



Influenza and other Respiratory Viruses Update-- 2014

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and

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Learning Objectives

1. Review of the 2013-2014 influenza season
2. Antiviral resistance surveillance
3. Emerging diseases impacting community health
4. Review of new diagnostic assays
5. Impact of new regulatory requirements
6. Discuss surveillance strategy for 2014-2015

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Influenza *The latest information*

www.cdc.gov/flu/index.htm

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What We're Dealing with Now

- Ebola virus
- EV-D68
- MERS CoV
- Dengue fever
- Chikungunya
- Pertussis
- Measles/mumps

... So what's the big deal with influenza?

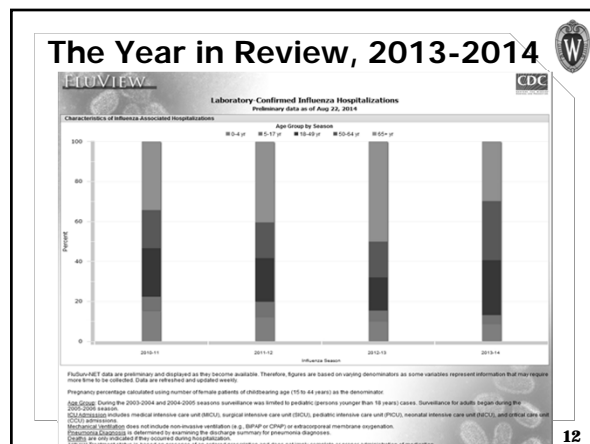
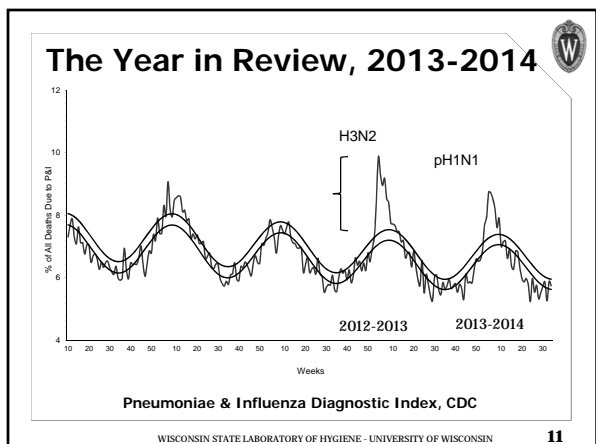
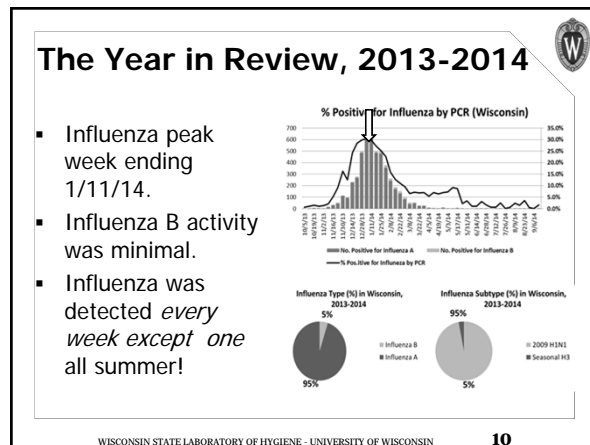
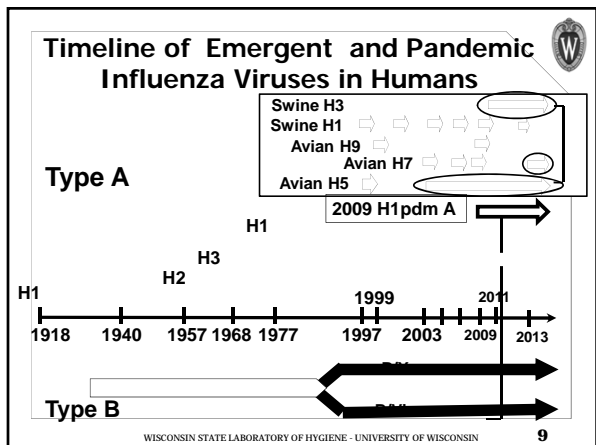
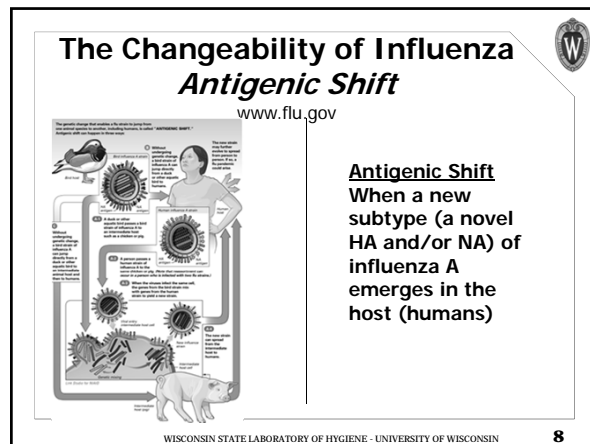
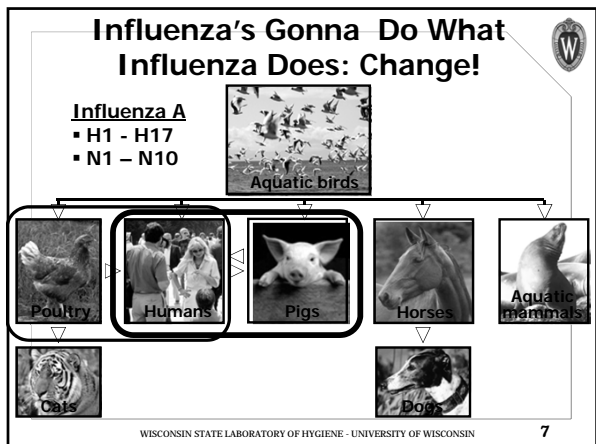
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The Changeability of Influenza *Antigenic Drift → Seasonal Influenza*

