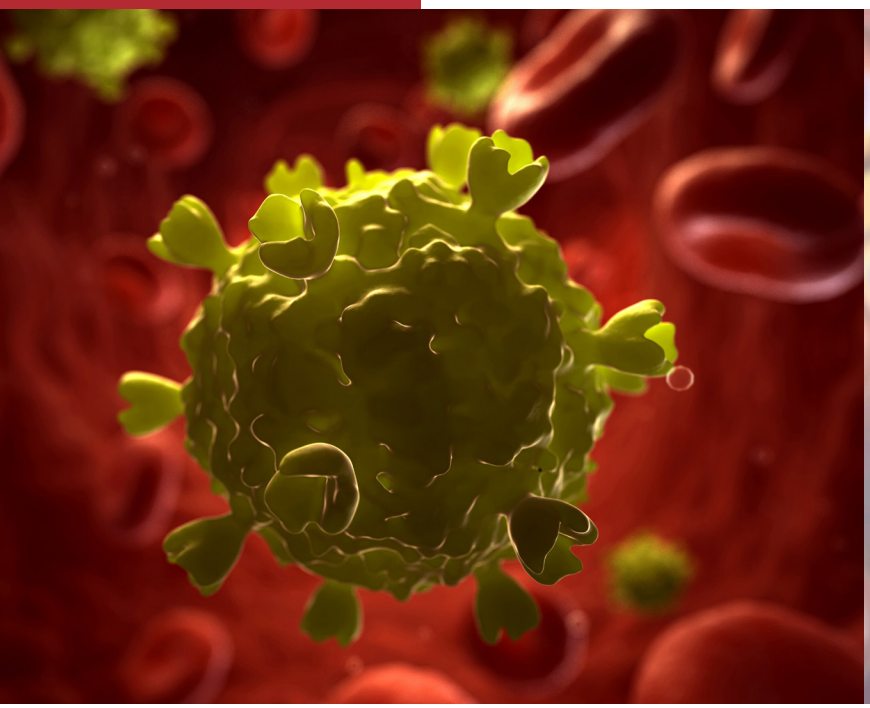
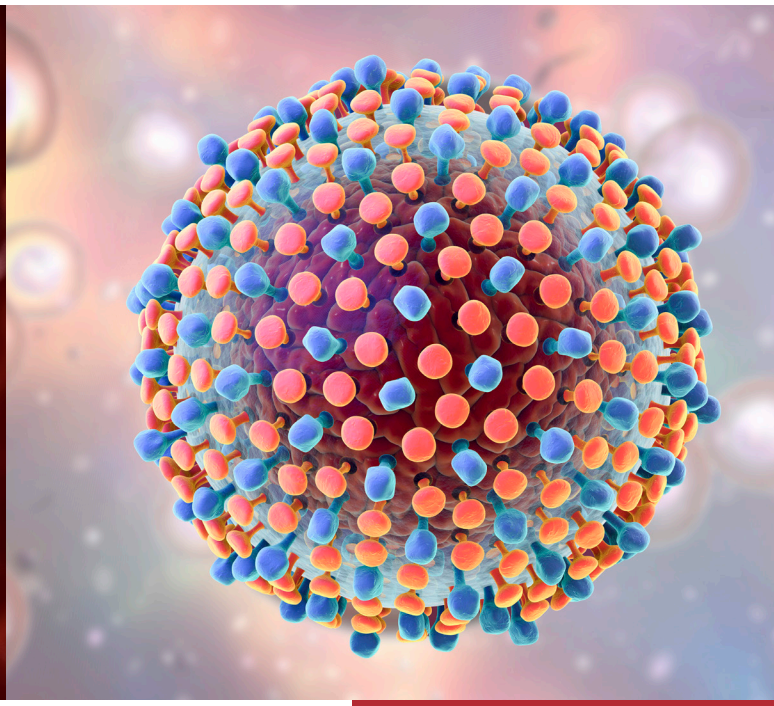
2017 HIV AND HCV DIAGNOSTICS SURVEY REPORT





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APHL ASSOCIATION OF PUBLIC HEALTH LABORATORIES®

Table of Contents

Background 3

Methods 3

Workforce 3

HIV Assay Utilization 4

Turnaround Time 6

Testing Volume and Specimen Types 7

Testing Volume Trends 7

HIV Infections Detected 9

Confirmation of Rapid Reactive Specimens 10

Trends in Oral Fluid Testing 11

Planned Changes To HIV Testing 11

Outreach, Training, Education on the Recommended Laboratory Testing Algorithm 12

On the Horizon—New HIV Testing Technology 13

Reimbursement Methods 13

Testing for HCV 14

Discussion 16

References 17

Acknowledgments 18

Background

The Association of Public Health Laboratories (APHL) periodically surveys its public health laboratory (PHL) members to assess their HIV and HCV diagnostic testing capabilities, capacities, and practices.

The goal of APHL's 2017 survey was to determine current practices of HIV and hepatitis C virus (HCV) testing in US PHLs, including 1) implementation and impediments to implementation of the HIV Laboratory Diagnostic Testing Algorithm,[1] 2) use of new and emerging assays, and 3) opportunities for providing additional support for testing. Survey findings will guide APHL's education and technical assistance activities, and inform policy development and advocacy.

Methods

APHL fielded its sixth survey using a 28-question online tool created by the APHL HIV and Viral Hepatitis Subcommittee and administered through Qualtrics®, a web-based survey instrument. APHL fielded the survey to all 106 member-institutions, including 55 state and 51 local PHLs between March and May 2018. The survey requested data on HIV and HCV testing capacity and practices from January 1, 2017 through December 31, 2017; therefore, all responses are for this period, unless otherwise indicated. Overall, 76% (81) of PHLs completed the survey, 89% (49) of state PHLs, and 63% (32) of local PHLs. Of the 81 respondents, 16 laboratories indicated one of four reasons for not performing HIV testing: 1) have never (or not in many years) performed HIV testing (n=6), 2) the laboratory no longer performs HIV testing due to the submitter switching to rapid/point of care testing (n=4) 3) the laboratory has stopped testing due to cost (n=4) or 4) no information was provided. Of note, two of the 16 PHLs that did not perform HIV testing did offer HCV testing. Table 1 summarizes the HIV and HCV testing practices reported by the responding laboratories.

Table 1: HIV and HCV Testing Practices in 2017

	State (n=49)	Local (n=32)	Total (n=81)
Performed HIV Testing in 2017	44	21	65
Percentage of PHLs with HIV Testing	*90%*	*66%*	*81%*
Performed HCV Testing in 2017	32	12	44
Percentage of PHLs with HCV Testing	*65%*	*38%*	*54%*
Performed HIV and HCV Testing in 2017	31	11	42
Percentage of PHLs with HIV & HCV Testing	*65%*	*38%*	*52%*

Historically, APHL has surveyed member PHLs approximately every three years, beginning in 2003. Survey questions requested data on HIV Diagnostic Practices for a one-year period. In 2014, APHL added questions about HCV testing practices to the surveys. Data from the current survey was compared to four previous HIV surveys conducted by APHL (2005, 2008, 2011, and 2014).[2–5] The 2003 dataset did not include local PHL responses, is limited in scope and was therefore not used for comparisons. In making comparisons across surveys (2005-2014), analysis of testing practices (e.g. test kit usage) using all survey responses was performed, unless otherwise noted. In order to properly evaluate trends in workforce, testing volume and other testing trends, data were compiled for the subset of PHLs (n=34, (three local and31 state PHLs) that completed the prior surveys (2005-2014).

