

Influenza Diagnostics Update

Michael Shaw



www.cdc.gov/H1N1flu



Actions for Diagnostic Preparedness Initiated 2007

1. Develop New Diagnostic Tests and Improved Diagnostic Capabilities
2. Improve Surge Capacity
3. Implement Proficiency Testing
4. Develop Policy and Regulatory Preparedness
5. Improve Access to Viruses and Reagents
6. Provide Guidance for Clinicians
7. Improve Virologic Surveillance



Influenza Diagnostics Landscape

(as of Summer, 2012)

Legend:

FDA-cleared	FDA-cleared after EUA	LDT, IUO, or RUO After EUAs Terminated	LDT, IUO, or RUO
-------------	-----------------------	--	------------------

Traditional Flu Testing

Traditional Cell Culture
Multiple Cell lines:
pRMK, MDCK, others

Shell vial cultures
•R-Mix & R-Mix Too



DFA/IFA Immunofluorescence

IMAGEN Influenza A and B

D3 FastPoint Influenza A/B

D3 Ultra 2009 H1N1 Influenza A Virus ID kit

SimulFluor Flu A/Flu B

ge™ A/H5N1 Flu Test

IQuum Liat Influenza A/2009 H1N1

Xpert Flu A Panel (A/2009H1 targets)

EUA-NAATs

Terminated June 26, 2010

GeneSTAT 2009 A/H1N1 Influenza

Influenza A H1N1 (2009)

Prodesse ProFlu-ST Influenza A assay

IMDx 2009 Influenza A H1N1 rt RT-PCR

Influenza H1N1 09 Prime rRT-PCR

State PHLs

DoD Qualified Labs



Moderate Complexity

LDTs RUO Kits

Esensor RVP (14+)

ARUP Labs: ELITech Molecular Diagnostics 2009-H1N1 Influenza A Virus rt RT-PCR test

TessArray RM-Flu

RealTime Ready Influenza A/H1N1

Viracor Labs 2009 H1N1 Influenza A RT RT-PCR

ResPlex II (Diatherix Labs 2009 H1N1-09 Flu test)

Infinity RVP Plus

NucliSENS Easy Q Influenza A/B

ResPlex III



High Complexity NAATs 510(k) Cleared

Real-Time RT-PCR Detection and Characterization Panel

Prodesse Profast+ (sH1/sH3/pH1N1) - Prodesse Profu (A, B, RSV)

xTAG RVP Assay (inc. A, B, H1, H3) RVP FAST (inc. A, B, H1, H3)

Simplexa Flu A/B and RSV Simplexa Influenza A H1N1 (2009)

JBAIDS Nucleic Acid Amplification, Novel Influenza A Virus, A/H109, H1, H3, H5 (Asian Lineage); Flu B

Quidel Molecular Influenza A+B Assay

artus® Infl A/B RG RT-PCR Kit

Idaho Technology Lim Array Respiratory Panel

Xpert Flu Assay (Flu A&B, 2009H1)

IQuum Liat Influenza A/B Assay

Verigene RVNATsp System Verigene RVNAT (RV+)

Antigen Tests Waived

Verigene BD Flu A+B

BinaxNOW A&B

Quickvue A+B

SAS FluAlert A SAS FluAlert B

Clearview Exact II Influenza A&B

Sofia™ Influenza A+B FIA

3M Rapid Detection Flu A+B test

Directigen EZ Flu A+B

Osom: Influenza A+B

TRU FLU A&B

Xpact(R) Flu A&B

SAS FluAlert A + B Test

Status® (BioSign) Flu A+B

Influenza Diagnostics Strategy

- 1. Point-of-Care Tests:** Reliable, simple point-of-care tests in outpatient and ambulatory settings
- 2. Hospital Tests:** Timely, accurate influenza tests in hospital settings
- 3. Support Manufacturers:** Greater support for manufacturers by providing viruses, reagents, specimens, and standards
- 4. Optimize Tests in Use:** Field assessment and optimization of new tests in practice settings to optimize their use during pandemics and emergencies
- 5. Multirespiratory Tests:** Capability to diagnose multiple respiratory pathogens
- 6. Immunity Tests:** Higher throughput and point-of-care tests to determine immune status
- 7. Novel Influenza Detection:** Rapid detection of reassortant and novel non-human influenza viruses



Commercially Available Influenza Point of Care Tests

- More than a dozen FDA-cleared rapid influenza diagnostic tests available
- All provide results in <20 mins, however many with low sensitivity and specificity
- Guidance developed by CDC to improve test practice and interpretation
http://www.cdc.gov/flu/pdf/professionals/diagnosis/testing_algorithm.pdf
- Working with FDA on new CLIA Waiver Guidance



Directions for Diagnostic Development: PCR Then, Sequencing Now

PCR for Influenza Diagnosis

2007: No FDA-cleared influenza PCR devices

- ✓ Sep 2007 – FDA clears first influenza A/H5 assay, developed by CDC, sponsored by BARDA
- ✓ Sep 2008 – FDA clears CDC, BARDA-sponsored 5-Target PCR; LDTs remain mainstay in high complexity clinical labs
- ✓ 2009-2010 – FDA approves EUA and clears CDC, BARDA-sponsored pdm H1N1 PCR

