Diagnostics and Medical Devices Division (DMD)

Rodney Wallace
Director (acting) DMD
Biomedical Advanced Research and Development Authority
BARDA

BARDA Industry Day
October, 2014
DMD Division

• Created in November 2013
• Combined diagnostics and device resources from:
  — BARDA Flu Division (Dx and Respiratory)
  — BARDA CBRN Division (Dx)
• Allows more efficient utilization of subject matter expertise:
  — Assay development (molecular & immunology)
  — Devices (ventilators, diagnostics)
  — Clinical lab experience
  — Radiation biology
  — Virology
Diagnostics and Medical Devices
Program Strategy

Our objective is to develop diagnostics and medical devices for response in Public Health Emergencies, informing patient management and reassuring concerned citizens.

- Developing diagnostics and medical devices for patient care
  - Aligned with the PHEMCE Implementation Plan
  - Aligned with the National Strategy for Pandemic Influenza

- Key Strategies
  - Leverage existing clinical diagnostic laboratory infrastructure, instruments, practices, and IT
  - Stimulate development of Point of Care (POC) and Near Patient diagnostics, moving testing closer to the patient
  - Stimulate improvements in available ventilators and respirators

Empowering Local Response

Types of Products Funded

Molecular Diagnostics

Antigen Diagnostics

Laboratory

Respirators

Ventilators

Point of Care

# Diagnostic Testing Spectrum

## 10-15 min, single test

- **Alternative:** Pharmacies, Outbreak field use, Homes
- **Outpatient:** Clinics, EDs, Phys. Offices
- **Hospital Lab**
- **Referral Lab, Acad. Med Ctr.**
- **Public Health Lab**
- **CDC**

## High throughput

- **CLIA-Waived**
  - Rapid Antigen Tests
- **CLIA Moderate**
  - PCR-based Tests (NAATs), Direct FA
- **CLIA High Complexity (LDTs, RUO)**
  - Sequencing

## Testing Types

- **POC Testing**
- **Near-Patient Testing**
- **Laboratory Testing**

## Alternative Testing Locations

- Outpatient: Clinics, EDs, Phys. Offices
- Hospital: Hospital Lab
- Referral: Referral Lab, Acad. Med Ctr.
- Public Health: Public Health Lab
- CDC

## Sequencing

- FDA Approval

Dx testing & communications (clinical & public health benefit)
DMD Project Areas

- Biodosimetry
- Pandemic Influenza Diagnostics
- Respiratory & Other Devices
- Biothreat Diagnostics
Biodosimetry

Lynne Wathen, PhD
Team Lead  Radiation and Chemical Agent Diagnostics
DMD/BARDA
BARDA Biodosimetry Needs and Desired Throughput

Point of Care Screening (1M people) ≤ 2 Gy

≥ 2 Gy

Plus

Follow on Care

High Throughput Screening - reports absorbed dose (400,000 people)
### BARDA Biodosimetry Target Product Profiles

<table>
<thead>
<tr>
<th><strong>Point of Care Device (POC)</strong></th>
<th><strong>High Throughput Device (HT)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type of result:</strong></td>
<td>Qualitative</td>
</tr>
<tr>
<td><strong>CONOPs:</strong></td>
<td>Initial Triage / Sorting</td>
</tr>
<tr>
<td><strong>Exposure level:</strong></td>
<td>2 Gy - threshold</td>
</tr>
<tr>
<td><strong>Ease of operation:</strong></td>
<td>Easy to operate, minimal complexity, requires minimal training, CLIA waived</td>
</tr>
<tr>
<td><strong>Device Characteristics:</strong></td>
<td>Integrated components—no separate sample preparation</td>
</tr>
<tr>
<td><strong>Intended use:</strong></td>
<td>Tents, shelters, open settings</td>
</tr>
<tr>
<td><strong># Patients / Event</strong></td>
<td>Up to 1,000,000 within 6 days</td>
</tr>
<tr>
<td><strong>Time to result:</strong></td>
<td>Rapid but individual sample result (15 to 30 minutes)</td>
</tr>
<tr>
<td>Developer</td>
<td>Point Of Care Technology</td>
</tr>
<tr>
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</tr>
<tr>
<td>SRI International</td>
<td>Protein Expression immunoassay</td>
</tr>
<tr>
<td>MesoScale Diagnostics</td>
<td>Protein Expression immunoassay</td>
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</table>
## BARDA High Throughput Laboratory Biodosimetry Programs