Workforce

APHL requested laboratories indicate the number of full-time equivalents (FTEs) that perform HIV testing. Among the 65 PHLs, performing HIV Testing in 2017, the average number of FTEs was 2.2 with a range of 0.15 to 11. The average number of FTEs at state PHLs (n=44) was 1.9 with a range of 0.15 to 7 while at the local PHLs (n=21) it was 2.3 with a range of 0.2-11 FTEs. The average number of FTEs dedicated to perform HIV testing in PHLs decreased from 2.9 (in 2008 and 2011) to 2.7 (2014) and 2.5 in 2017 based on the subset of 34 PHLs that have responded to all surveys.

HIV Assay Utilization

As the HIV assay market continues to evolve so too does the utilization of those assays. The HIV Laboratory Diagnostic Testing Algorithm[1] recommends initial testing with an antigen/antibody immunoassay (Ag/Ab IA). Recent updates from CDC provide guidance for utilization of the Alere Determine™ HIV-1/2 Ag/Ab Rapid Test in this first step for serum and plasma specimens, though instrumented Ag/Ab IAs are preferred.[6–8] If the Ag/Ab IA is reactive, the next step is to conduct supplemental testing with an HIV-1/HIV-2 antibody differentiation IA. Specimens with a negative or indeterminate result by the antibody differentiation IA should be tested with a nucleic acid test (NAT). As of 2017, 58 PHLs (18 local and 40 state) follow the recommended algorithm, including two PHLs that are utilizing the Alere Determine™ HIV-1/2 Ag/Ab Rapid Test as the first step in the algorithm for screening serum and/or plasma. This algorithm allows for the identification of acute and established HIV infections. Acute HIV-1 infection, the period between first detection of viral markers (RNA, DNA or p24) and when IgG antibodies can be reliably detected in blood, generally coincides with peak viremia and the greatest infectious risk to others.[1] Identification of acute HIV-1 infection is critical because the risk of HIV-1 transmission from persons with acute and early infection is much higher than that from persons with established infections.[9–12]

Screening Immunoassay

In 2017, of the 65 PHLs performing HIV testing, 63 PHLs reported HIV screening as part of their HIV testing activities. Of these 62 PHLs, 59 (94%) used an Ag/Ab IA for their initial test while three (5%) used an antibody immunoassay (Table 2). Two of the three laboratories that reported using the Alere Determine (trademark) HIV-1/2 Ag/Ab Combo (Rapid) used it to screen serum or plasma while the third used it in a CLIA-waived setting on fingerstick wholeblood.

Supplemental Antibody Assay

Since the last survey in 2014, the only FDA-approved HIV-1/HIV-2 antibody differentiation IA switched from the Multispot HIV-1/HIV-2 Rapid test (discontinued December 2016) to the Geenius™ HIV-1/2 Supplemental Assay.[13] The 2017 survey responses reflect the transition:

- 57 (90%) PHLs (19 local and 38 state) implemented Geenius™ HIV-1/2 Supplemental Assay
- 1 (2%) PHL utilized the HIV-1 western blot (WB)*
- 5 (8%) PHLs referred specimens to another laboratory for supplemental testing†

* This PHL indicated elsewhere in the survey that they plan to validate the Geenius™ HIV-1/2 Supplemental Assay by December 31, 2018.
† Anecdotally we know that this is due to a combination of low-test volume and costs associated with the assay

Table 2: Summary of HIV Immunoassay Utilization by PHLs for Screening[a,b]

Type of Assay	Name of Immunoassay	2005 (n=60)	2008 (n=52)	2011 (n=60)	2014 (n=70)	2017 (n=63)
Ag/Ab IA	Abbott Architect® HIV Ag/Ab			9 (15%)	17 (24%)	26 (41%)
	Alere Determine™ HIV-1/2 Ag/Ab Combo (Rapid)				1 (1%)	3 (5%)
	Bio-Rad GS HIV Combo Ag/Ab EIA			4 (7%)	28 (40%)	25 (40%)
	Bio-Rad BioPlex® 2200 HIV Ag-Ab					5 (8%)[c]
Subtotal		**n/a**	**n/a**	**13 (21.6%)**	**46 (66%)**	**59 (94%)**
Laboratory-based Ab IA	Bio-Rad GS HIV-1/HIV-2 Plus O EIA	9 (15%)	39 (75%)	36 (60%)	15 (21%)	2 (3%)
	Abbott HIV AB HIV 1/2	7 (12%)	2 (4%)	1 (2%)		
	ADVIA Centaur® HIV 1/O/2 Enhanced		3 (6%)	3 (5%)	3 (4%)	1 (2%)
	Ortho VITROS® Anti-HIV 1+2 Immunoassay			2 (3%)	2 (3%)	
	Bio-Rad Plus rLAV EIA	7 (12%)	5 (10%)			
	Avioq HIV-1 Microelisa			4 (7%)	3 (4%)	
	bioMerieux Vironostika HIV-1	37 (62%)				
Subtotal		**60 (100%)**	**49 (94%)**	**46 (76.6%)**	**23 (33%)**	**3 (5%)**
Rapid Ab IA	Uni-Gold™ Recombigen HIV			1 (2%)		1 (2%)
	Clearview® STAT PAK Assay		2 (4%)		1 (1%)	
	OraQuick ADVANCE®		1 (2%)			
Subtotal		**0 (0%)**	**3 (6%)**	**1 (2%)**	**1 (1%)**	**1 (2%)**

a. Number of laboratories using each assay (% of total). b. Some PHL only perform supplemental testing only and do not perform screening with an immunoassay. c. Two PHLs use to screen serum and/or plasma as part of the HIV Laboratory Algorithm, one PHL uses as a CLIA-waived test on fingerstick wholeblood.

Supplemental HIV-1 Nucleic Acid Assay

HIV-1 NAT should be performed on specimens that were reactive on the Ag/Ab IA or Ab IA and were negative or indeterminate on the HIV-1/HIV-2 antibody differentiation immunoassay. This test is critical to identify potentially acute HIV-1 infections but is only necessary for a small number of specimens and is prohibitively expensive for all PHLs to have available in-house.

- 21 (32%) PHLs (9 local and 12 state) perform HIV-1 NAT in-house
- 41 (65%) PHLs (12 local and 29 state) refer HIV-1 NAT to another laboratory
- 3 (4.6%) PHLs (three state) do not offer HIV-1 NAT

The in-house availability of HIV-1 NAT remained consistent with 21 respondents in the last three surveys, with the percentage of respondents varying slightly by year: 32% in 2017, 28% in 2014 and 32% in 2011. The number of laboratories that are referring specimens to other laboratories for HIV-1 NAT continues to increase from 34% (15 of 44) in 2011 to 62% (33 of 53) in 2014 and 65% (41 of 65) in 2017. Two of the three PHLs that do not offer HIV-1 NAT offered very limited HIV testing in 2017, one offered only oral fluid testing, one offered only confirmation of preliminary positives, and the third PHL recommended additional testing outside the PHL.