Antigenic Drift
Manifests in HA and NA as a result of continuous and gradual accumulation of point mutations in the HA and NA genes

www.flu.gov

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The Year in Review, 2013-2014

Antiviral Resistance Surveillance


Drug	2009 H1N1 % Resistant	Seasonal H3 % Resistant	Inf B % Resistant
Oseltamivir	1.2	0	0

Wisconsin: A total of 81 Influenza viruses were tested for neuraminidase inhibition and only 1 (2009H1N1) was characterized as resistant.

Data source: CDC Flu View (2014) Available at: <http://www.cdc.gov/flu/weekly/summary.htm> Accessed on: 8 October 2014.

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Early 2014-2015 Season....



PH Region	Date Received	Influenza type
NE	9/3/2014	FluA 09H1
N	9/13/2014	Flu A (H3)
N	9/13/2014	Flu A (H3)
N	9/18/2014	Flu A (H3)
S	9/18/2014	Flu B
N	9/25/2014	Flu A (H3)
SE	9/25/2014	Flu A (H3)
S	9/26/2014	Flu A (H3)
W	9/27/2014	Flu A (H3)
S	10/2/2014	Flu A (H3)
S	10/2/2014	Flu A (H3)
SE	10/3/2014	Flu A (H3)
SE	10/6/2014	Flu A (H3)
SE	10/6/2014	Flu A (H3)
SE	10/7/2014	Flu A (H3)

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It's NOT all about influenza.... other diseases of public health importance.....



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Enterovirus D68

Background


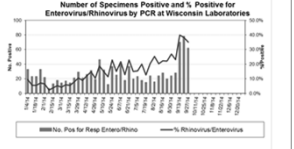
- Enteroviruses are very common respiratory viruses (10-15M/year).
- Transmission respiratory route (person-to-person)
- Cause a wide variety of illnesses.
- Types that circulate are variable & unpredictable.
- >100 EV types
- Peak activity during summer and fall.
- There are no vaccines or antiviral therapeutics.
- Children with asthma are more vulnerable.

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Enterovirus D68

Current Situation

- Mid-August to October 8, 2014, 664 cases reported from 45 states....**widespread activity**.
- As of October 8, there have been **11** CDC confirmed cases in Wisconsin.
- Not all hospitalized cases were diagnosed with EV68.** Others included rhinoviruses and other enteroviruses

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Enterovirus D68

Diagnostic Testing

- Genetically very similar to rhinoviruses.
- Most PCR assays cannot accurately discriminate!
- Some commercial PCR assays may have variable sensitivities for EV D68.
- Testing is *limited to severe adolescent cases* that meet WDPH established criteria.
- Combined NP/OP is the preferred specimen.
- WSLH is performing Enterovirus PCR on *approved* specimens.
- Specific EV D68 typing at CDC.

