



*United States Department of*

**Health & Human Services**

Office of the Assistant Secretary for Preparedness and Response



# **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

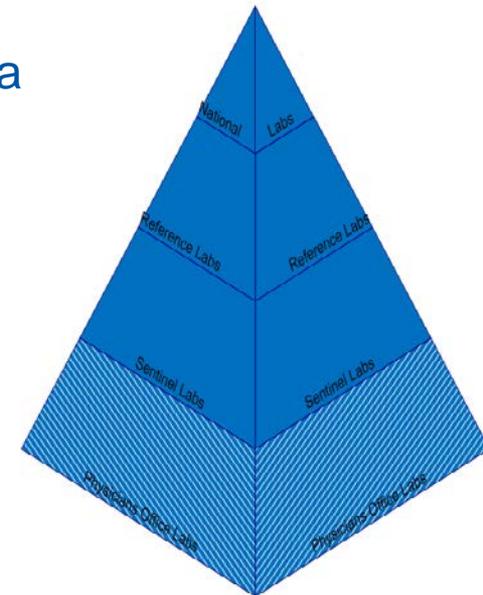


# Diagnostics and Medical Devices Program Strategy



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

Laboratory

## Molecular Diagnostics



## Antigen Diagnostics



Point of Care

## Respirators

## Ventilators





# Diagnostic Testing Spectrum



10-15 min, single test

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\***

**Laboratory Testing**

**Sequencing**

**FDA  
Approval**

**Dx testing & communications (clinical & public health benefit)**



# DMD Project Areas



**Biodosimetry**

**Pandemic  
Influenza  
Diagnostics**

**Respiratory  
& Other  
Devices**

**Biothreat  
Diagnostics**



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# **Biodosimetry**

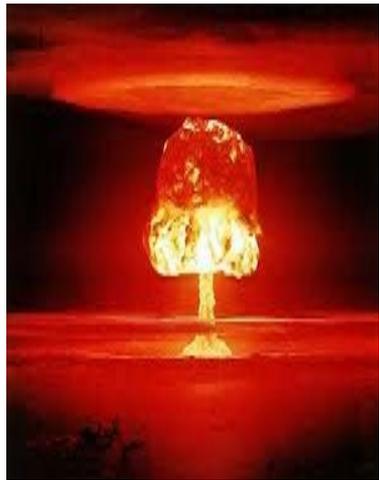
**Lynne Wathen, PhD**

**Team Lead Radiation and Chemical**

**Agent Diagnostics**

**DMD/BARDA**

# BARDA Biodosimetry Needs and Desired Throughput



**Point of Care  
Screening  
(1M people)**

**$\geq 2$  Gy**



**Follow on**



**Care**

**$< 2$  Gy**



**High  
Throughput  
Screening -  
reports  
absorbed  
dose  
(400,000 people)**



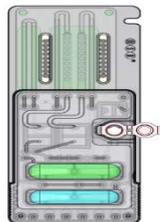
# BARDA Biodosimetry Target Product Profiles



	Point of Care Device (POC)	High Throughput Device (HT)
<b>Type of result:</b>	Qualitative	Quantitative (accuracy $\pm 0.5\text{Gy}$ )
<b>CONOPs:</b>	Initial Triage / Sorting	Injury Assessment / Treatment Tool
<b>Exposure level:</b>	2 Gy - threshold	Range: 0.5 – 10 Gy
<b>Ease of operation:</b>	Easy to operate, minimal complexity, requires minimal training, CLIA waived	Laboratory instrument—more labor intensive, requires training
<b>Device Characteristics:</b>	Integrated components—no separate sample preparation	May include separate components as needed. High automation desired.
<b>Intended use:</b>	Tents, shelters, open settings	Labs, hospitals, fixed facilities
<b># Patients / Event</b>	Up to 1,000,000 within 6 days	Up to 400,000 within 7 days (may need multiple assessments)
<b>Time to result:</b>	Rapid but individual sample result (15 to 30 minutes)	Up to 24 hours