Table 3: In-House HIV-1 NAT Testing Practices

	# of PHLs	Percentage
What specimen types are accepted? (n=21)		
Serum and Plasma	9	43%
Serum Only	6	29%
Plasma Only	4	19%
Whole Blood Only	1	5%
Serum, Plasma and Dried Blood Spot	1	5%
What reason(s) are HIV-1 NAT performed?[a]		
Diagnosis/Detection of Acute HIV-1	20	95%
Clinical Management/Viral Load	12	57%
Infant Diagnosis	6	29%
Supplemental test to confirm HIV-1 p24 Ag[b]	7[c]	33%
What type of HIV-1 NAT is performed?[d]		
Qualitative	13	62%
Quantitative	7	33%

a. Respondents could select more than one response. b. The question noted that this would apply for a situation where the only result from the initial screening test was HIV-1 Ag only, which is a result from the Alere Determine™ HIV-1/2 and the BioPlex® 2200 HIV Ag-Ab Assay.
c. Only three of the seven laboratories that reported this result use a screening assay that has an HIV-1 Ag only result. It is possible they receive specimens from an outside submitter that uses one of these assays. d. Respondents could select more than one response.

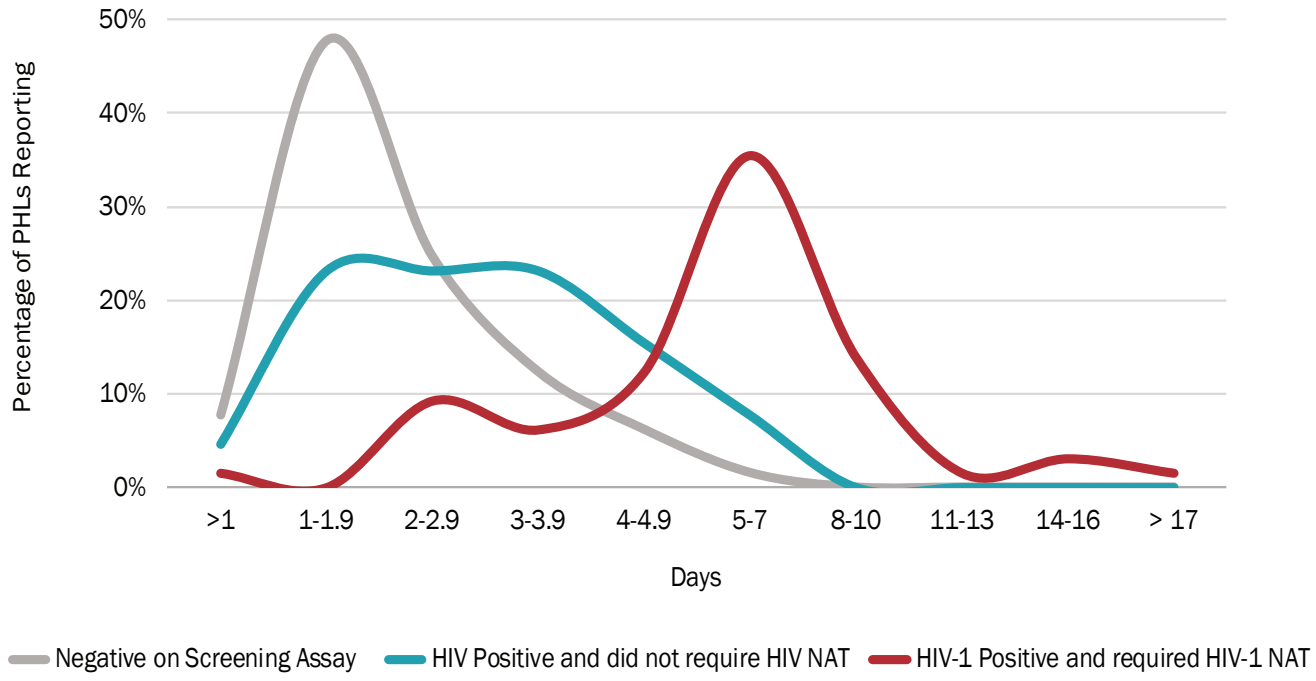
In 2017, of the 41 laboratories that referred specimens, 38 (93%) sent them to another PHL, two (5%) sent them to a commercial laboratory, and one referred to a clinical laboratory. Of the 38 (93%) laboratories that refer to another PHL, 28 (74%) utilize the APHL NAT Referral Project directly and an additional two local PHLs refer to their state PHL which participates in the project. The APHL NAT Referral Project remains an essential resource and is critical to maintaining PHL capacity for conducting the complete laboratory algorithm for HIV diagnosis.

- 38 (93%) refer to another PHL
  - 28 (74%) utilize the APHL NAT Referral Project
  - 1 (3%) refer to CDC
  - 9 (24%) refer to another PHL
- 2 (5%) refer to a commercial laboratory
- 1 (2%) refer to a clinical laboratory or hospital laboratory

Turnaround Time

Respondents provided the average turnaround time (TAT) in days from specimen receipt to reporting results for specimens that were a) HIV negative on their screening assay b) HIV positive and did not require HIV-1 NAT and c) HIV-1 Positive and required HIV-1 NAT (Figure 1). For the 65 PHLs performing HIV testing, the shortest average TAT was 1.81 days (median and mode of one day) for specimens that were HIV negative on the screening assay. The turnaround time for HIV positive specimens not requiring HIV-1 NAT was slightly longer on average, 2.62 days (median and mode 2 days) than the TAT for HIV negative specimens. Specimens that were ultimately HIV-1 positive and required HIV-1 NAT had the longest turnaround time, an average of 6.37 days (median 6 days and mode 7 days). Analyzing laboratories that perform HIV-1 NAT in-house (n=21) the TAT for HIV-1 positive specimens that required HIV-1 NAT was on average 4.53 days.

Figure 1: Average Turnaround Time for PHLs reporting, by days (n=65)



Testing Volume and Specimen Types

In 2017, the total number of specimens received for HIV testing by the 65 PHLs performing HIV testing was 1,133,772. The median number of specimens received per laboratory was 6,500 with a range of 29 to 197,878. The majority of specimens received were serum 776,944 (69%), or serum/plasma (unable to distinguish) 169,582 (15%) (Figure 2). The remainder of the specimen types were whole blood (105,400), plasma (51,471), oral fluid (29,672), dried blood spot (419) and unknown (7). Collectively 97% (1,103,667) were serum, plasma, or whole blood.

Testing Volume Trends

Overall, HIV testing volumes—reported as number of specimens received for HIV testing (screening and confirmation)—continue to decrease in PHLs. This analysis is based on responses from the subset of 34 PHLs (31 state and three local PHLs) that have responded to the last five APHL surveys (Figure 3). The peak of testing was in 2005 with 1,551,077 specimens received with a drop over time to the low of 735,134 in the most recent 2017 survey corresponding with a 53% decrease since 2005 (Figure 3).