<http://www.slh.wisc.edu/enterovirus-d68-confirmed-in-wisconsin/>

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MERS-Coronavirus

Current Situation

- Two confirmed cases in the US in spring 2014.
- As of June 11, 2014 699 cases and 209 deaths globally.
- Activity has *slowed* since the peak in May.

Epidemic curve of MERS-CoV cases,
8 June 2014 (WHO, 2014)

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MERS-CoV

What we know!

- Initially referred to as novel coronavirus.
- Virus is *different* than SARS-Coronavirus and seasonal coronaviruses OC43, HKU1, 229E & NL63.
- First cases documented in spring 2012 (nurse & university student)-Jordan.
- All cases linked to the Middle East.
- Age range 1 to 94.
- Severe morbidity and mortality.
- Limited human-to-human transmission.
- Genetically stable.

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Are we at Risk for MERS-CoV?

Points of entry and volume of travelers on flights to the United States and Canada from Saudi Arabia and the United Arab Emirates — May–June 2014. Source: (MMWR, 2014)

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Influenza

Diagnostic Technology Update

RIDTs **Automation** **NGS**
Multiplex **REGULATIONS**
PCRs **Rapid** **Molecular**

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Influenza Molecular Tests - PCR

Available at the WSLH

- CDC Flu rRT-PCR Dx Panel – FDA cleared
 - A, B, H1, H3, 2009H1, H5
- Flu B lineage testing – FDA cleared
- H7N9 available under EUA
- H3v evaluation for FDA approval
 - Multi-site PHL clinical study

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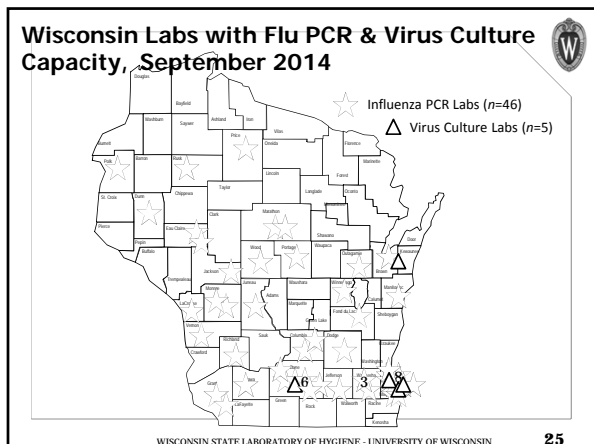
Influenza Molecular Tests - PCR

Commercially Available - FDA Cleared

- CDC periodically updates list
- More and more clinical labs using these
- Literature in general indicates high level of performance
- Concerns:
 - Detection of novel influenza A's
 - Variable subtyping capabilities

<http://www.cdc.gov/flu/professionals/diagnosis/molecular-assays.htm>

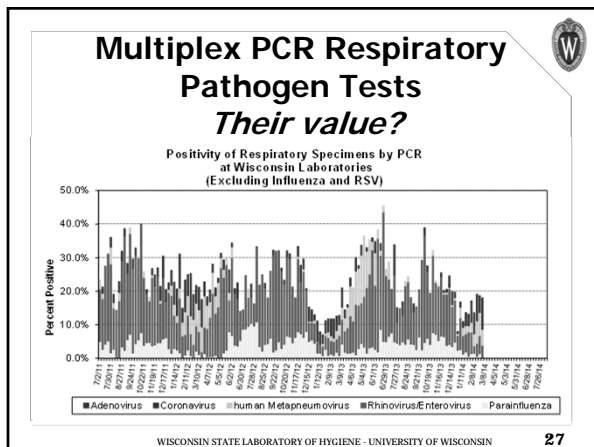
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Multiplex PCR Respiratory Pathogen Tests

Name	Manufacturer	# Targets	Targets 510(k) Cleared	Sample >Result	YR
FilmArray Respiratory Panel	BioFire	20	Viral & Bacterial	Yes	2012
eSensor Respiratory Virus Panel	GenMark Diagnostics	14	Viral only	No	2012
xTAG Respiratory Virus Panel	Luminex	12	Viral Only	No	2008
xTAG Respiratory Virus Panel FAST	Luminex	8	Viral Only	No	2011
Verigene Respiratory Virus Plus	Nanosphere	7	Viral Only	Yes	2011
Prodesse ProFlu+	Hologic Genprobe	3	Viral Only	No	2008
Simplexa FluA/B + RSV	Focus Diagnostics	3	Viral only	No	2012
Quidel Molecular RSV + hMPV	Quidel	2	Viral Only	No	2013