<table>
<thead>
<tr>
<th>Developer</th>
<th>HT Technology</th>
<th>Automation</th>
<th>Estimated Results per Day per Instrument</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duke/DxTerity</td>
<td>Gene expression</td>
<td>Semi-automated including ABI 3500 Dx</td>
<td>500</td>
</tr>
<tr>
<td>Northrop Grumman/</td>
<td>Cytology – micronuclei</td>
<td>Semi-automated including Applied Spectral Imaging Cytology Microscopes</td>
<td>1200</td>
</tr>
<tr>
<td>Applied Spectral Imaging</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arizona State University</td>
<td>Gene expression</td>
<td>Semi-automated including ABI 7500Dx or Life technologies QuantStudio</td>
<td>700</td>
</tr>
</tbody>
</table>
Biodosimetry Diagnostic Areas of Interest (AOI)

6.1 Development of a dosimetry self-assessment tool in order to determine if an individual has been exposed to ionizing radiation at a dose equal to or greater than 2 Gy.

6.2 Development, clinical evaluation, and/or agency clearance of rapid diagnostic systems for determining white blood cell counts from whole blood.

6.3 Development of a rapid point-of-care diagnostic assay for assessing whether an individual’s absorbed dose of ionizing radiation was above or below 2 Gy, and/or a centralized high-throughput assay system for determining absorbed doses of ionizing radiation in the range of 0.5 Gy to 10 Gy, from 24 to 168 hours post-exposure.

6.4 Development of an improvement on the current “gold standard” for assessing absorbed doses of ionizing radiation (the dicentric chromosomal assays (DCA)).
Influenza
Diagnostics Program

Roxanne Shively
Chief, Influenza Diagnostics
DMD/BARDA

**Flu DX Program Strategy - Objectives**

**Overall Objective:** better tests & better diagnostic practice to improve patient care, control/prevention, and pandemic preparedness

**Goals/Requirements:**

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; other respiratory pathogens, coinfections.

2. **Improve Diagnostic Surge Capacity**
   - New assays on existing platforms; distinguish other resp. 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 & response**
Flu DX Program Strategy

Better seasonal influenza diagnostics = Better pandemic Dx preparedness & response

Strategy and Approaches

• Advance development for clinical diagnostic needs

• Support independent evaluations to inform clinical diagnostic practice

• Facilitate clinical diagnostic practice by electronic real-time data aggregation, electronic prompts for clinicians

• Coordinate with CDC, FDA, NIH to optimize diagnostic efforts and resources
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**
- **Roche Real-Time Ready Influenza A/B**
- **Prodesse Proflu+ (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**
- **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

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

### Moderate Complexity

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

### High Complexity

- **Initial 4 contracts in Early Development**

- **BinaxNOW**
- **Quickvue**
- **SAS FluAlert A**
- **SAS FluAlert B**
Influenza Diagnostics Landscape: High complexity (as of Sep, 2014)

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

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

Traditional Flu Testing
EUA-NAATs Terminated June 26, 2010

NAATs 510(k) Cleared

Traditional Flu Testing

EUA-NAATs Terminated June 26, 2010

NAATs 510(k) Cleared

7500 Fast Dx
Lightcycler
Smartcycler
Luminex 100/200 xMAP
R.A.P.I.D (Lightcycler)
Integrated Cycler (3M)
Rotor-Gene
Nuclisens EasyQ
eSensor® XT-8
Abbott m2000
BD Max
Quant Studio Platforms
FDA-cleared