Figure 2: HIV Specimen Types Received for HIV Diagnostic Testing, by volume (percentage) (n=65)

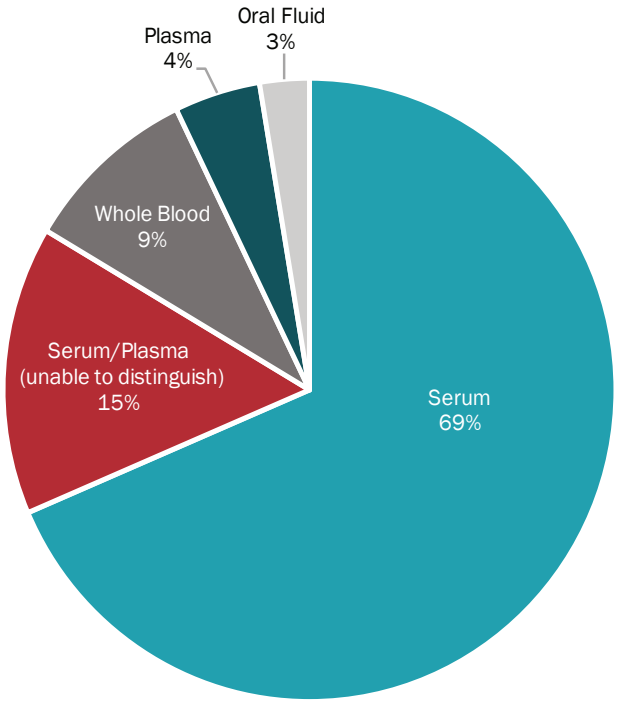


Figure 3: Samples received for HIV Testing - Volume Trends for PHL System, 2005-2017 (n=34)

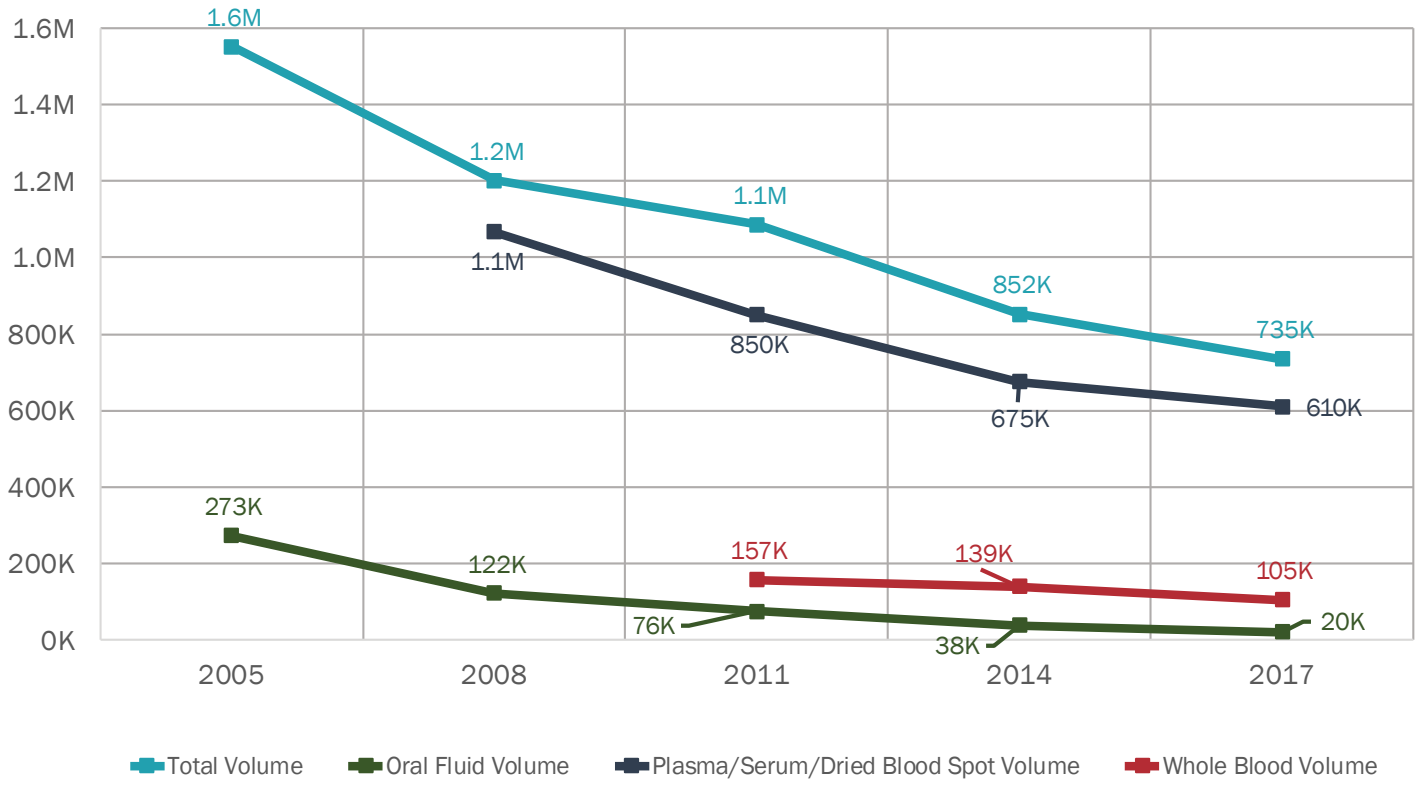


Figure 3: Comparison of total and oral fluid specimens received by PHLs that completed all APHL HIV surveys. The 2005 survey data cannot be parsed to determine test volume for plasma/serum or whole blood. The 2008 survey data cannot be parsed to determine whole blood volume.

In addition to analyzing testing volume trends overall, the contribution of particular specimen types was also examined (Table 4). The first item of note is the 15-percentage point drop in the proportion of oral fluid specimens compared to the total volume since 2005, which is an 83% decrease. During that time, there were major changes in the oral fluid testing market including the most recent discontinuation of the only FDA-approved supplemental assay for oral fluids. Additionally, of the 34 laboratories responding to all five surveys, 25 accepted oral fluid specimens in 2005, 18 in 2008, 18 in 2011, 12 in 2014 and only three laboratories in 2017. The second notable change was a 7% decrease in plasma/serum/DBS volume from 2005-2014 but an increase of 5% from 2014 to the 2017 survey.

Another impact on testing volume trends are the four state PHLs in this grouping that have provided data since 2005 that have discontinued HIV testing since 2014. One state PHL indicated that testing had transitioned to point-of-care but did not specify the exact date. Another PHL reported discontinuing testing in 2016 due to cost and staffing. The two remaining state PHLs discontinued testing during 2017 ultimately due to cost issues including low sample volume, challenges validating new assays and issues with third-party billing. Outside of this group an additional six laboratories reported discontinuing HIV testing since 2014. Even though they did not complete the 2014 survey, they cited similar reasons including costs, sample volume and submitters switching to rapid testing methods.

Table 4: Testing Volume Change Trends, by Specimen Type and Percent Contribution to Total Volume (n=34)

Specimen Type	Survey Year (Number of Specimens)					Percent Change Between Survey Years	
	2005 (1,551,077)	2008 (1,201,751)	2011 (1,085,714)	2014 (852,118)	2017 (735,134)	2005-2017	2014-2017
Proportion of Total Volume							
Oral fluid	18%	10%	7%	4%	3%	-83%	-25%
Plasma/ Serum/ DBS	Data Not Available	89%	78%	79%	83%	-7%	5%
Whole blood	Data Not Available	Data Not Available	14%	16%	14%	-	-12.5%

The 2005 survey data cannot be parsed to determine test volume for plasma/serum or whole blood. The 2008 survey data cannot be parsed to determine whole blood volume.

HIV Infections Detected

PHLs were asked to report test volume and results for testing in 2017 that included both screening and confirmation of preliminary positives. However, due to incomplete reporting only a subset of the data was suitable for analysis. For PHLs to be included in the analysis they had to have reported testing volumes for serum, plasma, serum/plasma (unidentified) and/or whole blood, and the number of results reported had to equal the number of specimens received (n=59). HIV infections included the following result categories:* Acute HIV-1 Positive,† HIV-1 Positive,‡ HIV-2 Positive,§ and HIV Positive.¶ Other result categories included Negative,** HIV-1 Negative, HIV-2 Inconclusive,†† Inconclusive‡‡ and Not Tested.§§ The 59 PHLs received 929,187 specimens and reported 12,048 HIV Infections reflecting an overall positivity rate of 1.3% (Figure 4). It is not possible to compare the positivity rate in 2017 to previous years due to the survey question being rephrased. Rather than asking for all results from all specimens (as was done in previous surveys) in 2017 the question was modified to request results from serum/plasma and whole blood samples only. So while the positivity rate (1.3%) was lower in 2017 than was reported in 2015 (1.5%) and 2011 (1.9%) the data is not directly comparable and a conclusion cannot be drawn based on this trend.

