Influenza Diagnostics Update

Michael Shaw
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

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Influenza Diagnostics Landscape
(as of Summer, 2012)

Traditional Flu Testing
- Traditional Cell Culture
  - Multiple Cell lines: pRMK, MDCK, others
- Shell vial cultures
  - R-Mix & R-Mix Too
- DFA/IFA
- Immunofluorescence

EUA-NAATs
Terminated June 26, 2010
- GeneSTAT 2009 A/H1N1 Influenza
- ARUP Labs: ELITech Molecular Diagnostics 2009 H1N1 Influenza A Virus RT-PCR test
- Viracor Labs 2009 H1N1 Influenza A RT-PCR
- IMDx 2009 Influenza A H1N1 rt RT-PCR
- Influenza H1N1 09 Prime rRT-PCR
- ResPlex II (Diatherix Labs 2009 H1N1-09 Flu test)
- Qiagen
- Infinty RVP Plus
- NucliSENS Easy Q Influenza A/B
- ResPlex III

High Complexity LDTs NAATs
510(k) Cleared
- Real-Time RT-PCR Detection and Characterization Panel Plus H1N1
- Prodesse Profast+ (sH1/sH3/pH1N1) (RSV)
- xTAG RVP Assay (inc. A, B, H1, H3)
- RealTime Ready Influenza A/H1N1
- RVP FAST (inc. A, B, H1, H3)
- Simplexa Influenza A/H1N1 (2009)
- JBAIDS Nucleic Acid Amplification, Novel Influenza A Virus, A/H109, H1, H3, H5 (Asian Lineage); Flu B
- artus® Infl A/B RG RT-PCR Kit

Low Complexity LDTs RUO Kits
- Quidel Molecular Influenza A+B Assay
- infinity RVP Plus
- artus® Infl A/B RG RT-PCR Kit
- ResPlex III

Antigen Tests Waived
- BD: V-Set Flu A+B
- Inverness medical: BinaxNOW A&B
- Quickvue A+B
- SA Scientific: SAS FluAlert A, SAS FluAlert B
- Clearview Exact II Influenza A&B
- Sofia™Influenza A+B FIA

Moderate Complexity
- Prodesse ProFlu-ST Influenza A assay
- Influenza A H1N1 (2009)
- DFA/IFA Immunofluorescence
- Xpert Flu A/B Panel (A/2009H1 targets)

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

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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
- 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

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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 unchartered, 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

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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

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Thank You