# BARDA Radiation Diagnostics Point of Care Biodosimetry Programs

Developer	Point Of Care Technology	Type	Estimated Results per Day per Instrument
SRI International	Protein Expression immunoassay	Dual Lateral Flow w/ Reader & Cell Extractor	400
MesoScale Diagnostics	Protein Expression immunoassay	Microfluidic Cartridge & Instrument	72



# BARDA High Throughput Laboratory Biodosimetry Programs

Developer	HT Technology	Automation	Estimated Results per Day per Instrument
Duke/DxTerity	Gene expression	Semi-automated including ABI 3500 Dx	500
Northrop Grumman/ Applied Spectral Imaging	Cytology – <i>micronuclei</i>	Semi-automated including Applied Spectral Imaging Cytology Microscopes	1200
Arizona State University	Gene expression	Semi-automated including ABI 7500Dx or Life technologies QuantStudio	700





# BARDA Broad Agency Announcement Number: CBRN-BAA-13-100-SOL-00013



## 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)).



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# ***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**



# 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.)

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** TessArray RM-Flu

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

**ViraCor** 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** 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 Scientific**  
SAS FluAlert A  
SAS FluAlert B

*Initial 4 contracts in Early Development*

**MesoScale**  
Influenza POC Test

**NANOGEN** Nanogen FluID

**Cepheid** Cepheid Xpert Flu A Panel

**IQ** IQuum Liat Influenza A/B

# Influenza Diagnostics Landscape: High complexity (as of Sep, 2014)

Legend:

FDA-cleared	LDT, IUO, or RUO After EUAs Terminated	LDT, IUO, or RUO
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**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

**MILLIPORE**  
SimulFluor Flu A/Flu B

**AVantage™ A/H5N1 Flu Test**

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

**GeneSTAT 2009**  
A/H1N1  
Influenza

**3M Influenza A H1N1**  
(2009)

**Prodesse ProFlu-ST**  
Influenza A assay

**IMDx 2009 Influenza A**  
H1N1 rt RT-PCR

**Influenza H1N109**  
Prime rRT-PCR

**State PHLs**

**DoD Qualified**  
Labs

**TessArray RM-Flu**

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

**Roche** RealTime Ready  
Influenza A/H1N1

**Viracor** Viracor Labs 2009 H1N1  
Influenza A RT RT-PCR

**Other LDTs**  
RUO Kits

**Infinity RVP Plus**

**NucliSENS Easy Q**  
Influenza A/B

**ResPlex III**  
GeneAmp 9700

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

**HOLOGIC GEN-PROBE**  
Prodesse Profast+ (sH1/sH3/pH1N1)  
Prodesse Proflu+ (A, B, RSV)

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

**FOCUS** Simplexa Flu A/B, RSV

Simplexa Influenza A H1N1 (2009)

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

**QUIDEL** Quidel Molecular  
Influenza A+B Assay

**artus®** Infl A/B RG  
RT-PCR Kit

**GenMarkDx** Esensor RVP  
(14+)

**Abbott Molecular**  
PLEX-ID Flu

**MD** Flu A/B and RSV  
(Abbott m2000)

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

**Traditional Flu**  
Testing

**EUA-NAATs**  
Terminated June 26, 2010

**NAATs**  
510(k) Cleared



# Influenza Diagnostics Landscape - POC/Near-Patient

(as of August, 2014)

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** Diagnostics  
Osom: Influenza A+B

