

Novel Influenza A H1N1 Update



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www.cdc.gov/H1N1flu



Objectives

- Describe the initial detection of the novel H1N1
- Give an update of current status
- Discuss issues around test development and use



Increasing Detection of Swine Flu



The NEW ENGLAND
JOURNAL of MEDICINE

Shinde, NEJM 2009

- Increasing numbers of swine influenza cases being detected over past five years from improved surveillance – *Shinde, NEJM 2009*
- Increasing efforts at states, CDC, and USDA to investigate human cases of swine influenza
- Limited secondary transmission



Swine Influenza A (H1N1) Infection in Two Children – Southern California, March–April 2009

On April 21, this report was posted as an MMWR Early Release on the MMWR website (<http://www.cdc.gov/mmwr>).

Novel Swine Influenza Detected

- Southern California, 2009 - *MMWR 58(15);400-02*
 - April 13 – 10 yo boy, recovered
 - April 17 – 9 yo girl, recovered
- Exposure to swine unknown
- Surveillance showed no other unsubtypeable influenza A PCR results

Detection of First Case



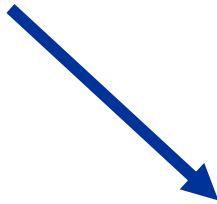
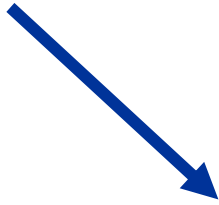
- **Mesoscale device used to diagnose influenza in 10 year old boy during clinical trial run by Naval Health Research Center (NHRC) in San Diego on April 1, 2009**
- **Result is influenza A positive, however, H1, H3, H5 negative**

Detection of First Case



- **San Diego public health notified**
- **Recommends sending specimen on to designated reference laboratory in Wisconsin as part of the clinical trial**

Detection of First Case



Wisconsin State
Public Health Laboratory

- **“Unsubtypable” confirmed by reference laboratory and by designated State Public Health Laboratory using FDA-cleared 5 Target PCR**