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Rapid Influenza Diagnostic Tests (RIDTs) A perennial discussion

www.cdc.gov/flu/professionals/diagnosis/clinician_guidance_ridt.html

www.jointcommission.org/siras.aspx

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Rapid Influenza Diagnostic Tests The Next Generation

- Incorporates reader instrument
- Reduces subjectivity
- Improved sensitivity
- CLIA-waved
- Data transmission capabilities
- A step in the right direction

Quidel Sofia Influenza A & B

B-D Veritor Influenza A & B

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Rapid Influenza Diagnostic Tests An Unique Application for Surveillance

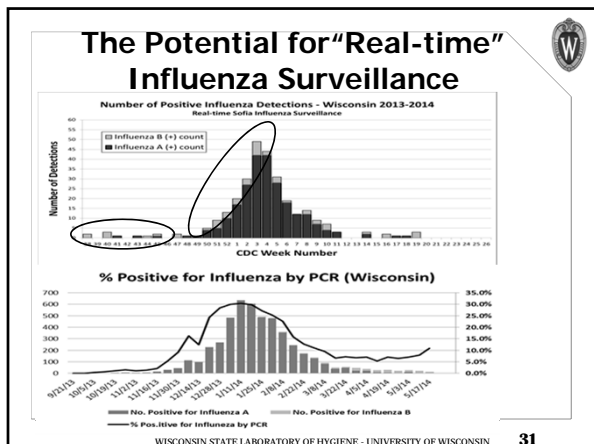
Virena Cellular-Linked (Cloud-Based) System for Near Real-Time Surveillance of Influenza Viruses A and B Using the Sofia® Fluorescence Immunoassay Platform

Figure 3. Virena wireless system

Figure 5. Transmission of Surveillance Data

Options for the Control of Influenza VIII Meeting, Sept. 2013, Cape Town, South Africa

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Improving RIDT Performance

There are new regulations in our future

<https://www.federalregister.gov/articles/2014/05/22#food-and-drug-administration>

- New nomenclature proposed:
Influenza Virus Antigen Detection test

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- ### If you are an RIDT(IVAD) user...
- **What would the new regulations entail?**
 - Reclassifying RIDTs from **Class I** to **Class II**
 - Add **"special controls"** to ensure device safety and effectiveness
 - Set minimum clinical performance criteria for sensitivity and specificity
 - Identify appropriate comparator tests for new assays
 - Accuracy assessed by manufacturers **each year** and when **novel strain emerges**
 - **When will this happen?**
 - **Possible impacts:**
Better tests? Fewer tests?
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Rapid Influenza Diagnostic Tests

Molecular Results in Minutes!

- Novel isothermal amplification technology
- Amplification of target NA at a single temperature
- Results in ~15min
- Point-of-care testing

J. Clin. Microbiol. published ahead of print 10 September 2014, doi:10.1128/JCM.01639-14

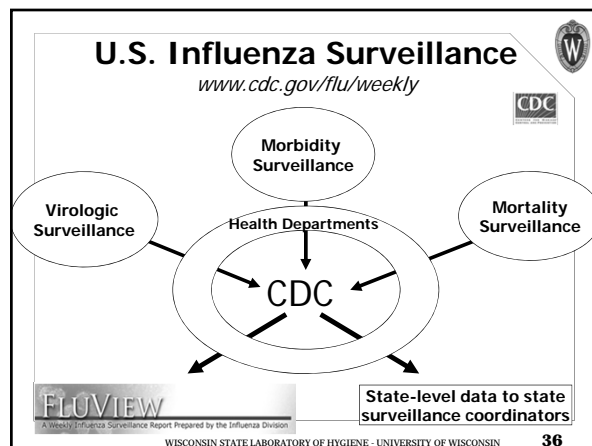
J. Clin. Microbiol. September 2014 52:3339-3344

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Update on Ongoing Efforts to "Right-Size" Influenza Virologic Surveillance

Right Size Roadmap
<http://www.aphl.org/aphlprograms/infectious/influenza/Pages/Influenza-Virologic-Surveillance-Right-Size-Roadmap.aspx>

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Influenza Virologic Surveillance Goals

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

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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.

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Using Alternative Data for Influenza Virologic Surveillance

• **What is Alternative Data ?**


Alternative data is existing virologic data from non-public health laboratory sources that can be used to supplement public health laboratory testing data for improved situational awareness.

