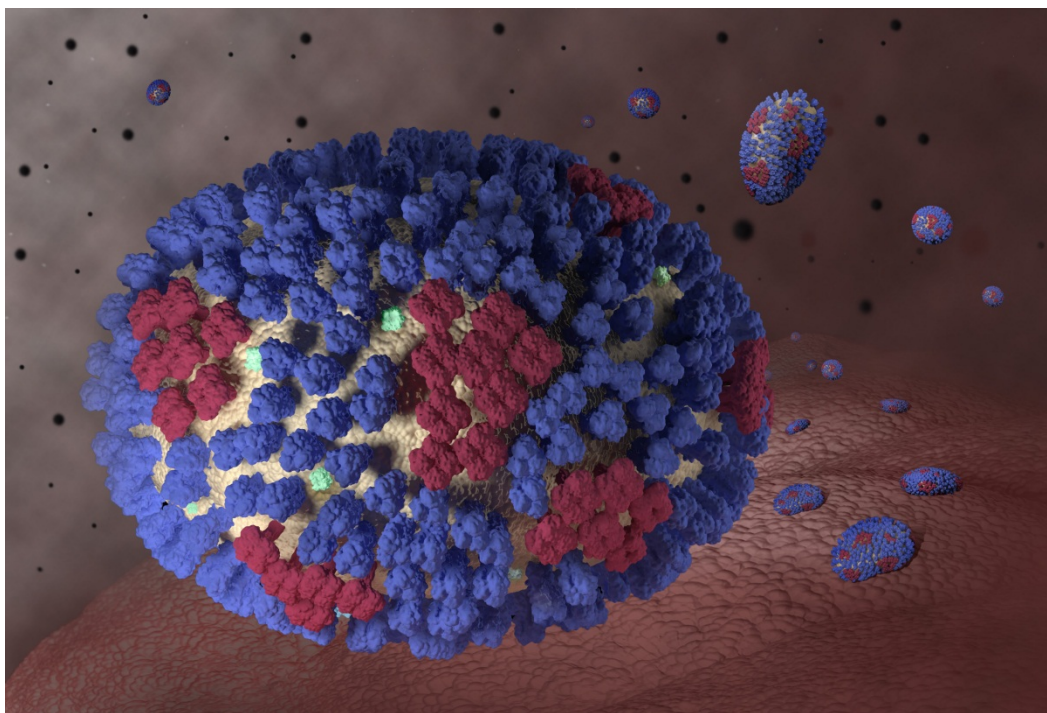


Right Size Influenza Virologic Surveillance

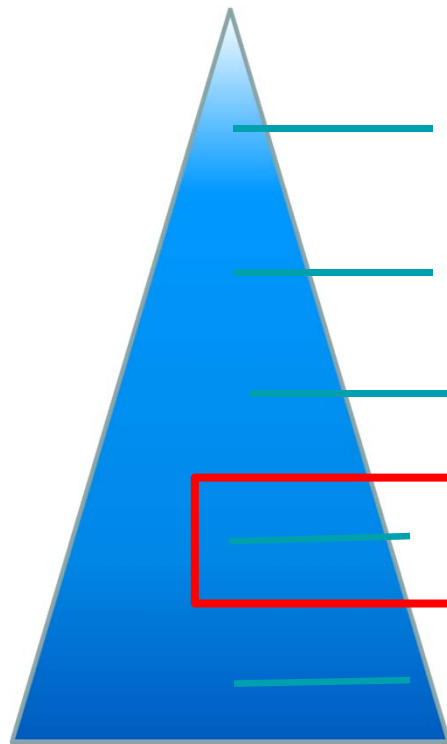


Dr. Pete Shult, PhD Wisconsin
State Laboratory of Hygiene

APHL Annual Meeting, Raleigh, NC
June 2013



Surveillance: Essential for directing prevention and control activities



Pediatric deaths reporting in all 50 States

Pneumonia and flu deaths reporting in 122 Cities

Flu hospitalizations from >80 counties in 15 states

Lab specimens from ~140 network laboratories in US

*Influenza-like illness visits at clinics and ERs
from ~3000 sites*

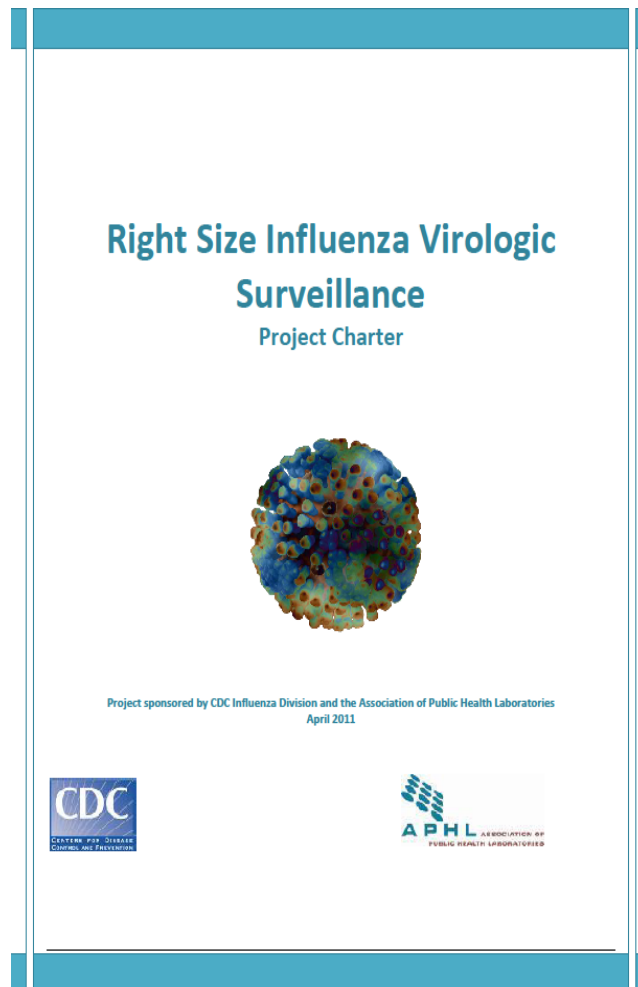
Reasons for Influenza Virologic Surveillance

- Provide situational awareness
- Inform vaccine strain selection
- Detect novel viruses or events
- Detect and monitor antiviral resistance

Surveillance Activities need to be:

- Relevant
 - PH decisions
 - Clinical community needs
 - Health Security
- Measurable
 - Data reliability
 - Impact
- Adaptable
 - Outbreaks/pandemics

The Influenza Virologic Surveillance Right Size Project and Roadmap - *The Process*



Influenza Virologic Surveillance Right Size Project - Rationale

- Post-pandemic AAR activity
- Need evidence-based decisions
 - Statistical, systematic approach lacking