Detection of First Case

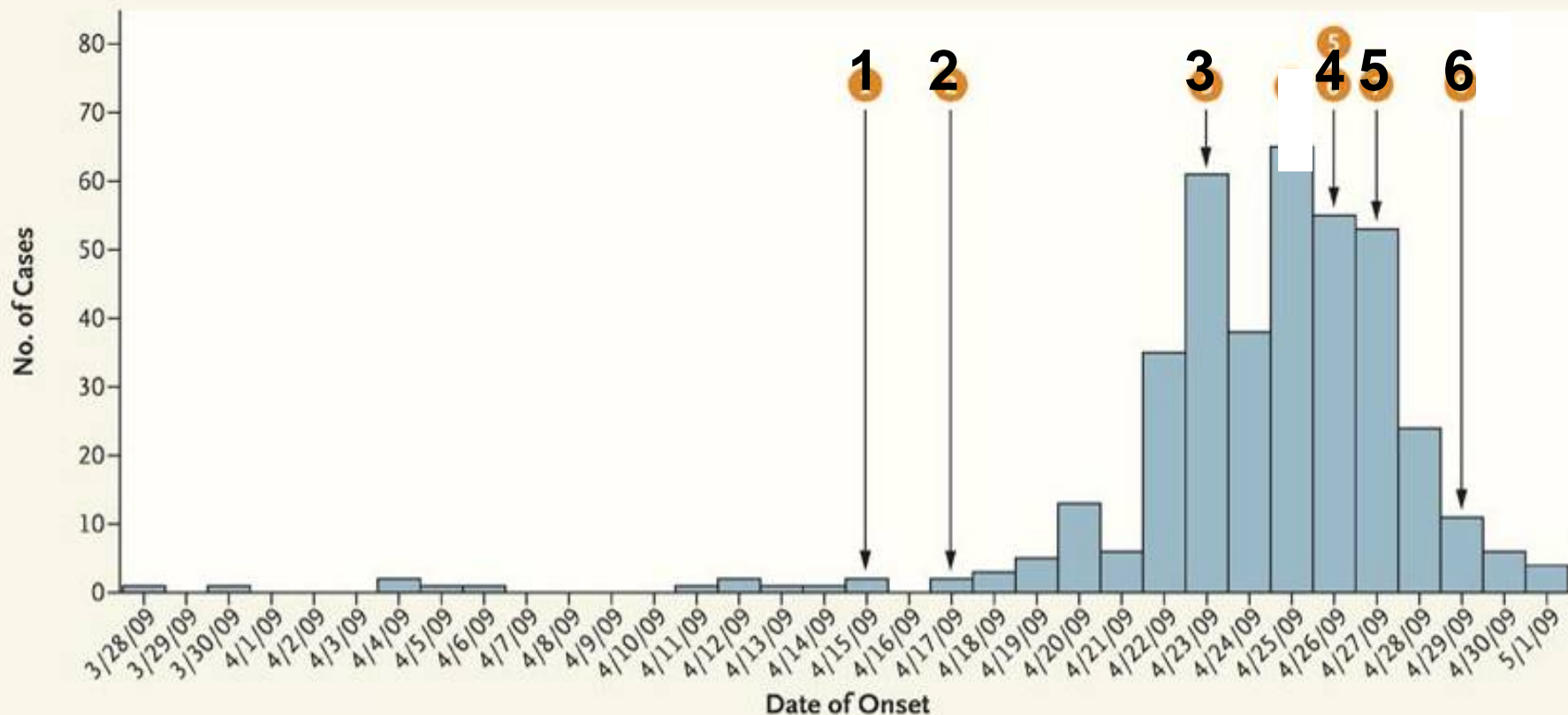


Wisconsin State
Public Health Laboratory



- Specimen tested at CDC
- Identified as a novel H1N1 Swine, triple reassortant, where are the infected swine?
- Novel case reported to WHO...end of story?

Confirmed Cases of Human Infection with Novel Influenza A (H1N1) with Known Date of Illness Onset, United States, March 28 – May 5, 2009



