The Association of Public Health Laboratories (APHL) and the Influenza Division of the Centers for Disease Control and Prevention (CDC) launched a three-year project in 2010 to define the core capabilities and the optimal “right size” for influenza virologic surveillance. The outcomes of the project will provide key state, national and global surveillance requirements to inform policy decisions and disease prevention efforts.

THE INFLUENZA VIROLOGIC SURVEILLANCE LANDSCAPE OF STATE PUBLIC HEALTH LABORATORIES

A Data Summary Based on the 2011 Right Size Influenza Virologic Surveillance Survey

The Association of Public Health Laboratories (APHL) and the Influenza Division of the Centers for Disease Control and Prevention (CDC) launched a three-year project in 2010 to define the core capabilities and the optimal “right size” for influenza virologic surveillance. The outcomes of the project will provide key state, national and global surveillance requirements to inform policy decisions and disease prevention efforts.

INTRODUCTION

The major outcome of the Right Size Influenza Virologic Surveillance Project will be the development of new guidelines for public health laboratory (PHL) virologic surveillance. Implementation of the right-size virologic surveillance guidelines will help CDC, PHLs, and surveillance programs to maximize use of available resources, redirect resources if necessary, and build new capacity as needed for optimal surveillance.

APHL developed and distributed the Right Size Influenza Virologic Surveillance Survey during 2011 as one of the project activities, since no definitive data-based descriptions of public health laboratory activities related to influenza testing and surveillance were available. The purpose of the survey was to collect data to characterize the current landscape of influenza virologic surveillance and testing practices and policies in state and local PHLs. Understanding existing laboratory capabilities and practices will inform efforts to develop new guidelines and define the core capabilities and the optimal “right-size” for influenza virologic surveillance. The survey captured how influenza testing priorities are established and funded, as well as challenges to the sustainability of public health laboratory influenza testing.
METHODS
The survey was launched on July 20, 2011, and closed September 26, 2011. This 59-question survey was administered electronically through MRInterview, a web-based survey instrument. The survey was distributed to 52 state and territorial public health laboratories (SPHLs), including the District of Columbia, and 34 local public health laboratories (LPHLs) that are known to perform influenza testing. Forty-six SPHLs completed the survey, resulting in a response rate of 92%. The response rate for LPHLs was 68%, representing 23 LPHLs.

Respondents were asked to base their responses on the period of October 1, 2010 through April 30, 2011 (the 2010-2011 influenza season) unless otherwise directed. They were also instructed to consult with epidemiologists and/or influenza coordinators as needed and to request a review by their laboratory director. Due to variations in the practices between SPHLs and LPHLs, this issue brief only presents the SPHL data. A separate issue brief, “Influenza Virologic Surveillance Landscape of Local Public Health Laboratories,” was published by APHL reporting the LPHL data summary.

PARTICIPATION IN NATIONAL SURVEILLANCE PROGRAMS
All of the responding SPHLs participate in the US influenza virologic surveillance system as US World Health Organization (WHO) Collaborating Laboratories. However, only 21 of 46 (46%) responding SPHLs participate in the National Respiratory and Enteric Virus Surveillance System (NREVSS) (based on both survey data and CDC records). The primary reasons for non-participation in NREVSS were evenly distributed among: a) not having adequate resources for all of the requested data submissions; b) belief that it is not worthwhile for the small volume of testing performed in their laboratory; and c) a lack of awareness of NREVSS.

INFLUENZA SURVEILLANCE PROGRAM ORGANIZATIONAL STRUCTURE AND COORDINATION
The data highlight the collaboration that occurs between SPHLs and epidemiologists/influenza coordinators, with the majority of state respondents co-formulating the policy for specimen submission, both for routine (80%; 37 SPHLs) and emergency situations (93%; 42 SPHLs). Communication between the SPHL and epidemiologists and/or the influenza coordinator occurs at least weekly for nearly one-third of responding states (29%; 13 SPHLs), and occurs as needed in more than half of responding SPHLs (56%; 25 SPHLs).
SPHL INFLUENZA SURVEILLANCE RESPONSIBILITIES