Legend:
FDA-cleared
LDT, IUO, or RUO After EUAs Terminated
LDT, IUO, or RUO

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

RealTime Ready Influenza A/H1N1

Viracor Labs 2009 H1N1 Influenza A RT RT-PCR

Prodesse ProFlu-ST Influenza A assay

IMdx 2009 Influenza A H1N1 rt RT-PCR

Other LDTs RUO Kits

ResPlex III GeneAmp 9700

Infinity RVP Plus

NucliSENS Easy Q Influenza A/B

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

Esensor RVP (14+)

Abbott Molecular PLEX-ID Flu

Flu A/B and RSV (Abbott m2000)

CDC Real-Time RT-PCR Detection and Characterization Panel Real-Time RT-PCR Detection and Characterization Panel Plus H1N1

Hologic Prodesse Profast+ (sH1/sH3/pH1N1)
Prodesse Profili+ (A, B, RSV)

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

Simplexa Flu A/B, RSV

Simplexa Influenza A H1N1 (2009)

IMDx 2009 Influenza A H1N1 rt RT-PCR

Influenza H1N109 Prime rRT-PCR

State PHLs

D3 FastPoint Influenza A/B

D3 Ultra 2009 H1N1 Influenza A Virus ID kit

DoD Qualified Labs

TessArray RM-Flu

ARUP Labs: ELITEch Molecular Diagnostics 2009-H3N1 Influenza A Virus rt RT-PCR test

IMAGEN Influenza A and B

Longhorn D3 Ultra 2009 H1N1 Influenza A Virus ID kit

Millipore SimulFluor Flu A/Flu B

AVantage™ A/H5N1 Flu Test

IMLabs SimulPoint Influenza A/B

SimulFluor A/H5 Flu Test

Simulfluor Flu A/Flu B

Simulfluor Flu A/Flu B

Simulfluor Flu A/Flu B

Simulfluor Flu A/Flu B
Influenza Diagnostics Landscape - POC/Near-Patient
(as of August, 2014)

**Rapid Antigen Tests**

*Waived*

- **BD**
  - Veritor™ Flu A+B

- **Alere**
  - Clearview Exact II
  - Influenza A&B

- **QUIDEL**
  - Sofia™ Influenza A+B FIA

**Moderate Complexity**

- **BD**
  - Directigen EZ Flu A+B

- **genzyme**
  - TRU FLU A&B

- **remel**
  - Xpect(R) Flu A&B

- **SAS**
  - FLU A+B Test

- **Status® (BioSign)**
  - Flu A+B

**PCR-based**

- **Simplexa Direct**
  - Flu A, B & RSV

- **IQunum Liat**
  - Influenza A/B

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

- **BiofireFilm Array**
  - Respir Panel

- **Verigene RVNATsp System**
  - Verigene RVNAT (RV+)

- **Alere**
  - Alere™ i Influenza A, B

**Others in the pipeline**

- **BD Max**
  - Meridian Illumipro-10

**FOUO – not for attribution**
## Flu DX Current Projects

<table>
<thead>
<tr>
<th>Project Title</th>
<th>Objective</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BD Technologies</strong></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>
</tr>
<tr>
<td><strong>Johns Hopkins Univ.</strong></td>
<td>• Assess performance of a rapid near-patient flu test for ED patients; &lt;br&gt;• validate and implement an electronic clinical decision guide for influenza testing; &lt;br&gt;• Assess cost-effectiveness of influenza testing and treatment strategies for adults presenting to the ED; &lt;br&gt;• Demonstrate feasibility of a data aggregation system across participating EDs</td>
</tr>
<tr>
<td><strong>Medical College of WI</strong></td>
<td>Standardized protocol to assess analytical variability with FDA-cleared rapid influenza tests for detection of influenza A and Influenza B virus types, sub-types, and variants</td>
</tr>
<tr>
<td><strong>InDevR, Inc</strong></td>
<td>Advance development of FluChip-8G, a microarray with sequence-specific influenza virus targets, image analysis and Digital Neural Network results interpretation.</td>
</tr>
<tr>
<td><strong>Alere, Inc.</strong></td>
<td>Advance development a next-generation CLIA-waived Influenza A&amp;B diagnostic test with PCR-equivalent performance</td>
</tr>
</tbody>
</table>
Advance development of influenza test systems and diagnostic tools for increased diagnostic capabilities with clinical benefit and providing for increased pandemic influenza preparedness