From these 59 PHLs, 646 (0.07%) HIV infections were reported as "Acute HIV-1 Infection" (Figure 4). Nearly all of the acute or early infections (80%, n=519) were identified by 32 PHLs that were using the HIV Laboratory Diagnostic Testing Algorithm.[1] Two additional PHLs reported 127 "Acute HIV-1 Infections," one was using an antibody immunoassay Ab IA rather than an Ag/Ab IA and the other was utilizing the Alere Determine™ HIV-1/2 Ag/Ab assay in a CLIA-waived setting and referring to another PHL that conducted the HIV Laboratory Diagnostic Testing Algorithm.[1]

All PHLs included in this analysis used an algorithm that includes an HIV-1/HIV-2 antibody differentiation assay for supplemental testing. In the absence of any FDA-approved assay for confirmation of HIV-2, the HIV-1/HIV-2 antibody differentiation assay allows for identification of HIV-2 infection. In 2017, five cases of HIV-2 were identified. In contrast, there were 415 specimens with inconclusive results ("HIV-1 negative, HIV-2 inconclusive" and "Inconclusive"). These specimens have not been fully identified as either HIV-1 or HIV-2 infections due to limitations of the testing algorithm, limitations of access to necessary testing, insufficient sample and policy or practice barriers. The remaining 113 "HIV Positive" specimens are considered untypable and/or undifferentiated and therefore would not require additional testing per the algorithm.

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* In the narrative, we use a shortened version of the actual wording of the responses on the survey. To ensure readers have a clear understanding of the potential responses we have included them as individual footnotes for each response.

† Acute HIV-1 Positive (e.g. IA+ and supplemental Ab-/indeterminate and HIV-1 NAT detected)

‡ HIV-1 Positive (e.g. IA+ and supplemental Ab testing confirms HIV-1)

§ HIV-2 Positive (e.g. IA+ and supplemental Ab testing confirms HIV-2)

¶ HIV Positive (e.g. IA+ and supplemental Ab testing untypable or undifferentiated)

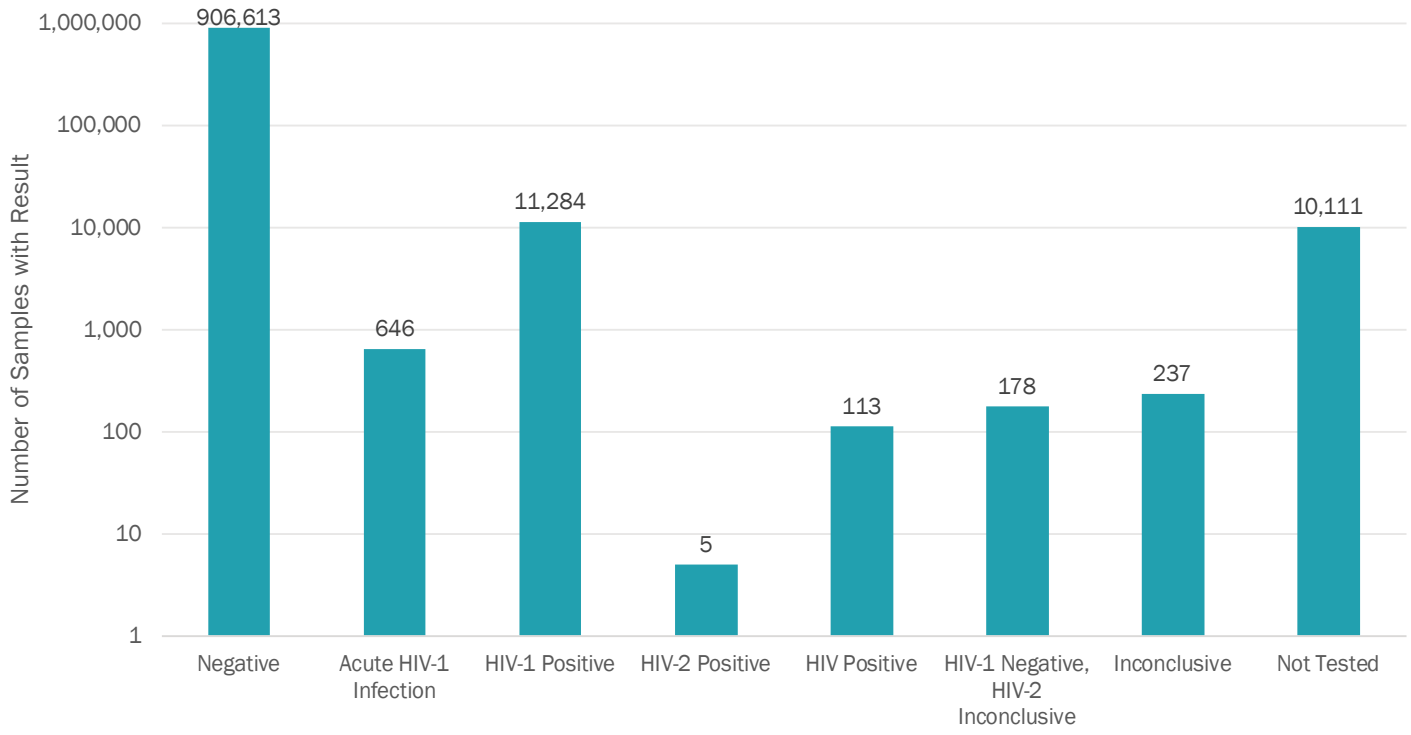
**Negative (e.g. screening test nonreactive or screening test reactive, supplemental testing (antibody and NAT) does not confirm)

†† HIV-1 Negative, HIV-2 Inconclusive (e.g. IA+ and supplemental Ab testing was either repeatedly HIV-2 indeterminate or HIV indeterminate and not detected by HIV-1 NAT)

‡‡ Inconclusive (e.g. IA+ and negative or indeterminate on supplemental Ab test and HIV-1 NAT was invalid or not performed)

§§ Not Tested (e.g. specimen rejected)

Figure 4: Reported HIV Diagnostic Results for Serum, Plasma and Whole Blood Specimens (n=59)



Confirmation of Rapid Reactive Specimens

In addition to diagnostic testing from primary specimens, PHLs also receive specimens from a variety of external sites for confirmation of preliminary positive or reactive rapid tests performed in CLIA-waived settings. There are different algorithms for confirmation of these specimens depending on the specimen type submitted. The Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations[1] includes information about performing the complete algorithm on serum or plasma specimens submitted for testing following a reactive, preliminary positive rapid HIV test. For other specimen types such as dried blood spot and/or oral fluid there are different confirmatory algorithms. Depending on the specimen type they receive and the needs within their respective jurisdictions PHLs may use alternative testing algorithms for specimens tested by rapid HIV tests at outside facilities.