**Meridian** Bioscience, Inc.  
TRU FLU A&B

**remel** Your link to G.C. Testing solutions  
Xpect(R) Flu A&B

**SA Scientific** SAS FluAlert A + B Test

**PBM** Status® (BioSign) Flu A+B

Antigen

## Others in the pipeline



BD Max



Meridian Illumipro-10

**FOCUS** Diagnostics  
Simplexa Direct Flu A, B & RSV

**IQ**um  
iQuum Liat Influenza A/B

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

**BIO**MERIEUX  
BiofireFilm Array Respir Panel

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

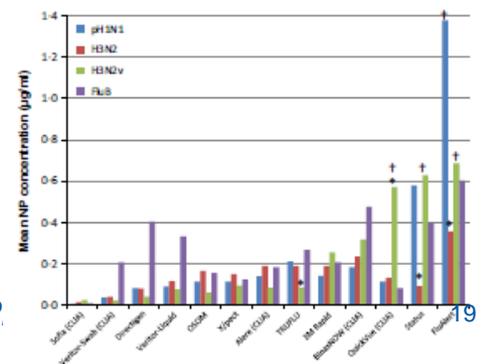
**Alere** Alere™ i Influenza A, B

PCR-based

FOUO – not for attribution

# Flu DX Current Projects

Project Title	Objective
<b>BD Technologies</b>	Advance development of a POC test to identify Flu A&B, and reduced susceptibility to neuraminidase inhibitors, directly from clinical isolates
<b>Johns Hopkins Univ.</b> (Grant/Cooperative Agreement)	<ul style="list-style-type: none"> <li>• Assess performance of a rapid near-patient flu test for ED patients;</li> <li>• validate and implement an electronic clinical decision guide for influenza testing;</li> <li>• Assess cost-effectiveness of influenza testing and treatment strategies for adults presenting to the ED ;</li> <li>• Demonstrate feasibility of a data aggregation system across participating EDs</li> </ul>
<b>Medical College of WI</b> (Rapid Influenza Test Evaluations)	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
<b>InDevR, Inc</b>	Advance development of FluChip-8G, a microarray with sequence-specific influenza virus targets, image analysis and Digital Neural Network results interpretation.
<b>Alere, Inc.</b>	Advance development a next-generation CLIA-waived Influenza A&B diagnostic test with PCR-equivalent performance





# Trajectory for the Future (Priorities)

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**



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# **Bio-threat Agent Diagnostics Program**

