Influenza Virologic Surveillance
Right Size Project

Launch
July 2013
Today’s Discussion Outline

• General Influenza Surveillance
• Right Size Rationale
• Roadmap
  o Requirements
  o Implementation
  o Sample Size Calculator
• “How To Use the Roadmap”
  o Roadmap Website
Overview of U.S. Influenza Surveillance
Weekly Updates at [http://www.cdc.gov/flu/weekly](http://www.cdc.gov/flu/weekly)

- **Morbidity Surveillance (3 components)**
- **Viral Surveillance (3 components)**
- **Mortality Surveillance (2 components)**

State-level data to state surveillance coordinators
U.S. Influenza Surveillance Components

- Morbidity Surveillance
  - ILINet outpatient surveillance
  - Influenza-associated hospitalization surveillance
  - State and Territorial epidemiologist reports

- Mortality Surveillance
  - 122 Cities mortality reporting system
  - Influenza-associated pediatric death reports
U.S. Influenza Surveillance Components

• Viral Surveillance
  – U.S. W.H.O. Collaborating Laboratories
  – National Respiratory and Enteric Virus Surveillance System (NREVSS)
  – Novel influenza A reporting
Goals for Influenza Virologic Surveillance

- Provide situational awareness
- Inform vaccine strain selection
- Detect novel viruses or events
- Detect and monitor antiviral resistance
Surveillance Activities need to be:

• Relevant
  o PH decisions
  o Clinical community needs
  o Health Security

• Measurable
  o Data reliability
  o Impact

• Adaptable
  o Outbreaks/pandemics
Influenza Virologic Surveillance
Right Size Project - Rationale

• Post-pandemic AAR activity
• Need evidence-based decisions
  o Statistical, systematic approach lacking
• National versus state needs
  o Lack of uniform standards and data
• Capacity as driver of testing decisions
• Funding/Sustainability
  o Lab capacity including workforce
  o Justify and optimize resources
The Influenza Virologic Surveillance Right Size Project and Roadmap - The Process
Influenza Virologic Surveillance Right Size Project - Objectives

• Define core capabilities and optimal “right-size” for influenza virologic surveillance to support state, national and global surveillance efforts and better help us to inform policy decisions and disease prevention efforts.

• Provide a statistical, systematic approach to virologic surveillance to enable better evidence-based decisions.

• Maximize available resources,
  o Build new or re-direct existing capacity as needed for optimal surveillance.

• Create a scalable approach to meet outbreak or pandemic surge needs.
The Influenza Virologic Surveillance
Right Size Roadmap

**Roadmap** to achieve an effective virologic surveillance system:

- **Requirements**: define state and national virologic surveillance needs, and associated functional requirements of state and local public health laboratories.

- **Implementation Guidance/toolkit** for CDC, state and local health departments and public health laboratories
  - Help operationalize the requirements

- **Sample Size Calculators** to determine effective sample size needed to detect/monitor key virologic surveillance objectives.
Influenza Virologic Surveillance Right Size Roadmap Development Process

- Conducted Multiple Stakeholder Meetings
  - March 2010 (advise the Charter, develop Objectives)
  - October 2011 (set Thresholds, discuss calculators)
- Presented Status Updates to APHL and CSTE
- Solicited input from Clinical/Commercial Laboratories and Healthcare providers
- Surveyed Public Health Laboratories for Current Influenza Landscape
- Obtained information from International Partners
- Roadmap Pilot Projects in 4 states
- Table top Exercise with participants from 15 states and 1 local jurisdiction
  - December 2012
Influenza Virologic Surveillance Right Size Benefits

- Roadmap and calculators well-received
- Standardization
- Enhance epidemiology/laboratory coordination
  - Facilitates valuable discussion between laboratory and epidemiology to better understand the influenza surveillance program’s importance and how to more effectively manage the program for future outbreak or funding reduction situations.
- Prioritization
- Planning and Budget Justifications
  - Allows laboratory and epidemiology to work together more frequently for program success
Influenza Virologic Surveillance Right Size Challenges

- State to state structural variations
- Fiscal realities differ for each state
- Prioritizing influenza surveillance activities for implementation during funding declines
- Funding to support could ease and/or speed implementation
Implementation: Partnerships

The most important partnership for effective virologic surveillance is the relationship between the PHL and the epidemiologists/influenza surveillance coordinators. Collaboration to implement these guidelines will be more successful if there is broad understanding of each partner’s role.

