CURRENT EFFORTS IN CBRN PRODUCT DEVELOPMENT AND BEYOND

George W. Korch
Senior Science Advisor
August 5, 2016

Resilient People. Healthy Communities. A Nation Prepared.

ASPR
All-Hazards Preparedness & Response

POLICY

Bioterrorism Act

Project BioShield

Pandemic & All Hazards Preparedness Act

National Health Security Strategy

MCM Enterprise Review

PHEMCE Strategy & Implementation Plan

PAHPA Reauthorized

2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016

9/11 and Anthrax

Re-emerging H5N1

Katrina, Rita, Wilma

Ike, Gustav

H1N1 Pandemic

Haiti earthquake

Deepwater Horizon and Tornadoes

Japan Earthquake Nuclear Event

Hurricanes Isaac and Sandy

Boston bombings

Ebola MERS Chikungunya

Zika

EVENTS

ASPR ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

ASPR Roles

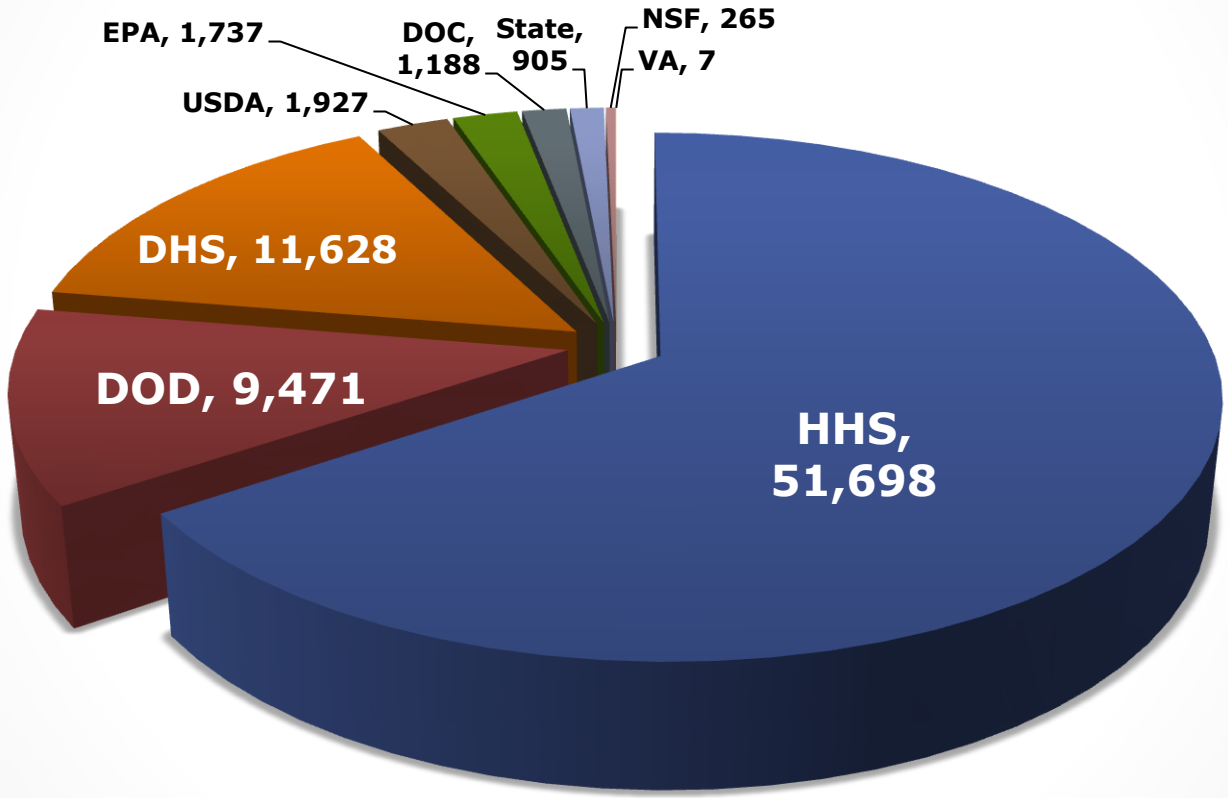
- Medical Countermeasure Development
- National Disaster Medical System Response
- Coordination of ESF 8 for National Response Framework
- International Coordination
- National Health Security Strategy
- National Science Response to Disaster