In 2017, 46 (71%) of the 65 laboratories performing HIV testing, received specimens for confirmation of preliminary positive rapid tests. From these 46 PHLs, 28 (61%) reported receiving a total of 2,893 whole blood, serum and/or plasma specimens for confirmation. Of these specimens 553 (19%) were ultimately reported as HIV negative. Additionally, 40 PHLs provided information on the specimen type used to perform the initial rapid screening test they were confirming: 30 PHLs provided data for rapid tests performed on whole blood, eight provided data on rapid tests performed on oral fluid and nine indicated the specimen type received for confirmation but did not know the specimen type used for the initial screen (Table 5). Laboratories were able to report as many specimen types as they receive for each of the different rapid test types.

Table 5: Number of PHLs reporting Specimen Types: Rapid Test versus Confirmation Testing

Specimen type used for rapid test/ prescreen		Proportion of PHLs reporting the Specimen Type Received for Confirmation					
		Serum	Plasma	Serum/Plasma (undistinguishable)	Whole Blood	Dried blood spot	Oral Fluid
	Whole Blood (n=30)	73%	13%	27%	10%	0%	0%
	Oral Fluid (n=8)	25%	0%	0%	0%	0%	75%
	Unknown (n=9)	89%	33%	22%	22%	22%	33%

Trends in Oral Fluid Testing

The Avioq HIV-1 Microelisa System is the only FDA-approved laboratory based IA for oral fluid specimens but several PHLs have performed validations of antibody or Ag/Ab IAs for off-label use with oral fluids. Of the 65 PHLs that responded to the survey, 49 (75%) reported that they did not conduct any screening of oral fluid specimens in 2017. Twelve (75%) of the 16 PHLs performing screening of oral fluid specimens utilized the FDA-approved Avioq HIV-1 Microelisa System, one (6.3%) used the Bio-Rad (GS) HIV-1/HIV-2 Plus O immunoassay off-label, three (16%) utilized the OraQuick ADVANCE® Rapid HIV-1/2 Antibody test, and one reported using the OraSure HIV-1 Western Blot (6.3%). The remaining four (25%) PHLs discontinued or changed testing, with three of the PHLs discontinuing testing entirely and one PHL switching to the Alere Determine™ HIV-1/2 Ag/Ab Combo.

In May 2017, OraSure Technologies notified users that the only FDA-approved test for confirmation of oral fluids, the OraSure HIV-1 Western Blot, would be discontinued with the last purchases by December 31, 2017 or when inventory was exhausted. In the survey information was requested about laboratory plans in response to the discontinuation of the Western Blot. Of the 16 PHLs performing Oral Fluid testing in 2017, 10 (63%) planned to discontinue oral fluid testing, 5 (31%) planned to validate another HIV assay (Geenius™ HIV-1/2 Supplemental Assay) for oral fluid specimen confirmation, and one (6%) was planning to move to a rapid/rapid algorithm.

Planned Changes To HIV Testing

All survey respondents (n=81) were requested to report on plans to add or change any HIV testing services before December 31, 2018 which was approximately 1.5 years from when they received the survey. Only 15 (19%) PHLs reported planning to add or change any testing during this period, 10 (12%) PHLs responded that they were unsure and the remainder of PHLs responded that they had no plans to add or change anything. Respondents were also asked about plans to eliminate or decrease any testing before December 31, 2018. In this case four PHLs (three state, one local) indicated they have plans to eliminate or decrease testing, two PHLs were unsure and the remainder had no plans to eliminate or decrease any HIV testing.

Screening Immunoassay

Additions or Changes

- Two PHLs plan to bring on new screening assay
- Four PHLs plan to replace existing screening assay with a new screening assay
- One PHL plans to refer screening to another laboratory

Eliminate or Decrease

- Three PHLs plan to or already have discontinued HIV testing, including screening
- One PHL plans to discontinue dried blood spot testing

Supplemental Antibody Assay

Additions or Changes

- Two PHLs plan to add a supplemental assay to be performed on site
- One PHL plans to replace existing supplemental assay with a new assay
- One PHL plans to modify an existing supplemental assay (for oral fluid testing)

Eliminate or Decrease

- Three PHLs plan to or already have discontinued HIV testing, including supplemental testing

Supplemental HIV-1 Nucleic Acid Assay

Additions or Changes

- Six PHLs plan to add an HIV-1 NAT to be performed on site
- One PHL plans to add an HIV-2 NAT
- One PHL plans to replace an existing HIV-1 NAT performed on site with a new HIV-1 NAT
- One PHL plans to modify an existing HIV-1 NAT (changing instrument for a laboratory developed test)

Outreach, Training, Education on the Recommended Laboratory Testing Algorithm

Public health laboratories frequently serve as a resource for the other laboratories in their jurisdiction, as well as epidemiologists and program staff. Thirty-two (40%) PHLs provided outreach, training, or education regarding HIV diagnostic testing in 2017. PHLs that provided outreach, training, or education identified the top five most common topics considering phone calls, emails, hotlines, meetings, or other formats for requests (Table 6). Each respondent indicated the three most common entities requesting training, education, or information. The most frequently named requesting entity was the HIV Prevention Program at the Health Department (n=21, 66%), followed by Clinicians/Providers (n=15, 47%), and HIV Patient Care at the Health Department (n=12, 38%). Other requesting entities were CLIA-waived sites (n= 7, 22%), Hospital Laboratories (n=4, 13%), Other (n=2, 6%), and one each for commercial laboratories and other PHLs.

The modality of the outreach, education or training included in-person seminars or meetings (44%), informal consultation via phone, email or other (38%), written guidance or information (19%), in-person training (13%), web-based seminar or meeting (6%), and web based training (6%).

Table 6: Most common topics that PHLs provided outreach, training or education

Topics	# of PHLs	Percentage
Result Interpretation	21	65.6%
Specimen Handling/Requirements	21	65.6%
Algorithm Interpretation	19	59.4%
Result Reporting	16	50.0%
Specimen Collection	16	50.0%
Implementation of the Recommended Diagnostic Algorithm (e.g. appropriate tests, sequence)	15	46.9%
Supplemental HIV Ab differentiation tests (performance or platforms)	10	31.3%
HIV Ag/Ab or HIV Ab Immunoassays (performance or platforms for screening tests)	8	25.0%
HIV-1 NAT/RNA for Diagnosis (performance or platforms)	7	21.9%
Rapid Tests (performance and selection of test kit)	4	12.5%
Rapid Tests (i.e. implementation and quality assurance)	3	9.4%
Cost of Tests	1	3.1%
Laboratory Developed Tests	1	3.1%
Other	1	3.1%
Guidance on Validating FDA Approved tests	0	0.0%
HIV1-NAT/RNA for Viral Load/Monitoring	0	0.0%

On the Horizon—New HIV Testing Technology

In order to better understand the needs and desires of PHLs regarding HIV testing technologies, respondents were asked to indicate whether they would be interested in different HIV assays/technology. The survey listed a number of possible or potential technologies and asked about whether the PHL would be interested in brining on that technology if were it were to become FDA-approved and/or recommended as part of the HIV Laboratory Diagnostic Algorithm (Table 7). These were not endorsements of any technology nor predictions or promises of these technologies coming to market. PHLs were most interested in an HIV-1 NAT with a dual-claim for diagnosis and viral load monitoring; of the 45 PHLs that noted interest, 40 are currently performing HIV testing. Of the nine PHLs that listed "Other," two provided specific responses: one indicated they would be interested in new methods for confirmatory testing for oral fluid reactive and the second mentioned a lower throughput HIV-1 and/or HIV-2 NAT.