- Epidemiologists/Influenza Coordinators
- Public Health Laboratories
- Policy Makers
- Clinical/Commercial Laboratories
- Clinicians
- CDC
Roadmap Requirements

Requirement: An essential component of virologic surveillance that is needed to produce reliable results to achieve state and national surveillance goals. These requirements should be interpreted as desired practices and not as criteria for receipt of federal funds.

We’re talking about *Functional Requirements* to:

- design and build an optimal virologic surveillance system,
- improve existing systems approaches,
- focus resources and efficiencies,
- inform policymakers, and
- justify national, state and local funding needs.
Right Size Influenza Virologic Surveillance Requirements

• Sampling (sample size and representativeness)
• Laboratory Testing
• Data Management
• Partnerships and Communications
• Quality Systems (performance metrics, benchmarks)
• Surge (outbreaks, novel events, pandemics)
• Financial Resources

Requirements developed based on multiple engagements over 2 years of stakeholder (epi and lab) input.
Surveillance Requirement - Sampling

- Establish a system that ensures efficient collection and timely flow of high quality specimens
- Establish a representative network of specimen submitters using ILINet providers, other primary care sources, and clinical and commercial labs
- Utilize a statistical, systematic approach to collect an appropriate, adequate number of specimens for testing.
- Utilize sampling approaches that ensure submitted specimens are clinically, temporally, geographically and virologically representative of the population.
- Send representative clinical specimens and/or virus isolates to CDC or a CDC-designated laboratory for national surveillance purposes.
Surveillance Requirement - Testing

• Utilize molecular detection, typing and subtyping methods (e.g., rRT-PCR).

• Maintain expertise and adequate testing capacity to achieve surveillance objectives.

• Ensure that staff members are knowledgeable in general principles of clinical virology, molecular biology and surveillance.

• Notify CDC immediately and ship unsubtypable influenza A viruses to CDC within 24 hours of detection to rule-out novel viruses.

• Routinely refer a representative subset of specimens/isolates to CDC or designated laboratory.

• Maintain capability to rapidly adopt new molecular test methods or modifications as required.

• Maintain additional influenza testing capabilities as appropriate for the jurisdiction.
Surveillance Requirement – Data Management

• Use electronic data systems that provide data in real time and utilize national standards (HL7, SNOMED, LOINC).

• All data submitted should provide:
  Specimen identifier and unique patient identifier,
  The state where specimen was collected,
  Date of birth of patient and/or age with unit (years, weeks, months, days),
  Specimen collection date,
  Specimen received date,
  Test method performed,
  Test result.

• Laboratories that have established Public Health Laboratory Interoperability Project (PHLIP) capability should also provide additional data elements if available.

• Consider incorporating data from rapid test sites and/or clinical laboratories
Surveillance Requirement – Partnerships and Communications

Establish and maintain partnerships and networks enabling communications that support the following:

- routine surveillance
- emergency preparedness and response
- data sharing
- specimen sharing

Several interrelated partnerships are needed among the public health and healthcare communities for routine surveillance including:

- CDC,
- State epidemiologist/surveillance coordinator,
- PHL,
- Clinical and commercial laboratories,
- Clinicians,
- Rapid Influenza Diagnostic Testing (RIDT) sites.
Surveillance Requirement – Quality Systems

Establish performance metrics, monitor performance and make improvements as needed to ensure national surveillance requirements are being met in an effective and efficient manner.
Surveillance Requirement – Surge

- Maintain a year-round virologic surveillance system that is flexible and scalable
- Incorporate the role and resource needs of the PHL in the state pandemic plan.
- PHL representatives should be part of state pandemic planning processes.
- Develop and maintain a laboratory pandemic surge plan
Surveillance Requirement – Financial Resources

• State influenza surveillance programs and PHLs should have adequate funding to support virologic surveillance requirements.

• State influenza surveillance programs and PHLs should coordinate planning and allocation of available funds (ELC, PHEP, EIP, state) to program and laboratory elements.

• National, state and local programs and PHLs should have effective cost accounting practices to justify resource needs and efficiently allocate available funds.

• CDC should have adequate funding to support CDC’s national virologic surveillance activities.