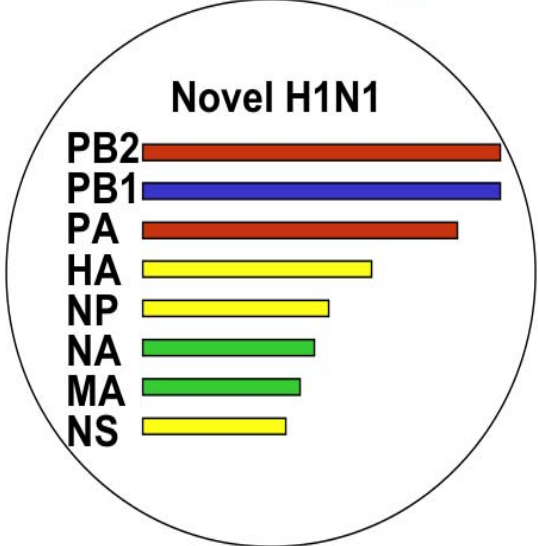
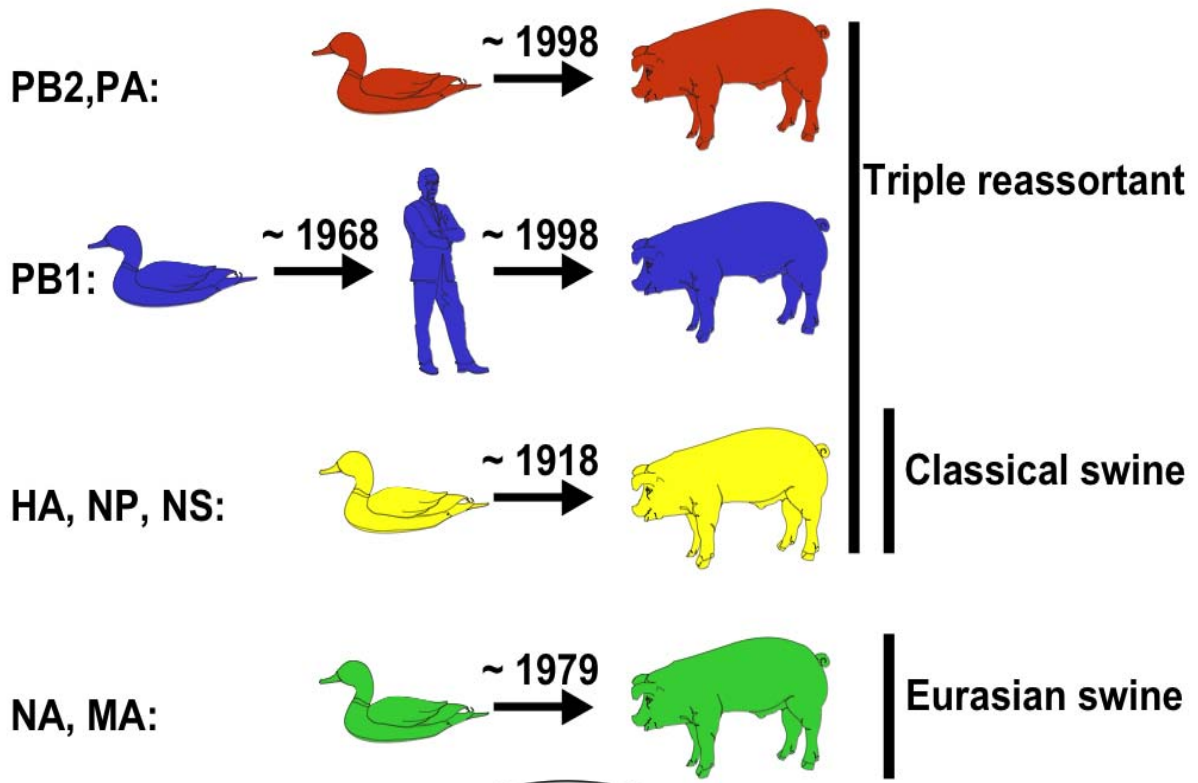
Novel Swine-Origin Influenza A (H1N1) Virus Investigation Team. *N Engl J Med* 2009;10.1056/NEJMoa0903810

1. Patient 1
2. Patient 2
3. Recognition of potential match between Mexico and US viruses
4. US declares a public health emergency
5. WHO raises to Pandemic Phase 4
6. WHO raises to Pandemic Phase 5

www.cdc.gov/H1N1flu



Gene Segment Host and Year of Introduction



**Origin of
“Swine-Origin”
H1N1
*Garten et al
Science, 2009***

Response to H1N1

- Strategic National Stockpile
 - Distributed 25% pro rata supply
- Enhanced Surveillance Initiated
- PCR panH1N1 kits for testing
 - Development at CDC, EUA at FDA, manufacture at ATCC, and ready to ship in ~ 2.5 weeks
 - Distributed Kits, so far:
 - Domestic: 95 labs
 - DOD: 15 labs
 - International: >250 labs in 140 countries
- Virus Characterization
 - >1000 genes sequenced from >260 viruses
 - Submitted to GenBank