All responding SPHLs perform testing for influenza as one of the laboratory’s responsibilities in their state’s influenza surveillance program. The survey data also document the additional responsibilities PHLs fulfill beyond performing tests. The overwhelming majority of responding SPHLs submit data/information to submitters, state epidemiologists/influenza coordinators and CDC (98%; 44 SPHLs) and provide virologic data for influenza surveillance reports (93%; 42 SPHLs) (see Figure 1). Eighty-nine percent of responding SPHLs (40 SPHLs) report to CDC; however, CDC receives reports from all states, indicating that either: a) someone else reports to CDC in the five responding states that indicated they do not report to CDC; b) the respondent was unaware of the reporting that occurs; or c) the respondent misunderstood the question.

A larger percentage of laboratories request samples for influenza surveillance in those states where the laboratory and state influenza coordinator/epidemiologists work together to enroll sites or the laboratory enrolls additional sites when compared to those states where only the state influenza coordinator/epidemiologists enroll and communicate with surveillance sites (62% vs. 19%).

Figure 1. SPHL Influenza Surveillance Responsibilities.

*Note: “Other” includes submitting specimens to CDC contract laboratories, providing test kits to submitters, and surveying sentinel laboratories for rapid influenza diagnostic tests (RIDT) results.
Influenza Specimen Submitters/Providers
Sentinel providers enrolled by the state influenza coordinator were the most frequently (93%) enrolled specimen submitters in states’ influenza programs during the 2010-2011 influenza season. The second most frequently identified enrolled group was clinical laboratories, at 85% (see Figure 2).

By comparison, the most frequently identified providers from which responding SPHLs actually received specimens for influenza testing during the 2010-2011 influenza season were clinical laboratories (100%; 46 SPHLs), followed closely by sentinel providers enrolled by the state influenza coordinator (98%; 45 SPHLs) (see Figure 2).

Influenza Specimen Submission Recommendations
All respondents provided specimen submission recommendations to providers; at least 87% (40 SPHLs) recommended specimen submission categories such as: epidemiologist request, sentinel provider selected by epidemiologist, pediatric death with influenza-like illness (ILI), and institutional or community outbreak (see Figure 3).
INFLUENZA PROGRAM OUTREACH ACTIVITIES

All responding states provide some type of support or incentives to influenza surveillance specimen submitters, with 85% or more of responding states (>40 SPHLs) offering free testing, free transport kits, and free shipping. Some of the more uncommon and unlisted incentives provided were medical reference materials, admission to a state conference, clinical consultations, children’s books, viral care kits, and framed artwork (see Figure 4).

In terms of financial support, all but one state defrayed the costs of specimen collection, and all but two states defrayed the costs of specimen transport for sample submitters who were enrolled in the laboratory influenza surveillance program during the 2010-2011 influenza season. In most cases, the SPHL provided collection supplies (80%; 37 SPHLs) and paid the specimen transport costs (48%; 22 SPHLs). No states provided reimbursement or payment for specimen collection or transport costs, although three states did provide payment for participation or per specimen.

For the purposes of this report, jurisdictional awareness and influenza testing data collection from clinical and commercial laboratories was considered to be a component of outreach activities. Thirty-three (73%) responding SPHLs stated that they know the number of clinical/commercial laboratories within their jurisdiction performing influenza testing by real-time reverse transcriptase polymerase chain reaction (rRT-PCR), culture and/or sequencing, although 17 (38%) qualified that knowledge as being “only the laboratories that communicate with the influenza surveillance program or public health laboratory.”

More than 80% of responding SPHLs (34 SPHLs) serve as a resource and/or provide guidance for technical information related to influenza testing, and 64% (29 SPHLs) perform initial subtyping of influenza positives and additional reference/specialized testing.