• Programs within CDC such as ELC and PHEP should collaborate.
Implementation Guidance

• Answers - “How to implement requirements?”
• Provides suggestions and model practices to operationalize the requirements.
• Incorporates information and model practices from pilot and exercise activities
• Aligns with the Requirements
Questions
Right Size Surveillance
Sample Size Calculators

• Determine the number of specimens that should be collected and tested to meet surveillance testing thresholds and data quality levels

• Utilize statistical sampling techniques to provide a quantitative understanding of surveillance data quality and limitations
Why use a statistical approach?

- Surveillance programs primarily conduct judgment and convenience sampling for virologic testing.
- Judgment & convenience sampling results cannot be generalized to the sampled population or easily compared between laboratories.
- Statistical-based (probability) sampling allows one to make inferences about the population of interest and more easily compare results across public health laboratories.
- Probability sampling provides a quantitative understanding of surveillance data quality and limitations.
Virologic Surveillance Goals

• **Situational Awareness:**
  – Determine the beginning and end of the influenza season and monitor the prevalence and spread of influenza viruses throughout the year. (Flu+/Medically Attended ILI+)

• **First Detection of a Novel Influenza:**
  – Detect a rare event/novel influenza virus among influenza positive surveillance specimens tested in all states at a low enough threshold for effective intervention and control measures. This objective relates to the initial detection of a novel virus which generally occurs as part of routine surveillance.

• **Novel Investigation:**
  – Determine the prevalence of the novel influenza virus (Novel Flu+/Total Flu+) within a state following the initial detection of a novel influenza virus (i.e. “deep dive”); confirm that the prevalence of a rare event does not exceed a specific percent positivity. Investigation of a novel event is typically performed using enhanced, targeted surveillance (Novel Flu+/Total Flu+)
## Thresholds

Defined as the level that triggers some action. The action may be as simple as defining a point in the influenza season or initiating investigation following detection of a novel virus.

<table>
<thead>
<tr>
<th></th>
<th>Situational Awareness</th>
<th>Novel event Detection</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Confidence Level (%)</td>
<td>Margin of Error (%)</td>
</tr>
<tr>
<td>Optimal</td>
<td>95</td>
<td>5</td>
</tr>
<tr>
<td>Mid-range</td>
<td>90</td>
<td>5</td>
</tr>
<tr>
<td>Minimum</td>
<td>85</td>
<td>5</td>
</tr>
</tbody>
</table>
Choose sample sizes based on acceptable error and level of confidence

<table>
<thead>
<tr>
<th></th>
<th>Relationship to Sample Size</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Margin of Error</strong></td>
<td>This is the amount of error that can be tolerated. A 2% error would mean that the calculated prevalence may be plus or minus 2% from the true answer. As this value decreases the sample size increases.</td>
</tr>
<tr>
<td><strong>Level of Confidence</strong></td>
<td>This is the amount of certainty that the true prevalence is equivalent to the estimated prevalence. As this value increases the sample size also increases.</td>
</tr>
</tbody>
</table>
Sample Size Calculator: Situational Awareness

Calculator A: Situational Awareness for Seasonal Influenza

- **Medically Attended ILI (MA-ILI)**: 2.2%
- **Total Population**: Alabama, 4,822,023
- **Expected prevalence of Flu+/MA-ILI**: 10%

### Sample Size

**Confidence level**: 95%

The graph, table, and output language below describe the **minimum sample size** (of unscreened MA-ILI specimens) needed to estimate the fraction of Flu+/MA-ILI with a specified **margin of error** and confidence level of 95%. This calculation is based on the estimated inputs provided above and assumes that the estimated level of Flu+/MA-ILI will be close to 10% and the total population under surveillance is 4,822,023. Use the mouse to view values in the sample size graph and scroll through sample size table.