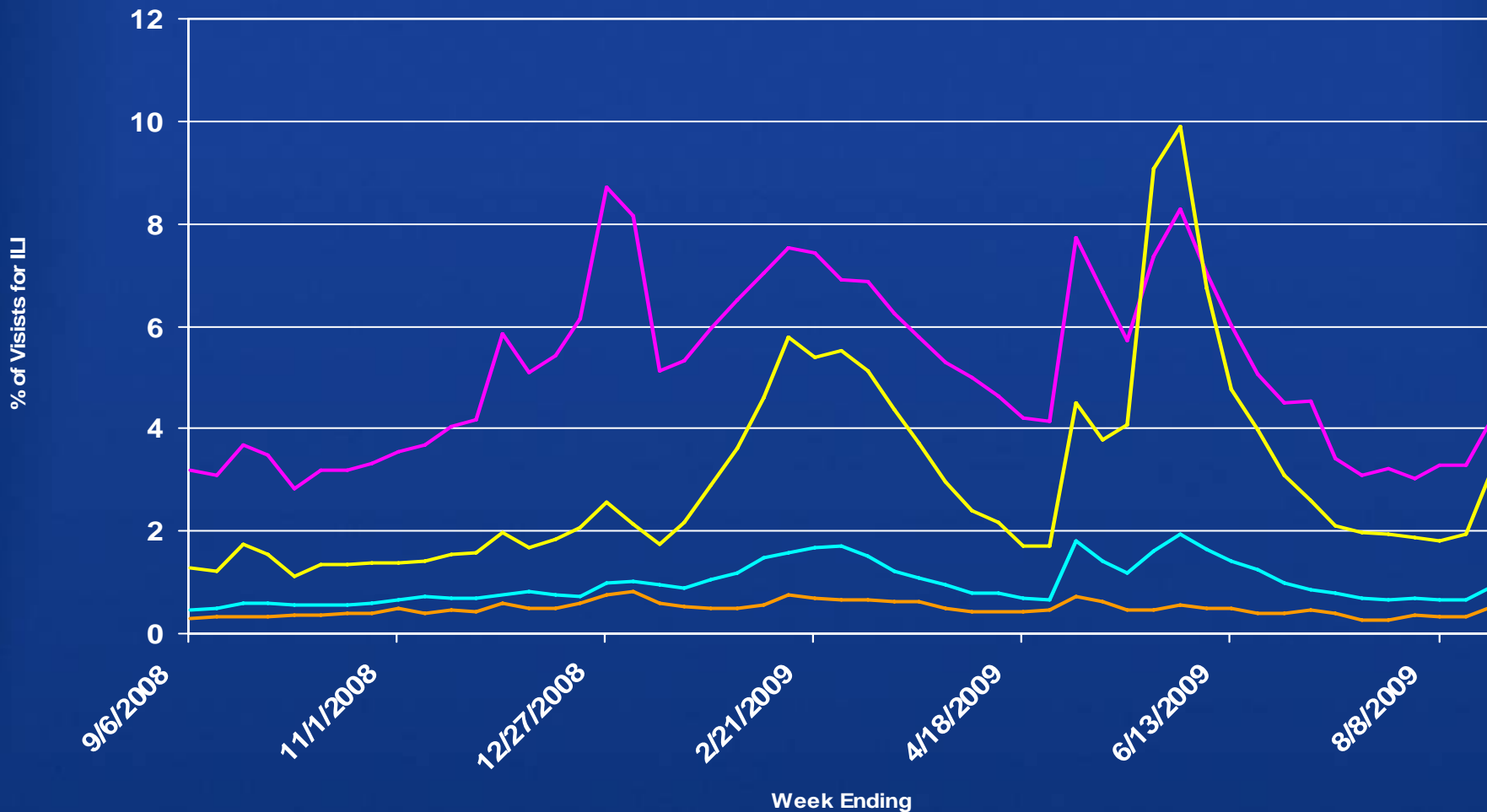


H1N1 Current Status

- Lab-Confirmed Cases
 - 44,317 total cases when reporting stopped in July
 - As of August 28, 2009
 - 8,842 hospitalized
 - 555 deaths
- Represents approximately 3 M cases
- Overall activity has declined since schools closed, but focal areas of activity have increased
- Viruses in US and Internationally show no evidence of significant genetic/antigenic change



Percentage of Visits for Influenza-like Illness (ILI) Reported by the US Outpatient Influenza-like Illness Surveillance Network (ILINet), novel 2009-H1N1 – 01 SEP 2009