Table 7: PHL Interest in Potential New HIV Testing Technology

Proposed Laboratory Assay	All Respondents (n=81)	Currently Performing HIV Testing (n=65)	Not Currently Performing HIV Testing (n=16)
HIV-1 NAT with a dual claim (single assay that is FDA approved for diagnosis and viral load monitoring)	56%	62%	31%
Rapid HIV NAT (HIV-1 and/or HIV-2)	33%	37%	19%
Alternative supplemental HIV-1/2 antibody differentiation assay	23%	26%	13%
HIV-2 NAT	23%	23%	25%
Alternative HIV-1/2 Ag/Ab differentiating combination immunoassay	22%	23%	19%
HIV-1 p24 Ag confirmatory assay	22%	23%	19%
Rapid HIV-1/2 Ag/Ab combination immunoassay	14%	12%	19%
Other, please specify	11%	9%	19%

Reimbursement Methods

Health department capacity to participate in third-party reimbursement for HIV/AIDS and viral hepatitis services is essential in the context of the Affordable Care Act. Funding for HIV diagnostic testing and other prevention services have become increasingly constrained. Federal funders require that health departments seek reimbursement from health insurers when possible. Leveraging revenue available through third-party reimbursement can help PHLs and HIV prevention programs to continue to provide essential services and carry out core public health functions.

All survey respondents were asked about reimbursement practices (Table 8). Of the 65 PHLs performing HIV testing, approximately half, 34 (52%) currently bill Medicaid, Medicare, private insurance or other payers for HIV diagnostic testing and an additional five PHLs plan to implement billing in the next 12 months. One additional laboratory that did not perform HIV testing in 2017 plans to implement HIV testing and billing in 2018. The mechanism of seeking reimbursement also varied with 25 (74%) of health departments billing insurers, five (15%) health departments billing providers, and four (12%) health departments were not sure about the billing mechanism. For the 34 PHLs that seek reimbursement, less than half (n=14) stated that the revenue went to the laboratory with two of those reporting that the revenue was earmarked for HIV testing. Additionally, 24 (30%) PHLs (18 state and six local) reported billing for HCV testing.

Table 8: Reimbursement/Billing Practices

	State	Local	Total
Seeking Reimbursement for HIV Testing? (n=81)			
Currently billing for HIV testing	20	14	34 (42%)
Plan to implement in next 12 months	2	2	4 (5%)[a]
No plans to implement billing in next 12 months	19	5	24 (30%)[b]
Don't know if PHL is billing for HIV testing	4	1	5 (7%)[c]
Don't offer HIV or HCV Testing	4	10	14 (17%)
For those currently billing, which payers? (n=34)			
Medicaid	18	11	29 (85%)
Medicare	7	6	13 (38%)
Private Insurance	8	8	16 (47%)
Other	5	5	10 (29%)
Providers/Clinics	3	1	4 (12%)
Grants	1	2	3 (9%)
Other	1	2	3 (9%)
Not sure	0	1	1 (3%)
For those currently billing, what mechanism? (n=34)			
Health Department bills insurers	16	9	25 (74%)
Health Department bills providers	1	4	5 (15%)
Not sure	3	1	4 (12%)
For those currently billing, where does revenue go? (n=34)			
Revenue to the Laboratory-Earmarked for HIV Testing	1	1	2 (6%)
Revenue to the Laboratory-Not Earmarked	6	6	12 (35%)
Revenue to Health Department	6	1	7 (21%)
Revenue to State/Local General Fund	3	3	6 (18%)
Other	0	1	1 (3%)
Not sure	4	2	6 (18%)

a. One of the two local PHLs that plans to implement billing is not currently testing for HIV but plans to implement testing and billing. b. One of the state PHLs did not perform HIV testing in 2017. c. All PHLs with this response performed HIV testing in 2017.

In order to assess whether PHLs were taking full advantage of their billing capacity the billing practices of the 42 PHLs performing both HIV and HCV Testing were examined (Table 1). Fifty percent of these PHLs report billing for both HIV and HCV testing services. An additional 13 PHLs (31%) reported having no plans to bill for HIV testing services and are not currently billing for HCV testing services and the three PHLs that reported not knowing their HIV billing practices are not billing for HCV testing services. The breakdown of the remaining billing practices are as follows:

- Two (5%) report billing for HIV testing services but not for HCV testing services
- One (2%) PHL reports plans to implement HIV billing in next 12 months and is billing for HCV testing services
- One (2%) PHL reports plans to implement HIV billing in next 12 months and is not billing for HCV testing services
- One (2%) PHL reports no plans to implement HIV billing and is billing for HCV testing services

Testing for HCV

The rapid evolution of effective treatment regimens for HCV infection provides an important prevention opportunity for public health departments. Screening for HCV is a key public health strategy for the prevention and control of HCV and as such, health departments and their PHL partners are building capacity to implement testing programs. In addition, health department HCV programming is frequently integrated into existing HIV prevention programming and therefore testing is also becoming increasingly integrated. To understand the current public health capacity to implement and expand testing for HCV, this survey

included several questions intended to obtain a snapshot of current PHL capacity to respond to public health efforts to expand HCV testing.

Forty-four (54%) of the responding PHLs perform HCV testing in some capacity. This is one less PHL than performed testing according to our 2014 survey, though not necessarily the same labs. Nearly all PHLs performing HCV testing, 42 (95%) perform HCV antibody IA-laboratory based, with HCV RNA for diagnosis offered by 19 (43%) and HCV RNA for patient management and or viral load monitoring offered by nine (20%) of PHLs. This is an increase of seven PHLs offering HCV RNA testing for diagnosis of HCV and a decrease of two for HCV RNA testing for patient management and/or viral load monitoring since the 2014 survey. During this period, several manufacturers were able to update or obtain intended use statements for HCV RNA assays such that the same assay can be used for both diagnosis and patient management. This change in the intended use and the rise of blood-borne infections associated with the opioid crisis may have contributed to more PHLs bringing on this testing. In addition to these tests a small number of PHLs offer HCV genotyping (n=6) and HCV sequencing (n=2). The assays utilized for HCV antibody and RNA testing are described in Table 9.

Table 9: HCV Assay Utilization

Type of Assay	Assay Name	n (%)
Anti-HCV Ab IA (n=42 PHLs)	Abbott Architect® Anti HCV	18 (43%)
	OraSure OraQuick® HCV Rapid Antibody Test	1 (2%)
	Ortho VITROS® Anti-HCV/Ortho® HCV Version 3.0	17 (40%)
	Siemens ADVIA Centaur® Anti-HCV	2 (5%)
	Subtotal	**42**
HCV RNA, for Laboratory Diagnosis of HCV (FDA intended use in parenthetical notation) (n=19 PHLs)	Abbott RealTime HCV (Monitoring treatment)	3 (14%)
	Roche cobas® HCV (Diagnosis and Monitoring treatment)	1 (5%)
	Roche COBAS® Ampliprep/COBAS® Taqman® HCV Test, v2.0 (Diagnosis and Monitoring treatment)	4 (19%)
	Hologic Hepatitis C Quant Dx Assay (Diagnosis and Monitoring treatment)	3 (14%)
	Hologic APTIMA HCV RNA Qual (Diagnosis)	7 (33%)
	Other HCV RT-PCR Qualitative - please specify: LDT	2 (10%)
	Other - please specify: Genotyping	1 (5%)
	Subtotal	**21[a]**
HCV RNA, for Patient Management/Viral Load for HCV (FDA intended use in parenthetical notation) (n=9 PHLs)	Abbott RealTime HCV (Monitoring treatment)	3 (30%)
	Roche COBAS® Ampliprep/COBAS® Taqman® HCV Test, v2.0 (Diagnosis and Monitoring treatment)	3 (30%)
	Hologic Hepatitis C Quant Dx Assay (Diagnosis and Monitoring treatment)	3 (30%)
	Hologic APTIMA HCV RNA Qual (Diagnosis)	1 (10%)
	Subtotal	**10[b]**

a. 2 PHLs reported using 2 different HCV RNA tests for laboratory diagnosis of HCV. b. 1 PHL reported using 2 different HCV RNA tests for patient management/viral load.