All-Hazards Approach

Vision

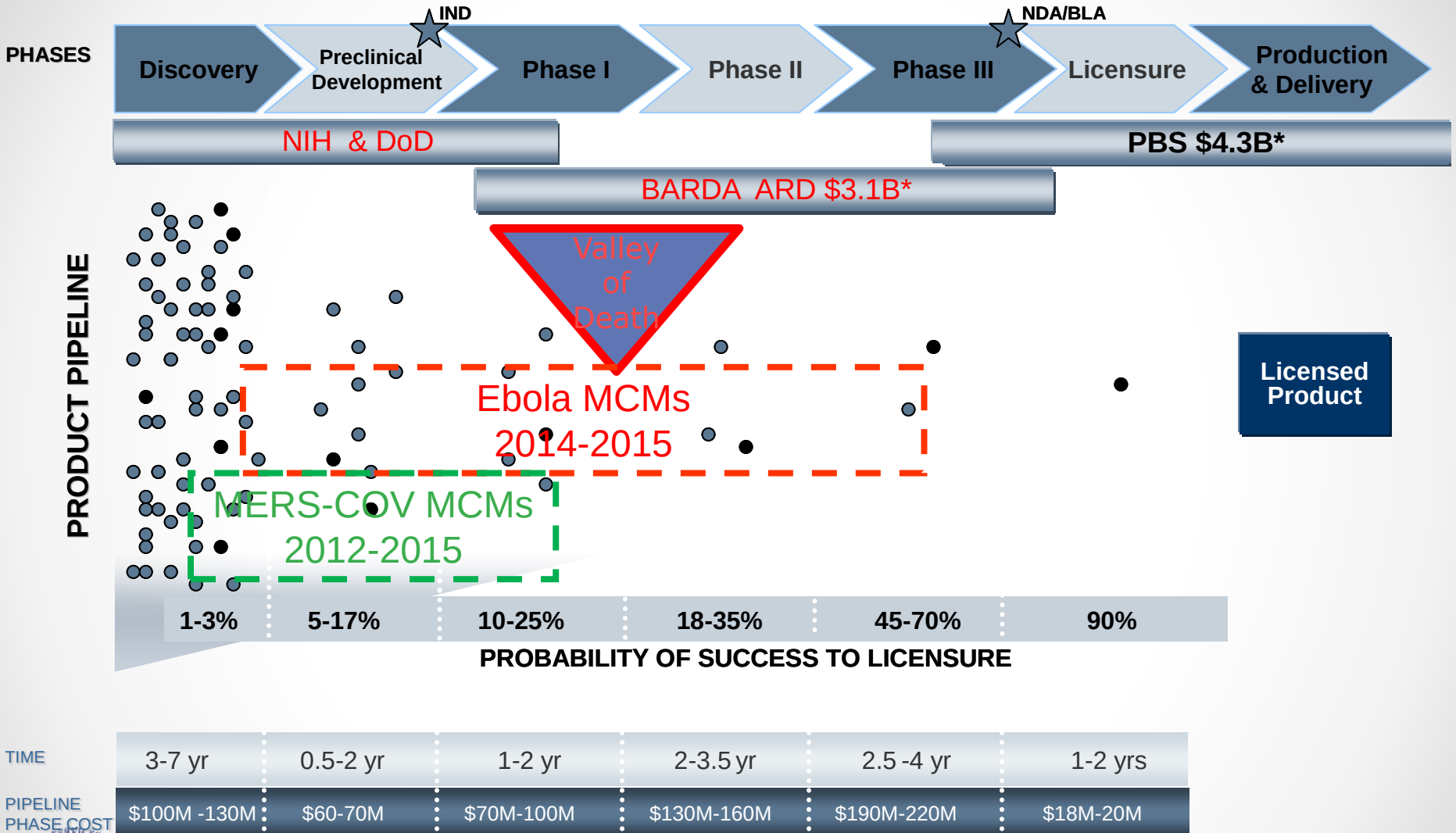
The right medical product to the right person in the right location at the right time

"Biodefense" Expenditures by Agency 2005-2014 ($B)