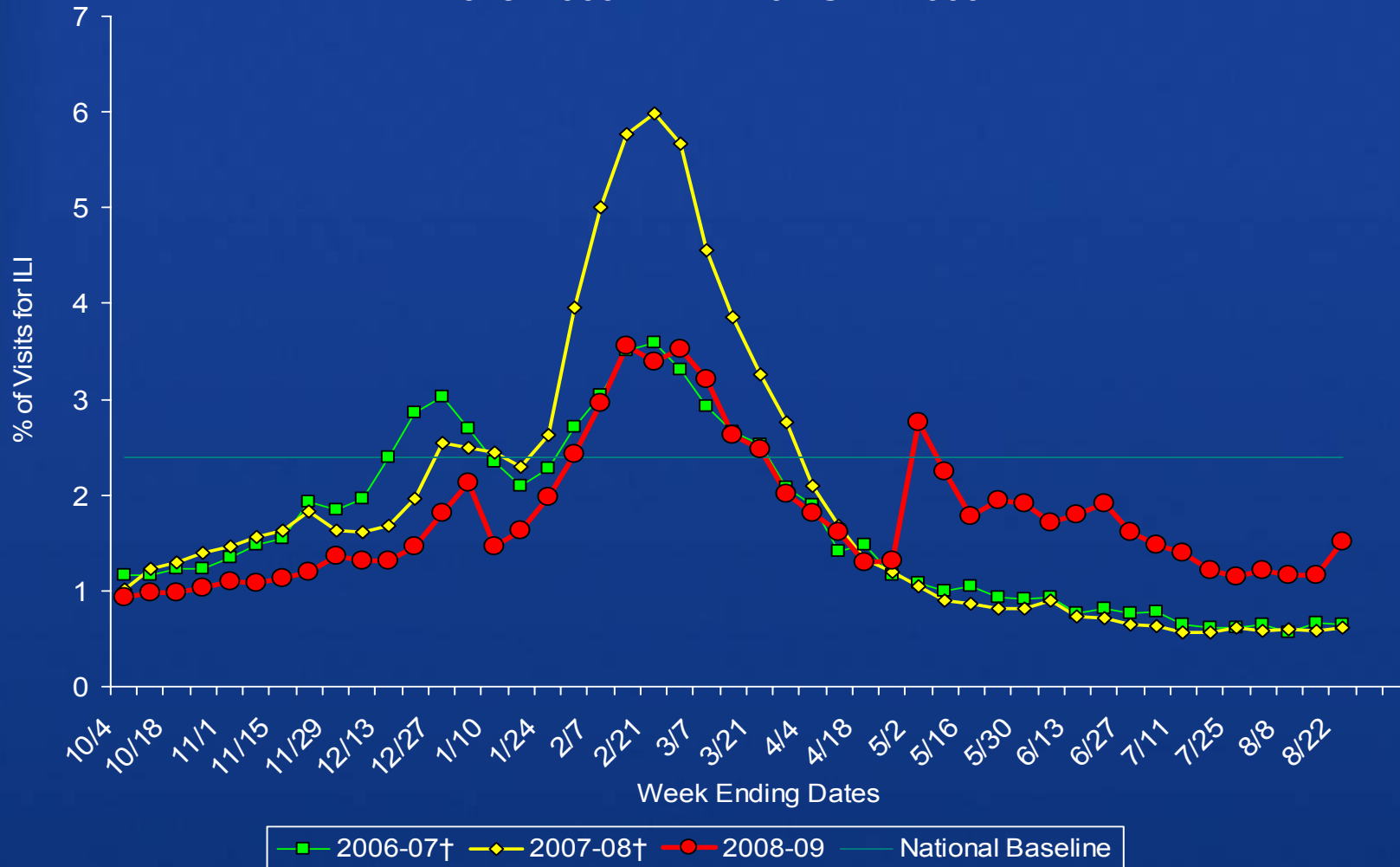
— %ILI 0-4
 — %ILI 5-24
 — %ILI 25-64
 — %ILI 65 and Older

Data are provisional and will not be officially released by the CDC until 1100 EDT
 Internal Use Only (FIUO)--For Official Use Only (FOUO) -Sensitive But Unclassified (SBU)
NOT FOR FURTHER DISTRIBUTION



Epidemiology/Surveillance

Percentage of Visits for Influenza-like Illness (ILI) Reported by the US Outpatient Influenza-like Illness Surveillance Network (ILINet), National Summary 2008-09 and Previous Two Seasons novel 2009-H1N1 – 01 SEP 2009