### Table: Incentives Provided to Influenza Surveillance Providers/Submitters by SPHLs. n=46

<table>
<thead>
<tr>
<th>Incentive</th>
<th>PERCENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Free testing</td>
<td>45</td>
</tr>
<tr>
<td>Free transport kits</td>
<td>41</td>
</tr>
<tr>
<td>Free shipping/courier services</td>
<td>40</td>
</tr>
<tr>
<td>Education/access to public health expertise</td>
<td>22</td>
</tr>
<tr>
<td>Certificate of participation</td>
<td>17</td>
</tr>
<tr>
<td>Rapid influenza diagnostic tests</td>
<td>13</td>
</tr>
<tr>
<td>Other*</td>
<td>7</td>
</tr>
<tr>
<td>Hand sanitizers</td>
<td>3</td>
</tr>
<tr>
<td>Payment for participation per specimen</td>
<td>3</td>
</tr>
<tr>
<td><strong>Note:</strong> “Other” incentives provided are described in the text.</td>
<td></td>
</tr>
</tbody>
</table>
INFLUENZA SURVEILLANCE DATA DISSEMINATION AND TEST RESULT REPORTING

When reporting influenza test results to submitters, the vast majority (91%; 41 SPHLs) of responding SPHLs use their laboratory information management system (LIMS) to generate reports. However, a variety of methods are then used to distribute these result reports to the submitters. US Postal Service mail is the most commonly used distribution method, (38%; 17 SPHLs), followed by fax (22%; 10 SPHLs) and email (4%; 2 SPHLs). Only 27% of responding SPHLs (12 SPHLs) use electronic reporting directly to submitters via their LIMS for result reporting.

By contrast, 67% of SPHL respondents (30 SPHLs) use electronic reporting via LIMS as the primary method of reporting influenza test results to state influenza coordinators and/or state or local epidemiologists. All SPHLs reported to their state influenza coordinator and/or state/local epidemiologists at least weekly during the 2010-2011 influenza season, with 51% (23 SPHLs) reporting in “real time” as results were generated.

According to CDC and the survey data, all SPHLs reported electronically to CDC during the 2010-2011 influenza season, with the majority (58%; 26 SPHLs) of reports sent via PHLIP (Public Health Laboratory Interoperability Project), followed by web-based Laboratory Internet Reporting System (22%; 10 SPHLs) and Public Health Laboratory Information System 2 (PHLIS2) (13%; 6 SPHLs) (see Figure 5). Ninety-five percent of responding SPHLs (43 SPHLs) reported to CDC at least weekly during the 2010-2011 influenza season; 51% (23 SPHLs) reported weekly. Forty-nine percent of SPHL respondents (22 SPHLs) are either capable of receiving result reports from CDC via electronic messaging using Health Level Seven (HL7) or are developing the capability.

Figure 5. Method of Reporting Influenza Laboratory Surveillance Data to CDC. n=45

Note: “Other” includes PHINMS.
FUNDING FOR INFLUENZA TESTING

SPHL estimates of annual costs related to influenza testing varied widely. Eleven responding SPHLs (24%) stated that they were unable to provide an accurate estimate of the costs; five additional SPHLs stated that they could only provide rough estimates or were unable to provide costs for some of the listed categories. Among the 34 SPHLs that submitted cost data, the estimated testing-related costs for the 2010-2011 influenza season ranged from $39,500 to $902,600 (median $229,375). Because of the incomplete data or rough estimates, these data should be interpreted with caution.

Survey data were analyzed to define the proportion of the costs funded by fee for service testing, state funding, and grant or cooperative agreement funding sources. The total Epidemiology and Laboratory Capacity (ELC) funding received by responding states during 2010 designated for influenza laboratory surveillance and/or testing ranged from $0 to $325,700, with an average of $88,728. Table 1 summarizes the percentage of funding expended by responding SPHLs for the 2010-2011 influenza season that was received from each of the listed funding sources.

