BARDA’s Role in Medical Countermeasure Development

The USG as a Source of Non-Dilutive Capital

Gary L. Disbrow, PhD
Deputy Director, CBRN Division
HHS/ASPR/BARDA

January 9, 2013
HHS Organization

BARDA MISSION

Develop and procure medical countermeasures that address the public health and medical consequences of chemical, biological, radiological, and nuclear (CBRN) accidents, incidents and attacks, pandemic influenza, and emerging infectious diseases

If a product fails, it should only be the result of failure of the product to achieve the desired safety or efficacy thresholds, and not as a function of our inability to provide the proper support from a technical, business and regulatory perspective
New 5yr Plan that focuses on the entire PHEMCE and not merely the SRF
INTEGRATED NATIONAL BIODEFENSE PORTFOLIO REQUIREMENTS

DoD-Unique
- Brucellosis Vx
- VEE/EEE/WEE Vx & Rx
- Plague Vx
- Botulism Vx
- SEB Vx & Rx
- Tularemia Vx
- Ricin Vx & Rx
- (other, unfunded)

Common
- Anthrax Vx & Rx
- Smallpox Vx & Rx
- Ebola / Marburg Vx & Rx
- Tularemia Rx
- Botulism Rx
- Radiation Rx
- Nerve agent Vx & Rx

HHS-Unique
- Smallpox Vx for special populations
- Burkholderia sp. Rx
- Plague Rx

DoD focus is on protecting forces prior to exposure. HHS focus is on response to threats to general civilian population after exposure

Vx = Prophylaxis  Rx = Therapeutic
Pandemic Influenza
Pandemic Flu Vaccine Strategy

- Cell-based Vaccines
- Recombinant and Molecular Vaccines
- Adjuvants
- Manufacturing Infrastructure

sanofi pasteur - 2007
Pandemic Influenza Antiviral, Diagnostic and Device Efforts

- **First drug used in an event under EUA – peramivir antiviral drug in 2009 H1N1 pandemic**

- **First 2009 H1N1 case recognized in MesoScale POC diagnostic device in clinical trial study**

- **POC diagnostic devices FDA cleared (3)**
  (Cepheid, Iquum, Focus Diagnostics)

- **Prototype next-generation ventilator under clinical evaluation**
  - low cost (< $3000)
  - user-friendly
  - universal component compatible
  - neonate and adult populations
Chem/Bio/Rad/Nuc
EVOLUTION OF CIVILIAN BIODEFENSE

- Chapter 1: pre-9/11, 1950s – 2001
- Chapter 2: post-9/11 to Project BioShield, 2001 – 2004
- Chapter 3: Project BioShield and PAHPA, 2004 – 2006
- Chapter 4: ASPR, BARDA & H1N1, 2007 – 2009
- Chapter 5: Enterprise Transformation, 2010 → beyond

Mid-1950’s on: DoD bio and chem defense programs

1990-1992 1st Gulf War
Iraqi BW, CW & nuke programs

NPS founded (1999)

“Animal Rule” (May 2002)

National Strategy for Pandemic Influenza (Nov 2005)

Project BioShield (Jul 2004)

PREP Act (Dec 2005)

PAHPA (Dec 2006) → BARDA (May 2007)

2009-H1N1 Pandemic (Apr 2009 -10)

PHEMCE Strategic and Implementation Plans (2012)

PHEMCE Review (Aug 2010)
Scoping the Challenge

Define, Design, Develop, Deliver and Dispense Medical Countermeasures to reduce the adverse health consequences of public health emergencies

A Nation Prepared

Complex array of Threats

Diverse population

Lengthy, risky and expensive product development

Prioritize medical countermeasure programs to effectively address mission goals

Strategies & dependencies for effective use

PRODUCT DEVELOPMENT MODEL

• Early Development
  — Emphasis on Proof of Concept
  — Integration of platforms, CROs, CMOs
  — Relies on tech-transfers, data and model sharing
  — Rapid Go/No Go Decisions

• Advanced Development
  — Emphasis on licensure and stockpiling
  — Scale-up, validation of manufacturing
  — Phase II/III, pivotal animal studies
  — Life cycle and sustainment important
IDEALIZED PIPELINE

PHASES
- Discovery
- Preclinical Development
- Phase I
- Phase II
- Phase III
- Licensure
- Production & Delivery

PRODUCT PIPELINE

NIH ($13.9 B)

BARDA ($1.6 B)

Project BioShield ($5.6B)

PROBABILITY OF SUCCESS TO LICENSURE
- 1-3%
- 5-17%
- 10-25%
- 18-35%
- 45-70%
- 90%

Valley of Death

Licensed Product


14
HIGH PRIORITY THREATS

- Radiological agents and Nuclear devices
- Cyanide and Nerve agents
- Emerging infectious diseases
  - Pandemic influenza
  - Multi-drug resistant pathogens
- Viral Hemorrhagic Fevers
  - Marburg
  - Ebola
- Gram negative organisms
  - Francisella tularensis (tularemia)
  - Yersinia pestis (plague)
  - Burkholderia mallei (glanders) and B. pseudomallei (melioidosis)
  - Rickettsia prowazekii (typhus)