- Influenza diagnostic capability closer to patients
  - Reliable, cost-efficient near-patient influenza testing
  - Rapid tests for seasonal virus subtypes, other respiratory pathogens
  - Rapid recognition of influenza antiviral resistance

- Improved, optimized methods for respiratory specimen collection
  - Collection at home, non-healthcare environments

- Sequence-based diagnostics:
  - Influenza A and Influenza B; novel, emerging viruses
  - Antiviral drug resistance markers.

Mechanism: Broad Agency Announcement BAA-13-100-SOL-00019
Bio-threat Agent Diagnostics Program

Donna Boston
Team Lead, Biothreat Diagnostics
DMD/BARDA
Objective: Develop rapid, accurate FDA-cleared bio-threat agent diagnostic assays/systems to inform patient management, for use in:

Laboratory settings
- Develop assays for high-throughput instruments to meet large diagnostics surge demand – e.g. 4.4M anthrax tests
- Leverage COTS platforms*

Point of Care settings
- Develop new or adapted platform/assay systems where existing platforms do not meet end user needs
- Greater benefit if has routine healthcare applicability*

* PHEMCE Strategy 2012: “Ensure a … product pipeline for MCM that emphasizes multi-functional capabilities … and includes consideration of viable commercial markets and/or routine public health applicability.”

www.medicalcountermeasures.gov
# Bio-threat Agent Diagnostics Program Objectives (cont.)

<table>
<thead>
<tr>
<th>Biothreat Agent</th>
<th>PHEMCE Rqmt</th>
<th>Currently Able to Fund</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Assay and Marker Studies</td>
<td>POC Assay Dev</td>
</tr>
<tr>
<td>Anthrax</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Botulinum toxins</td>
<td>In process</td>
<td>✔</td>
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<tr>
<td>Glanders &amp; Meloidosis</td>
<td>In process</td>
<td>✔</td>
<td></td>
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<tr>
<td>Filoviruses</td>
<td>In process</td>
<td>✔</td>
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<tr>
<td>Tularemia</td>
<td>In process</td>
<td>✔</td>
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<tr>
<td>Typhus</td>
<td>In process</td>
<td>✔</td>
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<tr>
<td>Smallpox</td>
<td>In process</td>
<td>✔</td>
<td></td>
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<tr>
<td>Plague</td>
<td>In process</td>
<td>✔</td>
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*ASPR: Resilient People. Healthy Communities. A Nation Prepared.*
<table>
<thead>
<tr>
<th></th>
<th>FY13</th>
<th>FY14</th>
<th>FY15</th>
<th>FY16</th>
<th>FY17</th>
<th>FY18</th>
<th>FY19</th>
</tr>
</thead>
<tbody>
<tr>
<td>CDC Anthrax Toxin Diagnostic</td>
<td></td>
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<tr>
<td>Clearance of CDC LRN Bio-threat Assays</td>
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<tr>
<td>MRI Global – Anthrax PCR Assay</td>
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<tr>
<td>nanoMR – Biothreat Identification System</td>
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<tr>
<td>Bio-marker/natural history studies – CDC and USAMRIID</td>
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**Future Bio-threat Agent Diagnostics Starts**

- **Existing**
- **FY14 new starts**

- ⭐ FDA clearance (LRN anthrax PCR assay cleared May 2014))
- ⭐⭐⭐⭐ Anticipated clearance

Bio-threat Agent Diagnostics Development Strategy

Agreement on Needs

Requirements Generation

Ensure Response Capability in LRN, smaller scale

Lab Based Platforms and Assays

POC Platform and Assay Development

Disease Specific Lab Test System(s)