**Graph**: Minimum Sample Size vs. Margin of Error

**Table**:

<table>
<thead>
<tr>
<th>Margin of Error</th>
<th>Sample Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.25%</td>
<td>184</td>
</tr>
<tr>
<td>4.5%</td>
<td>165</td>
</tr>
<tr>
<td>4.75%</td>
<td>149</td>
</tr>
<tr>
<td>5%</td>
<td>135</td>
</tr>
<tr>
<td>5.25%</td>
<td>122</td>
</tr>
<tr>
<td>5.5%</td>
<td>112</td>
</tr>
<tr>
<td>5.75%</td>
<td>102</td>
</tr>
<tr>
<td>6%</td>
<td>94</td>
</tr>
</tbody>
</table>

A sample size of **135** unscreened MA-ILI specimens is needed in order to be 95% confident that the true prevalence of Flu+/MA-ILI is **10% (+/- 5%)**.
Sample Size Calculators: Novel Event Detection

Calculator B: Rare/Novel Influenza Event Detection

Total Population: 4,622,023
Surveillance Scale: National

Flu+ Sample Size | MA-ILI Sample Size | Combined Samples | Data Confidence

Confidence level 95%
Expected prevalence of Flu+/MA-ILI 30%
Detection Threshold 0.1429% (1/700)

Combinations of Flu+ and unscreened MA-ILI sample sizes may be required to detect a rare/novel influenza specimen with prevalence (Rare+/Flu+) that has reached the detection threshold of 0.1429% (1/700), with a confidence of 95%. These calculations assume a total population of 4,822,023 and a Flu+/MA-ILI prevalence of 30%. Many more unscreened MA-ILI specimens are typically required than Flu+ specimens to achieve the same power of detection, particularly when the overall prevalence of influenza (Flu+/MA-ILI) is low.

To be 95% confident of detecting 1 or more rare/novel influenza events at a prevalence of 0.1429% (1/700) at a national level, the PHL must test 57 MA-ILI and 15 Flu+ specimens (with 30% Flu+/MA-ILI prevalence).
Situational Awareness for Seasonal Influenza

Inputs used to calculate the sample sizes for each state within these state population groups:
- MA-ILI = 2.2% (ILINet Baseline)
- Expected Flu+/MA-ILI = 10%

<table>
<thead>
<tr>
<th>State Population</th>
<th>Average Population*</th>
<th>95%</th>
<th>90%</th>
<th>85%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 2 Million</td>
<td>1094706</td>
<td>118</td>
<td>87</td>
<td>68</td>
</tr>
<tr>
<td>2-5 Million</td>
<td>3530463</td>
<td>132</td>
<td>94</td>
<td>73</td>
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<tr>
<td>5-10 Million</td>
<td>7193033</td>
<td>135</td>
<td>96</td>
<td>74</td>
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<tr>
<td>10-20 Million</td>
<td>15214169</td>
<td>137</td>
<td>97</td>
<td>74</td>
</tr>
</tbody>
</table>

Novel Event: National Thresholds – Low Season, 100% MA-ILI

Inputs used to calculate the sample sizes for each state within these state population groups:
- Laboratory receives and tests 100% MA-ILI specimens (unscreened)
- Expected Flu+/MA-ILI = 10%
- Confidence Level 95%

<table>
<thead>
<tr>
<th>State Population</th>
<th>Average Population*</th>
<th>1/200</th>
<th>1/165</th>
<th>1/143</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 2 Million</td>
<td>1094706</td>
<td>21</td>
<td>17</td>
<td>15</td>
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<tr>
<td>10-20 Million</td>
<td>15214169</td>
<td>290</td>
<td>237</td>
<td>205</td>
</tr>
</tbody>
</table>
How to Use the Roadmap?

Checklist: Recommended Steps for Utilizing the Roadmap

Each state will need to determine how best to implement the Roadmap recommendations. Although the requirements have been presented in a logical format, all these elements are inextricably linked. This checklist provides a series of steps that can be used collaboratively by epidemiologists/influenza coordinator and PHL leadership to assist in using the Roadmap and implementing the recommendations. Many of the recommended practices may already be in place in state or local influenza virologic surveillance systems.

- Review the document in its entirety to become familiar with the content. Although some sections may seem more relevant to program or laboratory functions, collaboration to implement these guidelines will be more successful if there is broad understanding of each partner’s role.

  - Individual sections may stand alone only when considered in context with the Introduction and the list of all Requirements. The on-line version of the Roadmap provides options to download specific sections pertinent to specific audiences (e.g., epidemiologists, PHLs, and policymakers).

- Identify key partners who should be included in discussions on specific sections or overarching surveillance decisions.

- Convolve a meeting (preferably in person) between program and laboratory staff to address all components of the roadmap document, including use of sample size calculators. Include external partners as needed to address relevant requirements.

- Refer to the list of Requirements and identify existing practices that meet the roadmap requirements as well as gaps in the virologic surveillance system. Utilize the Questions for Consideration provided in relevant sections.