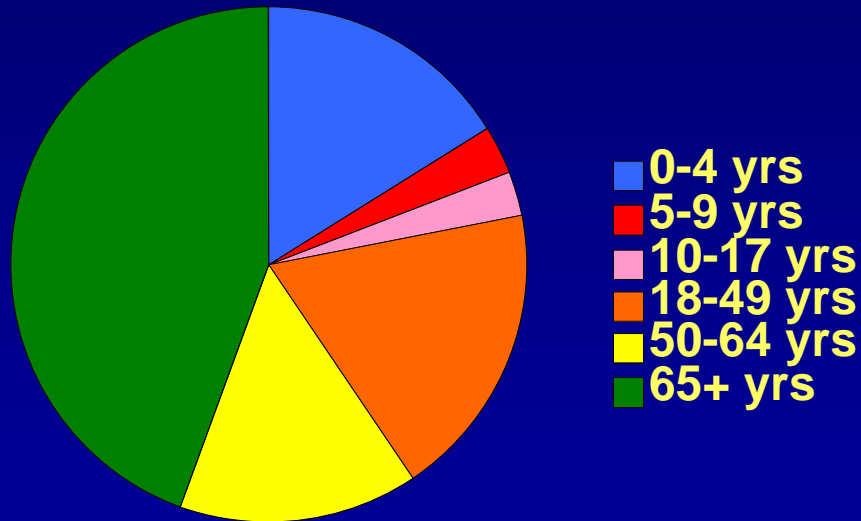
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Teens and young adults disproportionately affected

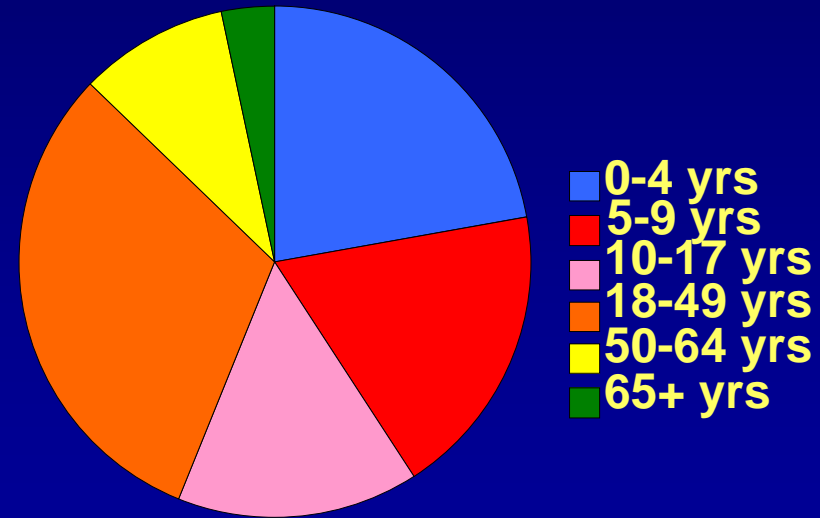
Few cases among elderly

Seasonal 2007-08



N=3,930

2009 H1N1 (April - Jun)



N=312

*April 12-June 30

www.cdc.gov/H1N1flu



Testing for 2009 H1N1

- Pandemic preparedness included diagnostic development
 - PCR for influenza at CDC
 - Point of Care devices through HHS-CDC contracts
- Pandemic preparedness included support
 - Public Health Laboratory staff
 - Equipment
 - Reagents
- New tests developed
 - EUA for Focus Diagnostics
 - LDTs for H1N1



PCR Assay

Lindstrom et al



CDC



CDC 5 Target PCR



Applied Biosystems



AB 7500 Fast DX RT-PCR



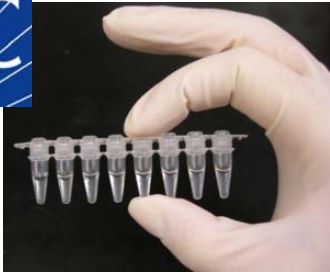
FDA

Sept 2008

- FDA cleared in September 2008 with special controls
- Five targets (A, B, H1, H3, H5)
 - All targets maintaining high sensitivity, specificity
- Reagents distributed from CDC to qualified laboratories