Marker & Disease Studies

Disease Specific POC Test System(s)

Legend

Agent Specific

All Threats

FY13 FY14 FY15 FY16 → out years

Bio-threat Agent Diagnostic Areas of Interest (AOI)

www.fedbizopps.gov

6.5 Development of an anthrax diagnostic assay system (may be part of a multi-pathogen panel):
   – For POC settings
   – For high-throughput testing on existing laboratory instrumentation

6.6 Hardware platform development – point of care:
   – 6.6.1 In vitro diagnostic (IVD) devices that would provide rapid, accurate point-of-care (POC) / “field-use” testing
   – 6.6.2 New and innovative sample preparation technologies needed for collecting and processing clinical samples potentially containing bio-threat agents of interest for use at point of care.

6.7 “Bio-threat Agent of Interest” knowledge development:
   – Marker identification and characterization, disease progression studies, etc.
Recent White House actions (September 2014):

• National Strategy for Combating Antibiotic-Resistant Bacteria
  — Includes five interrelated goals aimed at preventing, detecting, and controlling outbreaks of resistant pathogens recognized by CDC as urgent or serious threats (one of the goals specifically relates to creating POC diagnostics to identify resistance within bacteria)

• Executive Order
  — Creates a Joint Task Force led by HHS, USDA, and DOD

• President’s Council of Advisors on Science and Technology Report on Combating Antibiotic Resistance
  — Recommendations include incentives

• Implementation plans are being developed
• Details are forthcoming
  — Watch for BARDA CBRN Broad Agency Announcement updates in FY15
Respiratory and Other Devices

Richard Crawford
CMI Contractor
Supporting the Mission of
DMD/BARDA
Respiratory Devices

- Two Different Categories of Respiratory Devices
  - Respiratory Protection Devices
    - Surgical Masks
    - N95 Mask
    - Elastomers
    - Powered Air Purifying Respirator (PAPR)
  - Ventilators
    - Transport Ventilators
    - Advanced Homecare and Portable Ventilators
Respiratory Protection Devices (RPDs)

• Critical to response (influenza, biological threats, infectious disease)

• PHEMCE is reviewing stockpiling needs and approaches for RPDs
  — Review not complete
  — Some points are clear at this stage of the analysis
    • A severe influenza pandemic would require the largest number of RPDs
    • Multiple types of devices will be required for response.
      — N95’s. PAPR’s, surgical masks, etc.
    • Multiple surge response techniques will likely be needed
      — Stockpiling (centralized, user managed, vendor managed, etc.)
      — Domestic surge manufacturing during the event.

• Stay tuned for more details as the analysis continues.
<table>
<thead>
<tr>
<th>Developer</th>
<th>Type</th>
<th>Usage Population</th>
<th>Quantity Price</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phillips Respironics</td>
<td>All hazards transport ventilator, fully kitted</td>
<td>Neonate to Adult</td>
<td>$3,280 @ 10,000 units</td>
</tr>
</tbody>
</table>
Areas of Interest:

1.1 Development and characterization of improved respiratory protective devices (RPD). Support for advanced development of improved RPD such as masks or respirators to prevent influenza infections or harmful effects of biological hazards. RPD demonstrate improved features over currently available devices for functionality, usability, comfort, decontamination and re-use, cost efficiency, and durability to support a broad population (e.g., pediatric through adult), with a clear path to NIOSH certification and FDA clearance as applicable.

2.1 Development of improved full-featured continuous ventilators. Advanced development of new or improved ventilators to provide life support in clinical and non-clinical environments for severe respiratory conditions resulting from influenza infections or all-hazards events. Ideal ventilators should support neonate to adult populations, be capable of operation by unskilled or minimally trained care providers, include considerations for ease of stockpiling/maintenance, accommodate/provide accessories typically used in ventilatory standard of care, have a low cost per unit (<$3,000 per fully-kitted unit), and accommodate domestic surge production capacity.
Contact Information

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