The Enterprise will continue to address medical countermeasure needs to protect against high priority threats which have been determined by the Secretary of Homeland Security to pose a material threat sufficient to affect national security and/or which have the potential to seriously threaten national health security

- Bacillus anthracis (anthrax)
- Clostridium botulinum toxins (botulism)
- Variola virus (smallpox)
TOOLKITS FOR EMERGENCY PREPAREDNESS

ANTIBIOTICS
- Anthrax
  - Vaccines
  - Antitoxins

VACCINES
- Smallpox
  - Vaccines
  - Therapeutics

ANTITOXINS
- Botulism
  - Heptavalent Antitoxin

BACILLARY THREATS
- Antibiotics

RAD/NUCLEAR
- Ca- & Zn-DTPA
- Prussian Blue
- Potassium Iodide
- ARS Therapeutics
- Burn/Blast Supplies

CHEM
- CHEMPACKs

EMERGING DISEASES
- Vaccines
- Diagnostics
- Therapeutics

BARDA’s Cumulative Investments

<table>
<thead>
<tr>
<th>Year</th>
<th>ARD</th>
<th>SRF</th>
<th>Flu</th>
</tr>
</thead>
<tbody>
<tr>
<td>2004</td>
<td>.05</td>
<td>.77</td>
<td>.08</td>
</tr>
<tr>
<td>2005</td>
<td>.05</td>
<td>.77</td>
<td>.08</td>
</tr>
<tr>
<td>2006</td>
<td>2.58</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>2007</td>
<td>4.1</td>
<td>1.0</td>
<td>2.1</td>
</tr>
<tr>
<td>2008</td>
<td>6.41</td>
<td>2.0</td>
<td>4.4</td>
</tr>
<tr>
<td>2009</td>
<td>9.67</td>
<td>3.0</td>
<td>6.7</td>
</tr>
<tr>
<td>2010</td>
<td>9.96</td>
<td>3.0</td>
<td>6.9</td>
</tr>
<tr>
<td>2011</td>
<td>11.41</td>
<td>4.0</td>
<td>7.4</td>
</tr>
<tr>
<td>2012</td>
<td>12.30</td>
<td>5.0</td>
<td>7.3</td>
</tr>
</tbody>
</table>
CBRN Number of New Projects Per Year

Programs - Number of New Starts

Dollars in Millions

FY07 FY08 FY09 FY10 FY11 FY12

Project BioShield

Replenishment of Products
ARS Anti-Neutropenia Drugs
Chem/Anti-convulsive Drugs
FY13 Transfer to BARDA

Transfers to BARDA
$1574M

Other Transfers
$304M

$1022M Uncommitted

Anthrax Vaccines
$701M

Anthrax Therapeutics
$498M

Smallpox Vaccine
$542M

Smallpox Antiviral
$433M

Botulism Antitoxin
$481M

Rad/Nuc ($40M)

Revised Sept 2012

Licensed/Approved/Cleared

H5N1 Pandemic Influenza Vaccine
  Sanofi Pasteur

H1N1 Pandemic Influenza Vaccine
  5 Manufacturers

Flu/RSV Diagnostic
  Focus/3M

Anthrax Antitoxin
  HGS/GSK

Next-Gen Portable Ventilators
  Adult and Infant
  Newport

FLUCELVAX
  Novartis
Products Approaching Finish Line

H5N1 Vaccine with Adjuvant
- GlaxoSmithKline

Recombinant-based Influenza Vaccine
- Protein Sciences

Bot Antitoxin
- Cangene

Anthrax Vaccine
- Emergent
Stockpiled CBRN Countermeasures

Smallpox

Pentetate calcium trisodium injection
1000 mg
For intravenous or inhalation use only. See package insert for use information.
Rx only.

Pentetate zinc trisodium injection
1000 mg
For intravenous or inhalation use only. See package insert for use information.
Rx only.

Anthrax

BioThrax Vaccine Adsorbed
Contains 5 mL (0.5 mg per dose)
Rx Only

Radiation

ThyroShield Potassium Iodide Oral Solution
65 mg potassium iodide per mL
Black raspberry flavor

Botulism

Stress

MCMs THAT WE STILL NEED

• Anthrax vaccines
  – Faster-acting, stable, cheap
• Broad-spectrum antimicrobials
  – Novel drugs
• Radiation countermeasures
  – Acute radiation countermeasures
    • 7 subsyndromes
  – Oral decorporation agents
  – Biodosimetry/bioassays
• Viral hemorrhagic fever MCMs
• Diagnostics
• Volatile nerve agent countermeasures
• Thermal burn therapies
• Blood products
Animal Model Network

- Test Approved/Licensed products
- Studies not on the critical path
- Studies to inform CONOPS
ACCOMPLISHMENTS