Table 1. Percentage of Total Dollars Expended by SPHLs for Influenza Testing During the 2010-2011 Influenza Season According to Funding Source. n=45

<table>
<thead>
<tr>
<th>Funding Source</th>
<th>Mean %</th>
<th>Median %</th>
<th>Standard Deviation</th>
<th>Max %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epidemiology and Laboratory Capacity (ELC) Grant</td>
<td>31</td>
<td>25</td>
<td>26</td>
<td>100</td>
</tr>
<tr>
<td>CDC Public Health Emergency Preparedness (PHEP) funds</td>
<td>23</td>
<td>10</td>
<td>28</td>
<td>100</td>
</tr>
<tr>
<td>State Funds</td>
<td>23</td>
<td>14</td>
<td>28</td>
<td>100</td>
</tr>
<tr>
<td>Other*</td>
<td>16</td>
<td>0</td>
<td>28</td>
<td>100</td>
</tr>
<tr>
<td>CSTE Grant</td>
<td>5</td>
<td>0</td>
<td>13</td>
<td>59</td>
</tr>
<tr>
<td>Fee for Service Testing Fees</td>
<td>1</td>
<td>0</td>
<td>8</td>
<td>50</td>
</tr>
</tbody>
</table>

Note: The minimum % for all categories was 0%.

“Other” primarily includes PHER funding, but also includes other federal grants, immunization grants, and Affordable Care Act ELC grants. CSTE is the Council of State and Territorial Epidemiologists.

INFLUENZA TEST METHODS AND PRACTICES

An extensive menu of influenza testing methods is available to SPHLs including: molecular diagnostics, virus culture, and antiviral resistance testing. The survey asked PHLs to report which methods are used, testing limitations, and other testing characteristics, such as turnaround time.

While all but one responding SPHL perform rRT-PCR on a routine basis (i.e., at least once per week during the influenza season), use of the other testing methods varies (see Figure 6, page 8).

1Funding and influenza testing costs are being examined in more detail as a separate deliverable to the Right Size Influenza Virologic Surveillance Project.

2It should be noted that the funding levels of ELC cooperative agreement funds have decreased since this survey was administered.
INFLUENZA PCR AND VIRUS ISOLATION TESTING CAPACITY LIMITING FACTORS

Under routine testing conditions, the most significant factor limiting influenza PCR capacity identified by responding SPHLs was having insufficient staff to redirect to other tests/tasks. Lack of trained personnel and electronic data management capability were the next most commonly cited limiting factors (see Figure 7).

During a pandemic or surge response, SPHLs cited lack of trained personnel and, again, insufficient staff to allow for staff reassignment as the most significant inhibiting factors. SPHLs also indicated that data management capability and specimen receipt/accessioning were the next most significant limiting factors during a pandemic or surge response (see Figure 7).

For influenza virus culture, responding SPHLs most frequently identified factors related to adequate staffing issues, with the most frequently identified factor being the availability of trained personnel. The next most significant factors were availability of expertise and, as with PCR, insufficient staff to allow for staff reassignment to other tests/tasks (see Figure 7).
Of the 36 responding SPHLs that perform virus culture, the overwhelming majority (92%; 33 SPHLs) reported providing isolates for submission to CDC and detecting other respiratory viruses as reasons for performing virus culture (see Figure 8).

Of the SPHLs that self-identified as performing little or no virus culture, 18 (40%) indicated that the reason that they do not perform viral culture is a policy decision to use rRT-PCR for routine influenza testing, and 7 SPHLs cited the cost to maintain cell culture capability.

The policy decision factor is corroborated by the fact that, of the 10 SPHLs that do not perform virus culture, 100% perform rRT-PCR and 90% cited a policy decision to use rRT-PCR as the reason for limiting viral culture.
USE OF WHO INFLUENZA REAGENT KIT FOR IDENTIFICATION OF INFLUENZA ISOLATES

The 36 SPHLs that perform virus culture were asked which methods they use to identify and characterize cultured influenza viruses. The majority of SPHLs use the CDC rRT-PCR assay (86%; 31 SPHLs) and/or immunofluorescence utilizing commercially available monoclonal antibodies (64%; 23 SPHLs) to type and subtype cultured influenza viruses. Only 13 SPHL respondents (36%) identify isolates using the monoclonal antibodies from the WHO Influenza Reagent Kit for Identification of Influenza Isolates kits (WHO kits), provided by CDC (see Figure 9).

