Influenza Diagnostics Program

Roxanne Shively
Chief, Influenza Diagnostics Branch

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Influenza Diagnostics Landscape

(2006 U.S.)

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
- MILLIPORE SimulFluor Flu A/Flu B

Investigational/Research/Homebrew PCR-based (NAATs)

- artus Infla/B/H5 LC RT-PCR
- Real-Time Ready Influenza A/B
- Prodesse Profliu+ (A, B, RSV)
- Luminex xTAG RVP Assay (A, B, H1, H3)
- Cepheid Flu A/B Smartcycler ASR
- ARUP Labs: Nanogen Reagents Influenza A/B Virus rt RT-PCR test
- TessArray RM-Flu
- Viracor Lab Influenza A/B rtRT-PCR
- Genaco Resp. Panel w/ Influenza A/B Test

NAATs 510(k) Cleared

- A/H5: Asian Lineage

Antigen Tests

- Directigen EZ Flu A+B
- Osom: Influenza A+B
- Xpect(R) Flu A&B
- Directigen A/B

Moderate Complexity

-artus InfA/B/H5 LC RT-PCR
- Real-Time Ready Influenza A/B
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FDA-cleared

Inv./ RUO

Initial 4 contracts in Early Development

- MesoScale Influenza POC Test
- Nanogen FluID
- Cepheid Xpert Flu A Panel
- IQuum Liat Influenza A/B

Waived

- BinaxNOW
- Quickvue
- SAS FluAlert A
- SAS FluAlert B
Flu DX Major Program Accomplishments

• **3M/Focus Diagnostics Simplexa Direct FluA,B,RSV test:**
  – 510(k) clearance and Moderate Complexity categorization (for near-patient use)
  – First PCR-based test for FluA, B, RSV with moderate complexity
  – Cost-effective and adaptable to initial testing (can replace RIDT use in hosp. labs)

• **3 new CLIA waivers** for Rapid Flu Tests (RIDT Analytical Evaluations, collaboration with FDA&CDC)

• Support CDC RT-PCR rapid deployment strategy (2009 H1N1, H3N2v, H7N9)

• **2 EUAs** for POC-type products in 2009 followed by 510(k) clearances and moderate complexity categorizations.

• **First U.S. 2009 H1N1 case** recognized during on-going clinical study (Feb.-Apr. 2009)
Flu DX Program Strategy - Objectives

Overall Objective: better tests & better diagnostic practice for informing improved patient care and community mitigations

Goals:

1. Improve and expand influenza diagnostic response capabilities
   - Rapid testing (POC for outpatient, and near-patient for hospitalized, critical care settings)
   - Inform antiviral prescribing; inform clinical practice (adult and pediatrics)
   - Recognize novel virus infections in clinical settings

2. Improve Diagnostic Surge Capacity
   - New assays on existing platforms; distinguish other respiratory pathogens co-circulating with flu

3. Studies to provide data that support adoption of diagnostic options in clinical practice


Better seasonal influenza diagnostics = Better pandemic Dx preparedness
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Strategy and Approaches

• Advance development for clinical diagnostic needs

• Support independent evaluations to better inform clinical diagnostic practice

• Bring “surveillance” into clinical diagnostic practice by electronic real-time data aggregation within facilities, regions and states

• Coordinate with CDC and others to optimize diagnostic efforts and resources
### Influenza Diagnostic Testing Spectrum

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<thead>
<tr>
<th>10-15 min, single test</th>
<th>3+ days; high throughput</th>
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<tbody>
<tr>
<td>Alternative: Pharmacies, Outbreak field use, Homes</td>
<td>Outpatient: Clinics, EDs, Phys. Offices</td>
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<td>Hospital Lab</td>
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<td>Referral Lab, Acad. Med Ctr.</td>
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<td>Public Health Lab</td>
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<td>CDC</td>
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#### CLIA-Waived
- **Rapid Antigen Tests**

#### CLIA Moderate
- **PCR-based Tests (NAATs), Direct FA**

#### CLIA High Complexity (LDTs, RUO)
- **Sequencing**

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**POC Testing**

- Clinical benefit: ambulatory/out-patients

**Near-Patient Testing**

- Clinical benefit: hosp patients

**Dx testing & communications (clinical & public health benefit)**
# Flu DX Current Projects

<table>
<thead>
<tr>
<th>Project Title</th>
<th>Objective</th>
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<tbody>
<tr>
<td>BD Technologies</td>
<td>Advance development of a POC test to identify Flu A&amp;B, and reduced susceptibility to neuraminidase inhibitors, directly from clinical isolates</td>
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<td>Johns Hopkins Univ. (Grant/Cooperative Agreement)</td>
<td>• Assess performance of a rapid near-patient flu test for ED patients;</td>
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<td>• validate and implement an electronic clinical decision guide and prompt for influenza testing;</td>
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<td>• assess the cost-effectiveness of influenza testing and treatment strategies for adults presenting to the ED with ARI symptoms;</td>
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<td>• demonstrate feasibility of a data aggregation system across participating EDs</td>
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<td>3M/Focus Diagnostics Simplexa Direct</td>
<td>Project completed with 510(k) clearance and moderate complexity determination; 2nd season on U.S. market</td>
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<tr>
<td>Rapid Influenza Test Evaluations (Medical College of WI)</td>
<td>Standardized protocol to assess analytical variability with FDA-cleared rapid influenza tests for detection of influenza A and Influenza B virus types, subtypes, and variants</td>
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These are areas where we can help:

- First-of-a-kind IVDs face uncertain clinical markets
- IVDs are subject to both CLIA and FDA regulatory requirements
- Advancing technology challenges regulatory paradigms and existing standards
- Funding and resource constraints
- Influenza/respiratory market seasonality
Trajectory for the Future
Priority Development

- Influenza diagnostic capability closer to patients
  - Reliable, cost-efficient POC and near-patient influenza testing
  - Rapid tests for seasonal virus subtypes to guide infection control practice
  - Rapid recognition of influenza antiviral resistance

- Improved, optimized methods for respiratory specimen collection

- Sequence-based diagnostics:
  - Influenza A subtypes and influenza B lineages
  - Reassortants
  - Antiviral drug resistance markers

Mechanism: Broad Agency Announcement
Novel Swine Influenza Detected!!

First Case
• 10 year old boy in San Diego, CA
• Initially detected with investigational POC test
• Confirmed by CDC rRT-PCR in SPHL as unsubtypeable Influenza A virus
• Samples referred to CDC

Characterization of novel influenza A virus in CDC lab
• IHR report to PAHO as PHEIC
• Sequences posted
• Test kits produced and distributed to State labs (and international partners)
Thank You for your Attention!

The important thing in science is not so much to obtain new facts as to discover new ways of thinking about them.
~William Lawrence Bragg