

## INTRODUCTION

How much influenza surveillance is really needed? Do we need more or less laboratory testing? How do we know the surveillance data we have provides an accurate picture of what is really happening? These are frequent questions of public health decision makers in times of fiscal constraints, which escalate when the threat of novel viruses with pandemic potential seems imminent. The 2009 H1N1 events heightened awareness of these issues, demonstrating the need for a more strategic and evidence-based approach to virologic surveillance. The Department of Health and Human Services 2009 H1N1 Influenza Improvement Plan identified updated systems to ensure cost-effective virologic surveillance and implementation of standard reference methods for public health laboratory testing as key priorities.<sup>1</sup>

Public health laboratories (PHLs) and the Centers for Disease Control and Prevention (CDC) serve as the backbone of state and national virologic surveillance programs. The amount of virologic surveillance testing performed both at CDC and in PHLs has largely been determined by the capacity of the laboratory.

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. The resulting 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. The requirements provide scientific, evidence-based justification for program and laboratory resources to support virologic surveillance policy decisions. Implementation of the right size virologic surveillance guidelines will assist CDC and PHLs maximize available resources, redirect and build new capacity as needed for optimal surveillance. The primary audiences for this Roadmap are the state and local epidemiologists, influenza surveillance coordinators, PHL directors and other senior infectious disease laboratory staff responsible for coordinating policy, decisions, and relations with state epidemiologists for influenza virologic.

### Benefits of Right Sizing Influenza Virologic Surveillance:

- **Efficiency**
- **Standardization**
- **Data confidence**

### Background

A comprehensive system for influenza surveillance is important to confirm when and where influenza viruses are circulating each year and identify changes in the circulating viruses which may impact vaccine or treatment decisions or signal the emergence of a new virus with pandemic potential.

In the US, the influenza surveillance system is a collaborative effort between CDC and its many partners in state, local and territorial health departments, public health and clinical laboratories, vital statistics offices, healthcare providers, clinics, hospitals and emergency departments. The goals for national influenza surveillance include:

- Detect the onset, duration and spread of influenza activity in a geographic area.
- Measure and describe the severity of influenza during a season.
- Determine the populations affected and identify special risk groups.
- Monitor the prevalence of circulating virus types and subtypes and match to annual vaccine strains.
- Monitor genetic and phenotypic changes to circulating influenza viruses and evaluate their potential risk to public health and the need for changes to the annual vaccine composition.
- Identify and monitor novel subtypes that might signal a pandemic.
- Provide data to guide interventions in clinical and public health control measures.
- Provide information to key partners including: clinical decision makers, policy makers, emergency response officials, the media and the public.

Virologic surveillance is a key and complex component of the influenza surveillance system, informed by a variety of independent but related elements. Specific objectives of virologic surveillance include: seasonal influenza situational awareness and determination of virus strain prevalence, early detection of novel viruses or novel events, annual vaccine strain selection and antiviral resistance monitoring. The 2011 Right Size Influenza Virologic Surveillance Landscape survey provides the most recent and comprehensive summary of influenza testing and surveillance practices employed at both state and local public health entities.<sup>2</sup>

#### Influenza Surveillance

““ This is a lot of information that comes from a lot of different people — physicians, people at state health departments and state labs and in hospitals and vital statistics offices,” Brammer said. “Sometimes you step back and look at it and think it’s pretty amazing that this system keeps running week after week, and it always does. ””

--Lynnette Brammer  
Epidemiologist, Influenza Division, CDC

Source: The Washington Post, March 11, 2013<sup>30</sup>

**All state, and many local PHLs are participants in the US World Health Organization (WHO) Influenza Collaborating Laboratories Network. Influenza virologic surveillance is an essential function of all state health departments and requires a partnership between the PHL, epidemiologists including the influenza surveillance coordinators, and the health care community.**

At a minimum, virologic surveillance includes the ability to:

- Access a representative sample of clinical specimens from outpatient Influenza-like Illness Surveillance Network (ILINet) providers, other clinical primary care sources and clinical laboratories.
- Detect, type and subtype influenza viruses from clinical specimens in a timely manner using standard laboratory methods.
- Report results to providers, epidemiologists and CDC using standard electronic data systems.
- Rapidly refer unsubtypeable<sup>i</sup> influenza viruses to CDC to identify or rule out novel viruses.
- Routinely refer a subset of specimens and viruses to CDC or a CDC-designated laboratory for genetic and antigenic characterization and antiviral testing.
- Maintain the expertise, warm base (a minimum level of readiness or capacity) and surge capabilities necessary for pandemic response.<sup>3</sup>

This document is a “road map” to achieving an effective virologic surveillance system; it describes the system requirements and provides options and tools, including [sample size calculators](#), for decision-making processes and system implementation.