- Passing of Project BioShield and PAHPA
- Establishment of ASPR and BARDA
- Eight products in Strategic National Stockpile
- Three BLAs being filed 2012-2013
- First FDA approval of Animal Rule-regulated product Dec 2012
- Pipeline of over 100 products in development
- Establishment of long-term life-cycle management for MCMs
- Launch of broad-spectrum antimicrobial PPPs
- Core Services (Nonclinical, Clinical, ADM)
- FDA involvement in product development and licensure
SUSTAINING THE ENTERPRISE

• Innovation
  ─ Protein Expression
  ─ New platforms, delivery systems
• Product Improvements
  ─ Adjuvant technologies
• Stockpile Manufacturing Intermediates
  ─ Frozen stockpiles of immune sera and vaccines
• Multi-Purpose Products
  ─ Broad spectrum antibiotics
  ─ Anti-neutropenia/oncology drugs
• Integrate Stockpiling with Existing Drug Inventories
  ─ Vendor Managed Inventory
• Government furnished Core Services
  ─ Manufacturing
  ─ Animal Model development
  ─ Product Testing
  ─ Qualified reagents
Legislation Governing BARDA

• Project BioShield Act of 2004
  – Special Reserve Fund (~$5.6 B)
  – Emergency Use Authorization (FDA)
• Pandemic All-Hazards Preparedness Act of 2006
  – Established BARDA
  – Allowed for milestone payments in advance of delivery
  – Provided BARDA the authority to invest in advanced R&D
    • Yearly appropriations
• Federal Acquisition Regulation (FAR)
• Health and Human Services Acquisition Regulation (HHSAR)

Your company needs to have an understanding of Government regulations when you are seeking USG funding
Current Funding Mechanisms

• Advanced R&D
  – Broad Agency Announcements (BAA)
    • White papers and quad charts (first tier)
    • Full proposals by invitation (second tier)
    • Companies can submit full proposals at any time
    • No procurement of product
    • Cost plus fixed fee
  – Request for Proposals (RFP)
    • Allows for delivery of product under the contract
    • Cost plus fixed fee

• Procurement Contracts under Project BioShield
  – RFP
    • Fixed price (possibility for cost plus CLIN)
    • Product may be accepted once the sponsor has generated a data set sufficient for the potential use of the product during a declared emergency under Emergency Use Authorization (EUA)
• Contracts DO NOT have to be awarded to companies based in the US
  — FAR 25.001(b) Buy American Act not applicable in acquisitions subject to certain trade agreements (Subpart 25.4)
  — FAR 25.103 Exceptions
    • Public Interest – Domestic preference would be inconsistent with public interest
    • Non-availability – not produced in sufficient and reasonably available commercial quantities
    • Unreasonable costs
    • Resale
    • IT that is a commercial item
Contracting with BARDA

- BARDA awards contracts not grants
- Contracts for Advanced R&D
  - 1 or 2yr base
  - Incrementally funded
  - Milestone driven
  - In-Process Review with PHEMCE participation prior to execution of option
    - Those programs that fail to meet scientific milestones will be down selected
  - Purpose – generate the data set necessary for use under EUA
- Contracts for Procurement
  - Primarily procurement paid upon delivery of product
  - Small component for R&D to support licensure/approval
  - Product has to be “licensable” within 8yrs
Other Mechanisms

• Other Transaction Authority (OTA)
  — New R&D player/commercial firm will be participating (can be as one member of a consortium). Company that has the majority of their work in the commercial market
  — To a consortium
  — HHS Senior Procurement Executive has to approve use of OTA if does not include above

• Cooperative agreement
  — Principal purpose of transaction is the transfer of money, property, service, or anything of value to accomplish a public purpose
  — Substantial Federal involvement with the recipient during performance is anticipated
The USG “Business” Model

• Stockpile MCMs
  — Limited market
• This is an insurance policy
• USG wants products that are
  — Inexpensive
  — Have a long shelf life
  — Can be stored at RT
  — Single dose
  — Potential for self-administration

• Issues
  — Pharmaceuticals are not meant to be stockpiled
  — After a procurement contract is awarded maintaining industry’s interest in developing next generation products
CHALLENGES

• PAHPA reauthorization and continued funding
• Sustaining successful medical countermeasures and their developers
• Technology transfers from pipeline to Centers for Advanced Development and Manufacturing
• Developing readiness and ConOps plans for all MCMs
• Establishing a rapid response infrastructure for unknown threats
• Building and maintaining strong Public-Private Partnerships
Contacting BARDA

BARDA:
URL: http://www.phe.gov
BARDA e-mail: BARDA@hhs.gov

• Upcoming Events
• PHEMCE Strategy and Implementation Plan
• CBRN and Pan Flu Programs
• Business Toolkit

— www.phe.gov/amcg

MedicalCountermeasures.gov

• Tech Watch program
• Federally-sponsored conferences
• Funding opportunities
• Resources 7 core service programs
• Regulatory guidance
• Federal strategies and reports