- National versus state needs
 - Lack of uniform standards and data
- Capacity as driver of testing decisions
- Funding/Sustainability
 - Justify and optimize resources
- Workforce

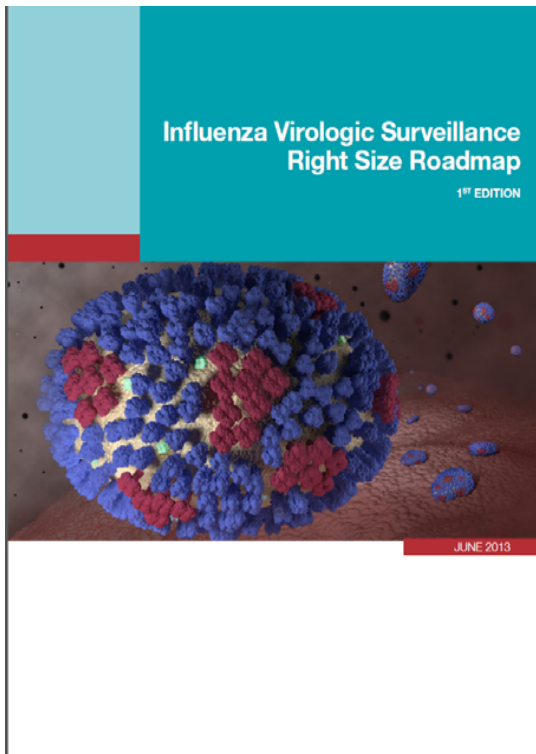


Influenza Virologic Surveillance Right Size Project - Objectives

- Define core capabilities and optimal “right-size” for influenza virologic surveillance, to support state, national and global surveillance requirements to inform policy decisions and disease prevention efforts.
- Provide statistical, systematic approach to support evidence based decisions
- Maximize available resources, redirect and build new capacity as needed for optimal surveillance.
- Create 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.
- Modeling tools to determine effective sample size needed to detect/monitor key virologic surveillance objectives.

Roadmap Requirements

Requirement: an essential component of virologic surveillance that is needed to produce reliable results to achieve state and national surveillance goals.

- Functional requirements that can be used 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
- Surge
- Financial Resources

Requirements developed based on multiple engagements over 2 years of stakeholder input.