PCR Assay

Lindstrom et al



CDC 5 Target PCR



AB 7500 Fast DX RT-PCR



Sept 2008

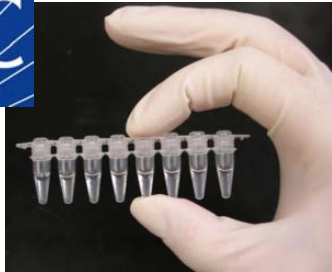
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May 2009

- FDA grants Emergency Use Authorization
- New targets: Influenza A (swine) and H1 (swine)
 - All targets maintaining high sensitivity, specificity
- Reagents distributed from CDC to qualified laboratories
- Qualified laboratories asked to verify accurate testing with 5 known positive specimens
- Protocol published at WHO website

PCR Assay

Lindstrom et al



CDC 5 Target PCR



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**2009/2010
Potential**

- ? Submission of additional targets for 510K
- ?Submission of EUA/510K for additional platforms



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Highlights

IRR website goes live!



Products

- Kits
- Proteins
- Reagents

Influenza Reagent Resource (IRR) was established by the Centers for Disease Control and Prevention(CDC)

- Reagents distributed by CDC's Influenza Reagent Resource under contract with ATCC, www.influenzareagentresource.org
- Orders available through fluorder@cdc.gov
www.cdc.gov/H1N1flu

Point of Care: Mesoscale Diagnostics



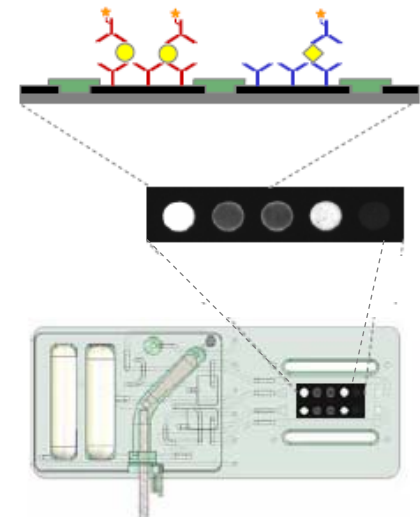
Put swab in cartridge



Insert cartridge into reader

- Detects A, B, H1, H3, H5 antigens
- Hands-off 15 min test
- Reader controls reagents, fluidics, detection, results
- Clinical trials underway
- Seeking EUA for use this fall
- CLIA complexity determination?

Monoclonal antibodies detect antigen with electrochemiluminescence



Rapid Influenza Diagnostic Tests

- Nine FDA-Approved Rapid Influenza Diagnostic Tests
- Evaluated seven RIDTs compared to PCR
 - Sensitivity ranged 18-69%
- Interpretation
 - Positive results = flu likely in specimen
 - Negative results = can not rule out flu
 - Caution with cohorting or return to settings where transmission is a concern



Antiviral Resistance

- Oseltamivir Resistance in US
 - H1N1 seasonal – 99.6% (1123/1128)
 - H3N2 – 0% (0/222)
 - B – 0% (0/635)
 - H1N1 novel – 0.6% (7/1117)
- Zanamivir Resistance
 - None reported for all subtypes/types
- Capacity for antiviral resistance testing is limited
 - Pyrosequencing: plan to expand at PHLs
 - Functional testing: difficult/costly to perform



Observations

- FDA Approval of CDC 5 Target Test
 - Costly to develop, to clear, and to maintain
 - Allowed for standard quality, rapid distribution
- EUA for swine primers
 - Easier to implement because of 5 target clearance
 - Allowed distribution to qualified laboratories
 - Ends when emergency ends
- WHO web posting of swine PCR protocol
 - Allowed for rapid increase in detection of 2009 H1N1
 - Led to laboratory developed tests
 - Distributed testing helps with surge, hard to verify accuracy
- Antiviral testing needs greater availability
- Rapid test performance is variable, clear need for POC detection



Questions?

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