- Include data from PCR(preferred) or RIDTs
- **Benefits to surveillance:**
 - Enhance influenza seasonal situational awareness
 - Identify positives during low prevalence periods
 - Detect potential geographic clusters
 - Detect institutional outbreaks

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Laboratory Surveillance Plan, 2014-2015

What YOU need to know!



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Influenza Surveillance in Wisconsin

Multi-element approach

1. Rapid Influenza Diagnostic Testing (RIDT) Sites
 - >50% of Influenza testing in WI.
 - Next gen tests have eliminated subjectivity and improved performance characteristics.
 - "Real-time" surveillance.
 - Confirmatory testing during periods of low prevalence!


WSLH can provide confirmatory testing for out-of-season positives and the first two positive influenza A and influenza B specimens.

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Influenza Surveillance in Wisconsin

Multi-element approach

2. Enrolled Surveillance Sites
 - 18 labs in 5 public health regions.
 - Provide randomized specimens weekly.
 - WSLH provides influenza PCR and multiplex PCR RVP testing.




Request to continue to submit the first 3 specimens per week with influenza test requests to WSLH.

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Influenza Surveillance in Wisconsin

Multi-element approach

- PCR Labs
 - “Gold Standard” testing.
 - Ability to type, subtype and antiviral resistance markers.
 - Provide weekly testing data summary reports.
 - 46 WI PCR labs!



Wisconsin Labs with Flu PCR & Virus Culture Capabilities, September 2014
 * Influenza PCR Labs (n=46)
 * Virus Culture Labs (n=5)

Request to report both the *number positive* and the *number tested* weekly.
 **Send Flu A unsubtypeable specimens when subtyping for both 2009 H1N1 and seasonal H3 were attempted (Ct<35).

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Laboratory-based Surveillance Summary

RIDT Sites:
 * Confirmatory testing for the *first 2 positive* Influenza specimens

Enrolled Regional Sites:
 * Send the *first 3 specimens collected per week* regardless of results

PCR Labs:
 •Report the *number tested* and *number positive*
 •Influenza A-Unsubtypable (Ct<35)


All Labs:
 •Send those with international travel histories
 •*Sampling* of influenza-related hospitalizations
 •Unusual presentations/results
 •Contact with swine

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Reporting Lab Results

There are two options.....

- Web-based reporting
 - http://
 - Select the method below to enter data; you must also select "Next".
 - Web-based Reporting
 - Print
 - Cancel
- FAX reporting
 - Wisconsin State Laboratory of Hygiene, University of Wisconsin
 - 1600 University Avenue, Room 1000, Madison, WI 53706-1600
 - Phone: 608-262-1021, Fax: 608-262-1021, Email: slh@wisc.edu
 - Website: www.wisconsin.gov
 - Wisconsin State Laboratory of Hygiene, University of Wisconsin
 - 1600 University Avenue, Room 1000, Madison, WI 53706-1600
 - Phone: 608-262-1021, Fax: 608-262-1021, Email: slh@wisc.edu
 - Website: www.wisconsin.gov



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NEW! Real-time reporting

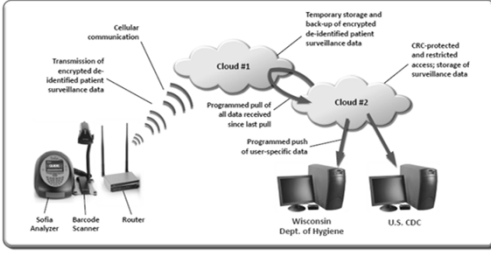


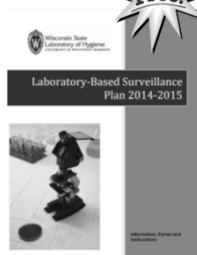
Image source: (2013) John Tamerius, Guidel Corp., Influenza Options VIII Meeting

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What is the WSLH able to provide to support participating labs?

- Specimen collection supplies.
- Specimen shippers & packaging supplies.
- NO cost specimen transport.
- Influenza confirmatory testing.
- Influenza PCR validation specimen panel.
- Weekly updated surveillance data (*B. pertussis*, *Influenza*, *RSV* & others).
- Laboratory Surveillance Reports

Free!





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Influenza Surveillance Strategy

WSLH Surveillance Coordinators

- Erik Reisdorf
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- Mary Wedig
 Electronic Reporting Coordinator
 Ph: 608-890-0353
mary.wedig@slh.wisc.edu

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Thank you!  

Your participation in the Wisconsin surveillance system is **vital** to monitor for emerging novel strains with pandemic potential and other pathogens that impact community health.

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