In addition to assay utilization, laboratories were requested to indicate their testing algorithm for HCV Diagnosis in their laboratory (Table 10). The CDC recommends that all HCV Ab reactive specimens be reflexed to an HCV NAT to confirm current infection, which is also required to initiate treatment.[14] The most common algorithm, reported by 16 (36%) PHLs, consisted of HCV Ab screening and automatic reflex of all HCV Ab reactive specimens to an HCV NAT. This is the most preferred approach as it ensures that all specimens are appropriately tested and minimizes turnaround times. One PHL reported that they repeat the HCV Ab screen before reflexing to HCV NAT and one PHL reflexes to an HCV NAT (quantitative) upon provider request. In addition to these 18 PHLs, an additional six PHLs perform the HCV Ab screening and refer Ab-reactive specimens for HCV NAT, either with (n = 1) or without (n = 5) requiring a provider request for the NAT. Four PHLs perform HCV Ab screening and recommend that a second specimen is sent for HCV NAT to another laboratory (n=3) or their laboratory (n=1). Two laboratories reported following an outdated algorithm of using a recommended signal to cutoff ratio from the HCV Ab screen to determine which specimens are reflexed to HCV NAT. Approximately one-third (30%) of PHLs perform HCV Ab screening alone with no reflex, referral or

recommendation to obtain HCV NAT. Lastly, one PHL performs referral HCV RNA testing only.

Table 10: HCV Diagnostic Algorithms Utilized by PHLs in 2017

	State	Local	Total
Laboratory performs HCV Ab screening and…	22	8	30 (68%)
Automatically reflexes all HCV Ab reactive specimens to an HCV NAT	12	4	16 (36%)
Repeats HCV Ab before reflexing HCV Ab specimens to an HCV NAT	1	0	1 (2%)
HCV Ab reactive specimens are only reflexed to an HCV NAT (quantitative) is performed upon request	1	0	1 (2%)
Refers HCV Ab reactive specimens for HCV NAT to another laboratory	3	2	5 (11%)
Refers HCV Ab reactive specimens for HCV NAT to another laboratory (upon provider request)	1	0	1 (2%)
Recommends a second specimen is sent for HCV NAT to another laboratory (or their own laboratory) to confirm HCV Ab reactivity	2	2	4 (9%)
HCV Ab reactive specimens are only reflexed to HCV RNA testing in-house if they are less than the recommended s/co	2	0	2 (5%)
Laboratory performs HCV Ab screening only	9	4	13 (30%)
Laboratory performs HCV RNA testing only	1	0	1 (2%)

Discussion

As of 2017, adoption of the HIV Laboratory Diagnostic Algorithm is quite high with 94% (59/63) PHLs reporting performing HIV screening using an Ag/Ab for their initial test and completing the algorithm with a supplemental antibody differentiation test and assured access to HIV-1 NAT. Nearly all PHLs have either switched to the Geenius™ HIV-1/2 Supplemental Assay (90%) and or have assured access to the test through referral (8%). While there were anecdotal reports that several PHLs would have to refer to another PHL for supplemental testing due to the cost of Geenius, the percentage of laboratories referring supplemental antibody testing was the same as 2014. Only one PHL is still utilizing the HIV-1 WB and they indicated elsewhere in the survey that they plan to validate the Geenius™ HIV-1/2 Supplemental Assay by December 31, 2018. In-house availability of HIV-1 NAT has remained steady at 21 (32%) PHLs and 65% of PHLs assure access to HIV-1 NAT through referral. Despite the steady numbers from 2014 to 2017 of HIV-1 NAT, several PHLs (n=6) expressed interest in adding HIV-1 NAT as an in-house test and one PHL plans to add HIV-2 NAT. Additionally, when asked about new technology, the majority of respondents (56%) were most interested in an HIV-1 NAT with a dual-claim for diagnosis and monitoring, followed by interest in a rapid HIV NAT (33%).

Adapting to changing technology is always challenging, and no less so as PHLs must do so in spite of decreasing workforce, and decreasing number and rate of samples being submitted to their laboratories. To evaluate these trends a subset of 34 PHLs that have responded to APHL surveys since 2005 were examined. The number of FTEs peaked in 2008 and 2011 with 2.9 and decreased slightly to 2.5 in 2017. In 2005, these PHLs reported receiving 1.5 million specimens for HIV Testing and this year reported 735,134 a decrease of 53%. The change in the oral fluid marketplace has resulted in a 14.8% decrease since 2005. In addition to these changes in the testing volume, it is also worth noting that four of the 34 PHLs in this group have reported that all HIV testing has stopped or will stop since this survey was fielded. These changes were reflected in questions about anticipated changes in the coming year with several PHLs planning to eliminate or discontinue certain aspects of HIV serologic testing.

For the first time, PHLs were asked to report TAT, and not surprisingly, the TAT for specimens that were negative for HIV based on the screening assay was on average 1.81 days compared to specimens that were HIV-1 Positive and did not require NAT, which took an average of 2.62 days from specimen receipt to reporting results. Moreover, while it was expected, the data now revealed that HIV-1 Positive specimens that required HIV-1 NAT to finalize the diagnosis took 6.37 days overall, nearly four additional days compared to those not requiring HIV-1 NAT.

Seeking reimbursement for testing services from insurers by the PHL or health department can be very challenging. However, implementation of billing capacity can be an important strategy to remain competitive. Of the 81 responding PHLs 42% are testing for HIV and currently billing for HIV testing with an additional 5% planning to implement billing in the next year. However,

35% of PHLs that are offering HIV testing either have no plans to implement billing or do not know if the PHL is billing. Improving awareness about the value in billing and building capacity to bill could be useful for PHLs and is an area that APHL can continue to explore.

The number of PHLs performing HCV testing is very similar to 2014 at 54% (n=44) despite one less PHL reporting. Of these PHLs 95% performed at least an HCV antibody IA and 43% offering HCV RNA testing for patient management and 20% offering HCV RNA testing for viral load monitoring which is an increase of seven PHLs compared to 2014 offering HCV RNA testing. The HCV Diagnostic Algorithm requires performing HCV RNA testing for any HCV Ab reactive specimen. Of the 44 laboratories, only one offers HCV RNA testing (serve as a reference center for submitters), 13 offer HCV Ab screening only and 30 offer HCV Ab screening and some form of either reflex or referral testing. Ensuring PHLs are able to offer the full diagnostic algorithm will be a focus of APHL's work for the next several years and has already begun with the support of an HCV NAT Reference Center that could be more fully utilized.

APHL and CDC will continue to explore opportunities to assist PHLs in responding to new and emerging technologies and mechanisms to assist with billing for HIV testing. APHL will continue to work with federal, state, local, non-governmental, and corporate partners to address HIV testing challenges and improve HIV testing practice in the country's PHLs.

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Berry Bennett, MPH
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Association of Public Health Laboratories

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8515 Georgia Avenue, Suite 700
Silver Spring, MD 20910
Phone: 240.485.2745
Fax: 240.485.2700
www.aphl.org