**In this context, 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.** These requirements should be interpreted as desired practices and not as criteria for receipt of federal funds. Each state will need to determine how to achieve these goals to meet both national and state needs, including considering options for shared services.

---

<sup>i</sup> Any influenza positive specimen that cannot be definitively typed and subtyped as a circulating seasonal influenza virus, influenza positive specimens producing non-standard or inconclusive results as defined in the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel Instructions for Use package insert.

The Roadmap recommendations were developed over three years based on extensive stakeholder input obtained through meetings, teleconferences, webinars and a table-top exercise held in December 2012. Stakeholders and exercise participants have identified numerous benefits to implementing the requirements. The right size approach:

- Standardizes virologic surveillance practices;
- Aids in the development and definition of public health surveillance priorities;
- Provides requirements, resources and statistical calculators to aid in planning and justifying budget and resource requests;
- Increases understanding and support of political leaders and the public;
- Allows epidemiologists and laboratorians to more systematically establish virologic sample sizes for different surveillance objectives and scenarios based on minimum thresholds of detection and acceptable confidence levels;
- Establishes common language between the laboratorians and epidemiologists resulting in improved communication between the two groups and better understanding of each other's needs;
- Provides information to assist decision makers in analyzing the impacts of budget cutbacks on national surveillance objectives (e.g., decreased confidence levels, reduced pandemic preparedness capacity, inability to perform testing such as virus culture).

“ Moves virologic surveillance from art to science ”

—Michael Pentella, PhD  
Director, Bureau of Laboratory Sciences  
Hinton State Laboratory Institute, Massachusetts

## Virologic Surveillance Requirements

The requirements listed here are the essential components needed for effective, efficient and economical influenza virologic surveillance.

A requirement is an essential component of virologic surveillance that is needed to produce reliable results to achieve state and national surveillance goals. These functional requirements 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.

**Sampling:** Provide year-round access to clinical specimens from ILINet providers and/or other primary care providers and clinical laboratories.

1. Establish a system that ensures efficient collection and timely flow of high quality specimens from the patient management tier of influenza surveillance to the CDC tier throughout the year.
2. 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<sup>ii</sup> influenza positives from clinical and commercial laboratories performing PCR methods that subtype currently circulating viruses.
3. 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 rare/novel influenza events. The sampling methodology should limit sampling bias where possible.
4. Utilize sampling approaches that ensure specimens submitted throughout the entire surveillance specimen submission and testing process are representative of:
  - Virus types and subtypes,
  - The entire year,
  - Geographic diversity of the population,
  - Age of influenza-like-illness (ILI) patients,
  - Disease severity,
  - Targeted populations when necessary for specific investigations.

<sup>ii</sup> Any influenza positive specimen that cannot be definitively typed and subtyped as a circulating seasonal influenza virus, influenza positive specimens producing non-standard or inconclusive results as defined in the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel Instructions for Use package insert.

5. Send representative clinical specimens and/or virus isolates to CDC or a CDC-designated laboratory for national surveillance purposes, including annual vaccine virus selection, based on annual CDC criteria and guidance.

**Laboratory Testing:** Ensure capability to detect type, subtype and characterize influenza viruses from clinical specimens in a timely manner using reliable laboratory methods.

1. Utilize molecular detection, typing and subtyping methods (e.g., rRT-PCR) for influenza virologic surveillance.
2. Maintain instrumentation, personnel, expertise and adequate capacity to test the volume of specimens needed to achieve surveillance objectives.
3. 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.
4. Notify CDC immediately and ship unsubtypeable influenza A viruses to CDC within 24 hours of detection to rule-out novel viruses.
5. Routinely refer a representative subset of specimens (and viruses) to CDC or a CDC-designated laboratory for genetic and antigenic characterization.
6. Maintain capability to rapidly adopt new molecular test methods or test modifications if a new influenza virus with pandemic potential emerges or when new technology provides improvements to virologic surveillance.
7. Maintain additional influenza testing capabilities (as defined in this document) as appropriate for the jurisdiction or utilize shared testing services models to ensure access to testing.
8. CDC: Identify, characterize, and rapidly conduct risk assessments of emerging novel influenza viruses; develop, deploy and evaluate CDC assays to assure optimum performance; utilize sequencing methods; and evaluate new technologies; and develop technical standards and guidance for virologic surveillance.