Sampling Requirements

- Establish a representative network of specimen submitters using ILINet providers and/or other clinical primary care sources. Also, collect specimens from hospital/clinical laboratories to ensure that a subset of specimens represents hospitalized patients. Capture unsubtypable influenza positives from clinical and commercial laboratories performing PCR methods that subtype currently circulating viruses.
- Utilize a statistical, systematic approach to collect an appropriate, adequate number of specimens for testing that will provide reliable data with acceptable confidence limits to meet surveillance objectives and recommended thresholds of detection, including timely detection of novel events. The sampling methodology should limit sampling bias where possible.

Laboratory Testing Requirements

- Utilize molecular detection, typing and subtyping methods (e.g. rRT-PCR) for influenza virologic surveillance.
- Ensure that staff members are knowledgeable in general principles of virology, molecular biology and surveillance, as well as appropriate specimen collection, handling and transport methods.
- Maintain additional influenza testing capabilities (as defined in this document) as appropriate for your jurisdiction or utilize shared testing services models to ensure access to testing.

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



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

Threshold: 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.

	Situational Awareness		Novel event Detection			
			High Season		Low Season	
	Confidence Level (%)	Margin of Error (%)	Confidence Level (%)	Threshold (%)	Confidence Level (%)	Threshold (%)
Optimal	95	5	95	1/700	95	1/200
Mid-range	90	5	95	1/600	95	1/165
Minimum	85	5	95	1/500	95	1/143

Sample Size Calculator: Situational Awareness

Abbreviations

MA-ILI+ : number of medically attended patients diagnosed with influenza-like-illness
 Flu+ : number of medically attended patients diagnosed with influenza-like-illness that have influenza
 Rare+ : number of Flu+ patients that have a rare type of influenza

Calculators

▼ Sample Size Calculator for Flu+/MA-ILI+

Medically Attended ILI **2.2%**
 Total Population **6000000**
 Expected Flu+/MA-ILI+ **10%**

Sample Size | Sample Size Table | Sample Power

Confidence level **95%**

Minimum sample size (of non-prescreened 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 assumes that the estimated level of Flu+/MA-ILI+ will be close to 10% and the total population under surveillance is 6,000,000). Use your mouse to view values in the sample size graph and scroll through sample size table.

Margin of Error	Minimum Sample Size
1%	2237
1.25%	1640
1.5%	1236
1.75%	958
2%	760
2.25%	616
2.5%	500

A minimum of **760** MA-ILI+ specimens are required to estimate the actual Flu+/MA-ILI+ fraction with **95%** confidence and error bars of +/-**2%**. (This assumes that Flu+/MA-ILI+ is approximately **10%**.)



Sample Size Calculator Tables

- Quick Glance Tables Available in Roadmap.

Situational Awareness

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%

State Population	Average Population*	Confidence Level (5% Margin of Error)		
		95%	90%	85%
Less than 2 Million	1094706	121	87	69
2-5 Million	3530463	132	94	73
5-10 Million	7193033	135	96	74
10-20 Million	15214169	136	97	74

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%

State Population	Average Population*	Detection Threshold (MA-ILI specimens only)		
		1/200	1/165	1/143
Less than 2 Million	1094706	25	20	17
2-5 Million	3530463	70	57	49
5-10 Million	7193033	143	117	101
10-20 Million	15214169	302	249	215

Influenza Virologic Surveillance Right Size Roadmap Development Process

- ❑ Conducted Multiple Stakeholder Meetings
 - March 2010
 - October 2011
- ❑ 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

Table Top Exercise Key Findings

- Roadmap and calculators well received
 - Standardization
 - Enhance epidemiology/laboratory coordination
 - Prioritization
 - Planning and Budget Justifications
- Potential Barriers
 - State to state structural variations
 - Fiscal realities
- Recommendations
 - Expand implementation guidance
 - Include performance metrics

Influenza Virologic Surveillance Right Size Project: Next Steps

- Disseminate 1st Edition to public health user community for use in 2013-2014 influenza season.
- Capture lessons learned, enhance calculators to address biases.
 - Provide Roadmap 2nd edition 2014-2015.

Influenza Virologic Surveillance Right Size Project Roll Out July 2013

- National Teleconferences:
 - July 11, 2013 at 3pm ET
 - July 16, 2013 at 3pm ET
- Sample Size Calculator Webinars
 - July 23, 2013 at 3pm ET
 - July 25, 2013 at 1pm ET
 - July 29, 2013 at 2pm ET
 - July 31, 2013 at 3:30pm ET
- Watch for APHL communications.

Thank you!