



United States Department of

Health & Human Services

Office of the Assistant Secretary for Preparedness and Response



Influenza Diagnostics Program

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ASPR: Resilient People. Healthy Communities. A Nation Prepared.

Influenza Diagnostics Landscape

(2006 U.S.)

Legend:

FDA-cleared	Inv./ RUO
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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 InfA/B/H5 LC RT-PCR

ARUP Labs: Nanogen Reagents Influenza A/B Virus rt RT-PCR test

Roche Real-Time Ready Influenza A/B

TessArray RM-Flu

GEN-PROBE Prodesse Proflu+ (A, B, RSV)

Viracor Lab Influenza A/B rtRT-PCR

Luminex xTAG RVP Assay (A, B, H1, H3)

GENACO Genaco Resp. Panel w/ Influenza A/B Test

Cepheid Flu A/B Smartcycler ASR

NAATs

510(k) Cleared



Antigen Tests

BD Directigen EZ Flu A+B

genzyme Osom: Influenza A+B

remel Xpect(R) Flu A&B

BD Directigen A/B

Moderate Complexity

High Complexity



Waived

BinaxNOW

QUIDEL Quickvue

SAS FluAlert A

SAS FluAlert B

Initial 4 contracts in Early Development

MesoScale Influenza POC Test

NANOGEN Nanogen FluID

Cepheid Xpert Flu A Panel

IQuum Liat Influenza A/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**

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Better seasonal influenza diagnostics = Better pandemic Dx preparedness



Flu DX Program Strategy



Better seasonal influenza diagnostics = Better pandemic Dx preparedness

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



10-15 min, single test

3+ days; high throughput

Alternative:
Pharmacies,
Outbreak field
use, Homes

Outpatient:
Clinics, EDs,
Phys. Offices

Hospital
Lab

Referral
Lab, Acad.
Med Ctr.

Public
Health
Lab

CDC

CLIA-Waived

CLIA Moderate

CLIA High Complexity (LDTs, RUO)

Rapid Antigen Tests

PCR-based Tests (NAATs), Direct FA

Sequencing

POC Testing

Near-Patient Testing

Clinical benefit: ambulatory/out-patients

Clinical benefit: hosp patients

Dx testing & communications (clinical & public health benefit)

Flu DX Current Projects

Project Title	Objective
BD Technologies	Advance development of a POC test to identify Flu A&B, and reduced susceptibility to neuraminidase inhibitors, directly from clinical isolates
Johns Hopkins Univ. (Grant/Cooperative Agreement)	<ul style="list-style-type: none"> • Assess performance of a rapid near-patient flu test for ED patients; • validate and implement an electronic clinical decision guide and prompt for influenza testing; • assess the cost-effectiveness of influenza testing and treatment strategies for adults presenting to the ED with ARI symptoms; • demonstrate feasibility of a data aggregation system across participating EDs
3M/Focus Diagnostics Simplexa Direct	Project completed with 510(k) clearance and moderate complexity determination; 2 nd season on U.S. market
Rapid Influenza Test Evaluations (Medical College of WI)	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



Influenza Diagnostics Landscape - POC/Near-Patient

(as of August 2013)

Legend: FDA-cleared FDA-cleared after EUA

Rapid Antigen Tests Waived



BD Veritor™ Flu A+B

Alere Clearview Exact II Influenza A&B

QUIDEL CORPORATION Sofia™ Influenza A+B FIA



Alere BinaxNOW A&B

SA Scientific SAS FluAlert A
SAS FluAlert B

QUIDEL CORPORATION Quickvue A+B

Moderate Complexity

Response Biomedical Corporation Rapid Detection Flu A+B test

BD Directigen EZ Flu A+B

genzyme Osom: Influenza A+B

Meridian Bioscience, Inc. TRU FLU A&B

remel Xpect(R) Flu A&B

SA Scientific SAS FluAlert A + B Test

PBM Status® (BioSign) Flu A+B

Antigen

Others in the pipeline



Meridian Illumiprio-10

FOCUS Simplexa Direct Flu A, B & RSV

IQUM iQuum Liat Influenza A/B

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

Idaho Technology Inc. BiofireFilm Array Respir Panel

Nanosphere Verigene RVNATsp System
Verigene RVNAT (RV+)

PCR-based

FOUO – not for attribution





Why work with BARDA?



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

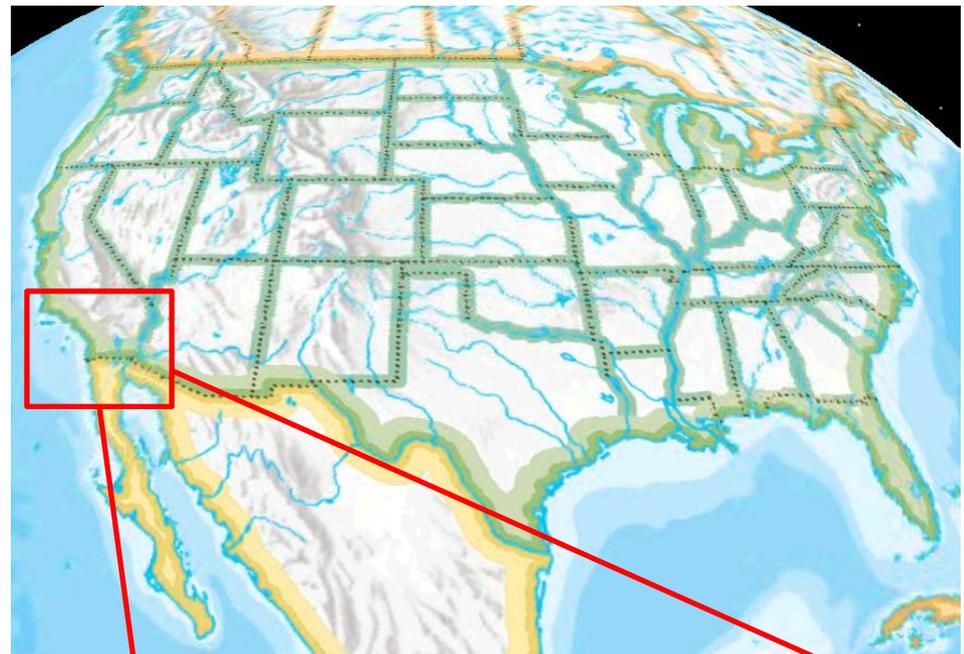
Novel Swine Influenza Detected!!

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)



**Southern California
April 2009**



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*