2012: Seventeen FDA-cleared influenza PCR devices

- ✓ PCR IVDs on nine platforms (+ numerous LDTs)
- ✓ Lab practice shifting towards moderate complexity; near-patient testing



Directions for Diagnostic Development: PCR Then, Sequencing Now

Sequencing for Influenza Diagnosis

- ✓ Improved accuracy, rapidly decreasing cost, commercial platforms now available
- ✓ Technology ready, regulatory pathway uncharted, opportunity for USG push as with PCR
- ✓ High multi-use potential:
 - ✓ Influenza and other pathogens can use same platform and technology
 - ✓ Antimicrobial resistance and clinical markers detected at same time
 - ✓ Rapid capability to identify emerging novel influenza since no new reagents needed, only software/database upgrades
 - ✓ Optimized specimen collection will facilitate sequencing and traditional methods
 - ✓ Tiered efficiency with obtaining necessary information for clinical and public health practice
 - ✓ Real-time data and data aggregation improves public health efforts



Other Testing Needs: Experience from the Field

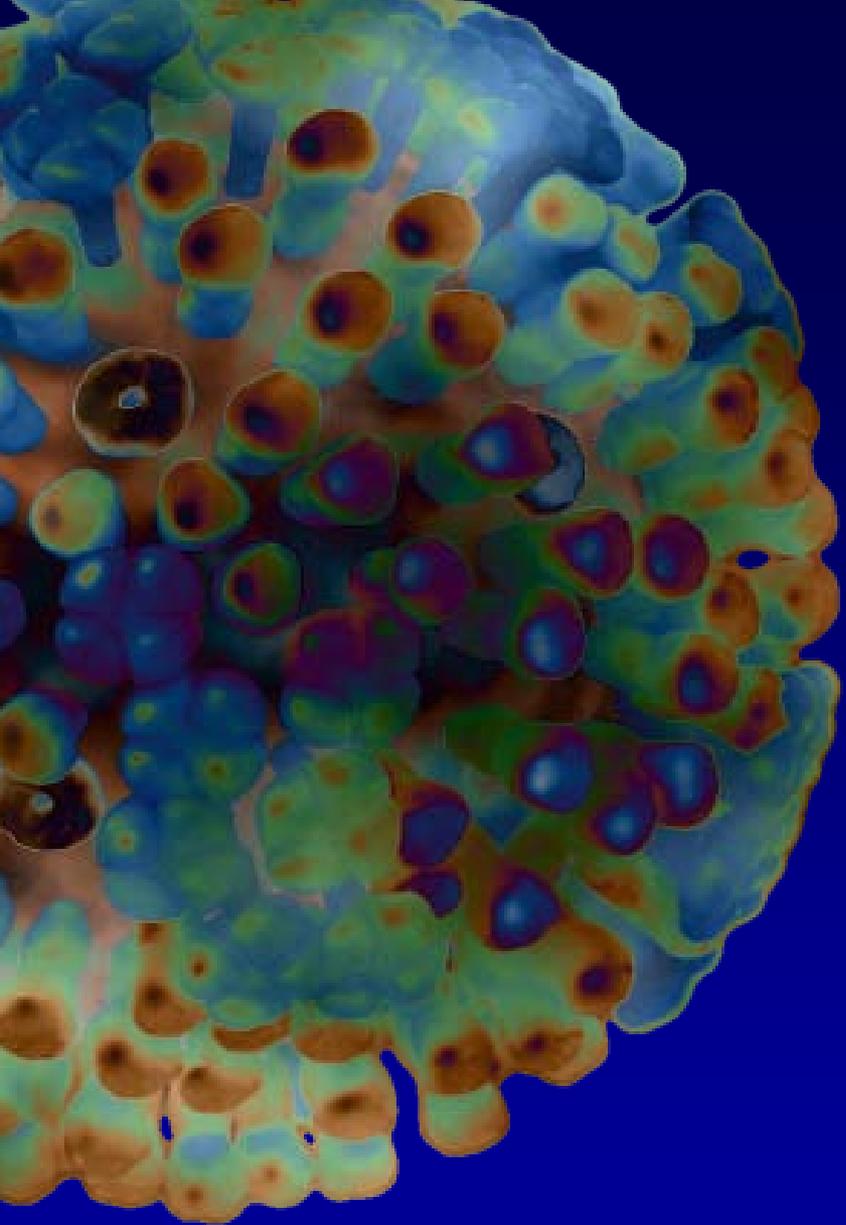
Rapid Influenza Immunity Testing:

- A point of care and high-throughput assay to evaluate influenza immune status
- Determine R_0 in an outbreak situation
- Screening of at risk populations for exposure to novel influenza viruses.
- Evaluation of immune status prior to intervention in the event of limited vaccine and antivirals supplies.
- Determine the effectiveness of intervention strategies

Antiviral Resistance Testing:

- Rapid screening for known resistance markers
- Functional assays to detect atypical markers





Thank You



www.cdc.gov/H1N1flu