- Use the sample size calculators (or the pre-calculated sample size tables in Appendix B) to assess the reliability of data (confidence levels and error rates) obtained through current sampling practices and testing volumes.

- Determine which elements or practices will provide the most significant improvement to the existing surveillance system (i.e., the most “bang for your buck”). Draft a plan for implementing recommendations. Identify the changes that can be most easily executed. Consider a staged implementation, rather than an immediate redesign of the entire system.

- Identify available funding and resources from all sources. Prioritize capabilities; ensure flexibility and capacity to respond to seasonal variations and emergence of a novel virus.

- Engage public health leaders and policymakers to garner support for implementation.
The most important partnership for effective virologic surveillance is the relationship between the PHL and the epidemiologists/influenza surveillance coordinators. Collaboration to implement these guidelines will be more successful if there is broad understanding of each partner’s role.

- Epidemiologists/Influenza Coordinators
- Public Health Laboratories
- Clinical/Commercial Laboratories
- Policy Makers
- Clinicians
- CDC
Influenza

Influenza Virologic Surveillance Right Size Roadmap

The CDC APHL influenza Virologic Surveillance Right Size project was launched in 2010 to systematically define the rationale, vital capabilities, and optimal "right size" for influenza virologic surveillance. This website provides the resulting Roadmap and other valuable information and tools.

SAVED TOPICS: Infectious Diseases, Influenza, Pandemic Influenza, Public Health Lab Systems

Influenza Virologic Surveillance Roadmap - Full Document PDF
The Roadmap consolidates requirements for all components of virologic surveillance in one document, and provides tools to assess and improve the precision of the system to support disease surveillance, response and control efforts and policy decisions. Use this link to download the entire roadmap including appendices.

Individual Roadmap Sections
For printing and easy reference the roadmap sections are separated into individual, printable documents below. Although some sections may seem more relevant to program or laboratory functions, collaboration to implement these guidelines will be more successful if there is broad understanding of each partner's role. Individual sections may stand alone only when considered in context with the introduction and the list of all Requirements.

Introduction & Virologic Surveillance Requirements
How to Use the Roadmap
Objectives: Thresholds & Representativeness
Individual Roadmap Sections
For printing and easy reference the roadmap sections are separated into individual, printable documents below. Although some sections may seem more relevant to program or laboratory functions, collaboration to implement these guidelines will be more successful if there is broad understanding of each partner’s role. Individual sections may stand alone only when considered in context with the Introduction and the list of all Requirements.

Introduction & Virologic Surveillance Requirements

How to Use the Roadmap

Objectives: Thresholds & Representativeness

Requirements Intent - Complete Requirements Section PDF
A requirement is an essential component of virologic surveillance that is needed to produce reliable results to achieve state and national surveillance goals. These are functional requirements that can be used to design and build an optimal virologic surveillance system, measure and improve existing systems approaches, focus resources and efficiencies, inform policymakers, and justify national, state, and local funding needs.

Implementation Guidance - Complete Implementation Guidance Section PDF
Suggestions and tools to assist state and local PH directors and laboratory, epidemiologists and influenza surveillance coordinators in operationalizing the Roadmap requirements.

Roadmap Sections By Topic
Sampling
Sample Size Calculator Tools
The calculators can be used to estimate the desired number of specimens to be tested to ensure adequate confidence in influenza surveillance data and detection of novel viruses. Alternatively, they can be used to demonstrate the level of confidence in the data obtained.

Sampling Requirements Intent
Sampling Implementation Guidance
Appendix A: Surveillance Sampling Process Map
Appendix B: Pre-Calculated Sample Size Tables

Laboratory Testing
Laboratory Testing Requirements Intent
Laboratory Testing Implementation Guidance
Appendix C: Laboratory Methods

Data Management
Data Management Requirements Intent
Data Management Implementation Guidance
Influenza Virologic Surveillance
Right Size Project: Next Steps

• National Teleconferences

• Sample Size Calculator Tutorial Webinars

• State Right Size Implementation

• Capture lessons learned, and enhance calculators to address influenza surveillance biases.
Right Size Roadmap Website:
www.aphl.org/Right-Size-Influenza

Right Size Calculator Website:
www.aphl.org/Right-Size-Influenza/Calculators
Questions?

For additional questions please email fluquestions@aphl.org.