Twenty-four responding SPHLs (53%) do not use the WHO kit reagents; 11 (24%) of those laboratories keep the reagents for emergency or problem virus situations. Twenty-one responding SPHLs (47%) indicated that they use the WHO kit reagents for at least one purpose; the purpose cited was evenly distributed among using the monoclonal antibodies for immunofluorescence tests, using the hemagglutination inhibition (HI) reagents for typing and subtyping, and using the HI reagents for influenza B lineage typing.

INFLUENZA ANTIVIRAL SUSCEPTIBILITY/RESISTANCE TESTING

As previously mentioned, 11 responding SPHLs (24%) performed antiviral susceptibility/resistance testing during the 2010-2011 influenza season. All 11 SPHLs performed pyrosequencing using CDC protocols.

In addition, two laboratories performed neuraminidase inhibition testing, and one laboratory performed pyrosequencing using other reference protocols. Two laboratories also reported using whole gene dideoxy sequencing.
CONCLUSION

The data from the survey highlight the extensive role SPHLs play in influenza virologic testing and national influenza surveillance. The survey data also document the additional roles SPHLs fulfill beyond test performance. For example, the survey results provide insight into the role SPHLs play in providing data and reports based on their testing, as well as enrolling, communicating, and educating specimen submitters and providers. Additionally, the vast majority of SPHLs also provide technical guidance and/or act as technical resources in their jurisdictions. The survey data document these outreach activities and the relationships between SPHLs and their jurisdictions. The relationship between SPHLs and their clinical and commercial laboratories and healthcare providers is likely to become increasingly important as influenza virologic surveillance evolves. The survey data document outreach activities and relationships developed by some PHLs and may inform the development of guidance in best practices for PHLs that do not have well-established relationships with partners.

It is encouraging to document that collaboration occurs between SPHLs and epidemiologists/influenza coordinators, with the vast majority co-formulating their policies for specimen submission, both for routine and emergency situations. The survey data also demonstrate that specimen submission policies are not static documents that are created and shelved; rather, these policies are living documents with 80% of SPHLs stating they reviewed their specimen submission policies at least annually or as needed.

As was expected, the survey data confirm that rRT-PCR has become the most commonly used routine influenza testing method. The percentage of SPHLs that perform virus culture may decline further in response to the fiscal challenges currently facing PHLs. The minimal use of the WHO kit reagents reported in the survey coincides with the declining use of virus culture and the increased use of PCR testing methods for influenza surveillance. Although one of the reasons that SPHLs retain the WHO kit reagents is for potential use for “problem virus situations,” it seems unlikely that SPHL use of these reagents would provide a more appropriate response than accessing CDC’s expertise and capabilities. The survey data, combined with an understanding of the changes in influenza virologic surveillance, bring into question whether there remains a need to provide the WHO reagent kits to US PHLs.

Finally, the survey data clearly demonstrate concerns about funding. This may be the time to define who bears the responsibility for funding influenza surveillance programs, whether it be state, federal, other funding, or a combination of the three. The survey data indicate that accurately capturing funding and expenditure information can be difficult; however, identifying all of the necessary elements of an influenza surveillance program and its associated costs can be accomplished and may become even more important in light of the current fiscal challenges.

Despite fiscal challenges, SPHLs have been able to maintain an extensive menu of influenza test and surveillance-related activities. However, the survey data highlight the urgency and need for the Right Size Virologic Surveillance Project to address the future landscape of influenza virus isolation and testing at PHLs in order to have a sustainable, efficient, and data-driven surveillance system.
Association of Public Health Laboratories

The Association of Public Health Laboratories (APHL) is a national non-profit organization dedicated to working with members to strengthen governmental laboratories that perform testing of public health significance. By promoting effective programs and public policy, APHL strives to provide member laboratories with the resources and infrastructure needed to protect the health of US residents and to prevent and control disease globally.

Funders
As part of the Right Size Influenza Virologic Surveillance Project, this report was supported by Cooperative Agreement Number # U60HM000803 from CDC. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of CDC.

© Copyright 2012, Association of Public Health Laboratories. All Rights Reserved.