**Donna Boston**  
**Team Lead, Biothreat Diagnostics**  
**DMD/BARDA**



# Bio-threat Agent Diagnostics Program Objectives



**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](http://www.medicalcountermeasures.gov)

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



*B. anthracis*

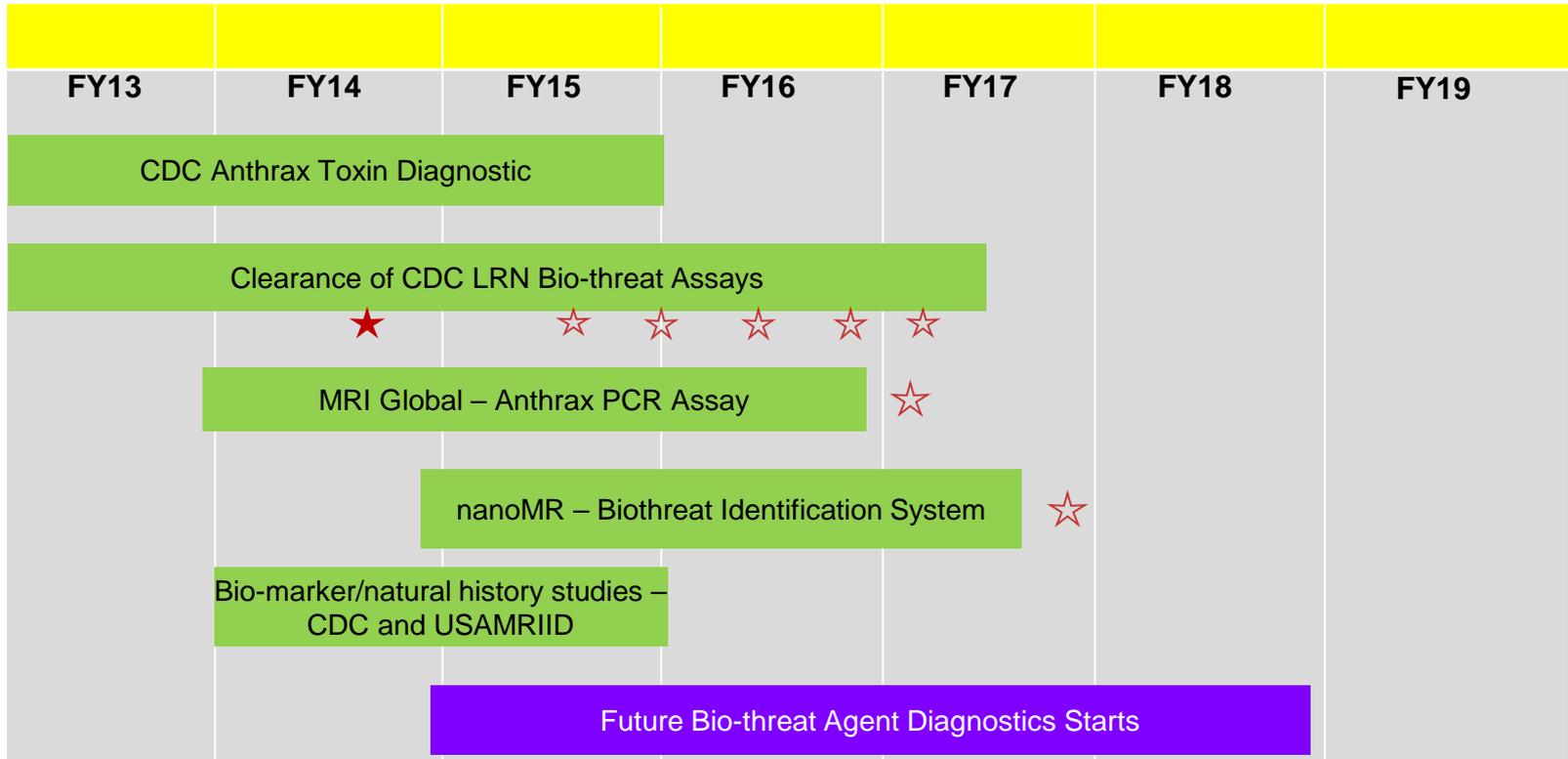


Smallpox

Biothreat Agent	PHEMCE Rqmt	Currently Able to Fund		
		Assay and Marker Studies	POC Assay Dev	Lab Assay Dev
Anthrax	✓	✓	✓	✓
Botulinum toxins	<i>In process</i>	✓		
Glanders & Meloidosis	<i>In process</i>	✓		
Filoviruses	<i>In process</i>	✓		
Tularemia	<i>In process</i>	✓		
Typhus	<i>In process</i>	✓		
Smallpox	<i>In process</i>	✓		
Plague	<i>In process</i>	✓		