**Data Management:** Report results to providers, epidemiologists and CDC.

1. Use electronic data systems that provide data in real time and utilize national standards (HL7, SNOMED, LOINC).
2. 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.
3. Laboratories that have established Public Health Laboratory Interoperability Project (PHLIP) capability should also provide the following data elements, if available:
- Submitter information,
  - Provider identifier for the CDC Program (i.e., ILINet provider, Emerging Infections Program (EIP), other),
  - Current influenza vaccination status,
  - Antiviral treatment,
  - Travel information,
  - Patient death information,
  - Additional geographic information (e.g., county, city, zip),
  - Patient location at time of testing (inpatient, outpatient, long-term care facility),
  - Whether specimen was related to an outbreak,
  - Whether specimen was sent to CDC and if so, include specimen identifier,
  - Date of illness onset.
4. States should consider incorporating data from rapid test sites and/or clinical laboratories to supplement influenza surveillance data.

### **Partnerships and Communication**

Establish and maintain partnerships and networks enabling communications that support routine surveillance and emergency preparedness and response, data sharing and 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.

### **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.

**Surge**

1. Maintain a year-round virologic surveillance system that is flexible and scalable for rapid, effective response to support diagnostic needs and case counts in rare/novel influenza event investigations, enhance surveillance for outbreak and pandemic scenarios and has criteria to determine when to scale up and ramp down.
2. Incorporate the role and resource needs of the PHL in the state pandemic plan. PHL representatives should be part of state pandemic planning processes.
3. Develop and maintain a laboratory pandemic surge plan that addresses criteria for specimen triage, algorithm changes to improve throughput, and resource needs (e.g., staff, equipment, space, reagents and supplies).

**Financial Resources**

1. State influenza surveillance programs and PHLs should have adequate funding to support virologic surveillance requirements.
2. State influenza surveillance programs and PHLs should coordinate planning and allocation of available funds (Epidemiology and Laboratory Capacity [ELC], Public Health Emergency Preparedness [PHEP], EIP, state) to program and laboratory elements (staff, information technology, all supplies, reagents and equipment maintenance).
3. National, state and local programs and PHLs should have effective cost accounting practices to justify resource needs and efficiently allocate available funds.
4. CDC should have adequate funding to support CDC's national virologic surveillance activities as well as state/local surveillance activities that rely on federal funds.
5. Programs within CDC such as ELC and PHEP that provide funding to support other state and local programs should collaborate to ensure that changes in one program do not unintentionally impact other individual programs.

## How to Use the Roadmap

The success of the influenza virologic surveillance system in any jurisdiction requires a strong partnership and collaboration between epidemiology and the PHL, as well as active support of leadership and policy makers. The infrastructure, capabilities and surveillance system of each state differ, requiring each state to independently evaluate its current surveillance system and determine how to incorporate the right size surveillance recommendations. The Roadmap is designed to help identify "where you are, where you want to get to and how to get there" to achieve more effective and efficient virologic surveillance.

The primary audiences for this Roadmap are the state and local epidemiologists, influenza surveillance coordinators, PHL directors and other senior infectious disease laboratory staff responsible for coordinating policy, decisions, and relations with state epidemiologists for influenza virologic. The list of requirements and the descriptions of these essential elements in the Requirements Intent Section will also be useful to policymakers and leadership making resource and funding decisions. Guidance and information in this document will assist each state in identifying strengths and weaknesses in the existing virologic surveillance system, determining the optimal amount of surveillance required and identifying priority implementation activities. The Roadmap will also be a useful tool to assist in crisis management, whether the crisis is the result of detection of a novel virus, a large outbreak or a crisis of resources due to fiscal constraints. This is not intended to be an SOP (standard operating procedure) manual, but rather a guide, or "roadmap," to assist states in achieving an effective influenza virologic surveillance system.

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.

In addition to the previous Introduction and list of Requirements, this document includes three major sections:

1. Virologic Surveillance Objectives: Thresholds and Representativeness which defines the key surveillance objectives, describes specific considerations to ensure that specimens are broadly representative of the population as a whole and establishes national thresholds for detection. In this context, a threshold is defined as the level (proportion) which triggers some action.

A major outcome of the pilot studies was having epidemiology and laboratory staff come together in-person to discuss the influenza program in detail, using the roadmap document to facilitate the discussion.

2. Requirements Intent, which describes the essential elements for an effective national influenza virologic surveillance system and the rationale for applying these requirements at the state local and national level is explained.
3. Implementation Guidelines, which provides suggestions to assist states operationalize the requirements. The calculator tools that can be used to estimate the appropriate sample size for key surveillance objectives are described and guidelines for using the on-line calculator tools are provided. The model practices provided in this section are based on experience with the surveillance system since its inception in the late 1990s, a series of stakeholder meetings, a table-top exercise conducted in December 2012 testing the utility of the roadmap recommendations and data gathered through pilot projects conducted in four states during the 2012-2013 influenza season.

**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 categorical 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 policy makers).
- Identify key partners who should be included in discussions on specific sections or overarching surveillance decisions.
- Convene 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 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.