# Bio-threat Agent Diagnostics Projects



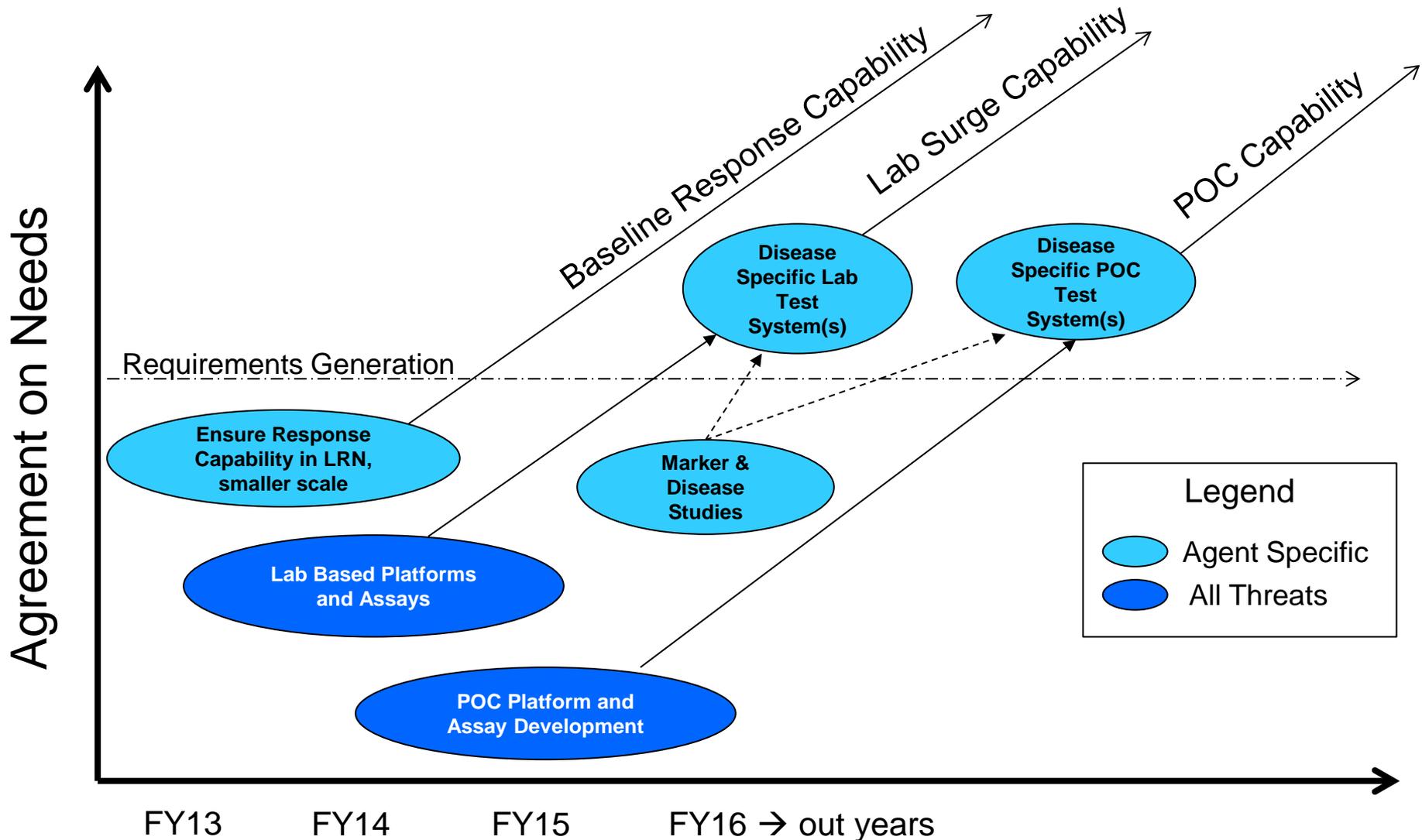
■ Existing ■ FY14 new starts

★ FDA clearance (LRN anthrax PCR assay cleared May 2014))

★ Anticipated clearance



# Bio-threat Agent Diagnostics Development Strategy





# BARDA Broad Agency Announcement CBRN-BAA-13-100-SOL-00013



## Bio-threat Agent Diagnostic Areas of Interest (AOI)

[www.fedbizopps.gov](http://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.



# Interest in Diagnostic Development for Antimicrobial Resistance



## 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



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# Respiratory and Other Devices

**Richard Crawford**

**CMI Contractor**

**Supporting the Mission of**

**DMD/BARDA**

- 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.



# BARDA Ventilator Development Programs



Developer	Type	Usage Population	Quantity Price
Phillips Respironics	All hazards transport ventilator, fully kitted	Neonate to Adult	\$3,280 @ 10,000 units



# BARDA Broad Agency Announcement Number: BAA-13-100-SOL-00019



## 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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