Funding figures extracted from Center for Health Security

Development is Expensive, Lengthy and Risky

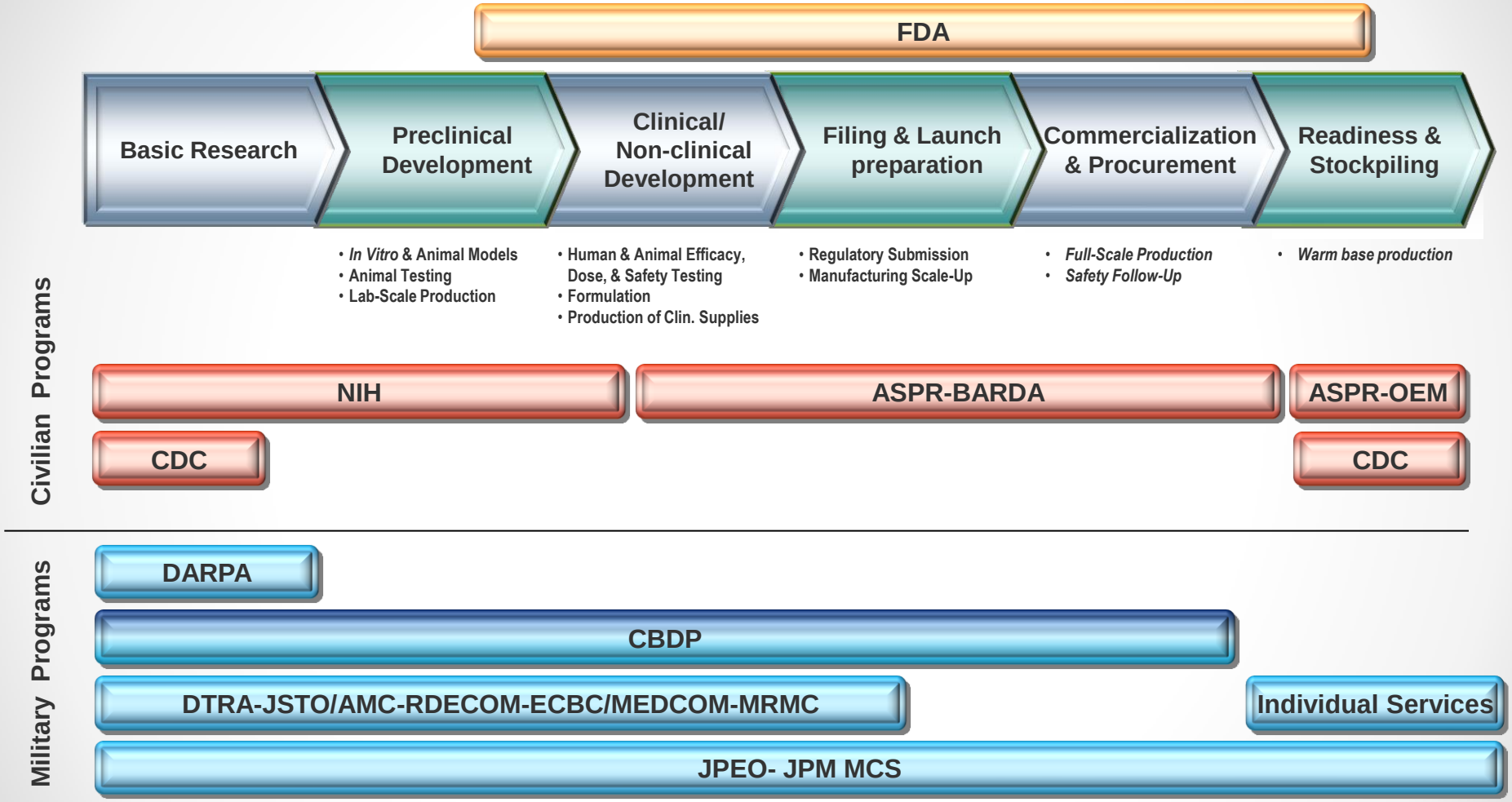


* Represents $1.8B transferred from PBS to support ARD FY09-13, $415M FY14, FY15

* $1.8B transferred to ARD, $255M FY14, FY15

ASPR
ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

No Single Entity Leads the Entire MCM Development Portfolio



High-Priority Threats

- Bacillus anthracis (anthrax)*
- Clostridium botulinum toxin (botulism)*
- Cyanide
- Emerging infectious diseases
  - Pandemic influenza
- Gram negative organisms
  - Francisella tularensis (tularemia)
  - Yersinia pestis (plague)
  - Burkolderia mallei (glanders) and B. pseudomallei (meliodosis)
  - Rickettsia prowazekii (typhus)
- Multi-drug resistant Bacillus anthracis (MDR anthrax)

The PHEMCE 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

- Nerve agents
- Radiological agents (e.g., radiological dispersal devices)
- Nuclear devices
- Variola virus (smallpox)*
- Viral Hemorrhagic Fevers
  - Marburg
  - Ebola

ASPR
ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

2007 PHEMCE Implementation Plan:
Priority Medical Countermeasure Acquisitions

Near-Term
FY 2007-2008

- Broad-Spectrum Antibiotics
- Anthrax Vaccines
- Smallpox Vaccines
- Therapeutic Drugs for Acute Radiation Injury

Mid-Term
FY 2009-13

- Broad-Spectrum Antibiotics
- Diagnostics
- Anthrax Antitoxins
- Filovirus MCMs
- Smallpox Antivirals
- MCMs for ARS and DEARE
- Radionuclide-Specific MCMs
- Rad/Nuc: Biodosimetry/ Bioassays
- Enterprise CHEMPACKS

Long-Term
Beyond 2013

- Broad-Spectrum Antivirals
- Volatile Nerve Agent Antidotes

Reference: *HHS PHEMCE Implementation Plan for CBRN Threats*, Federal Register, Vol. 72 No. 77, April 23, 2007.

ASPR
ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

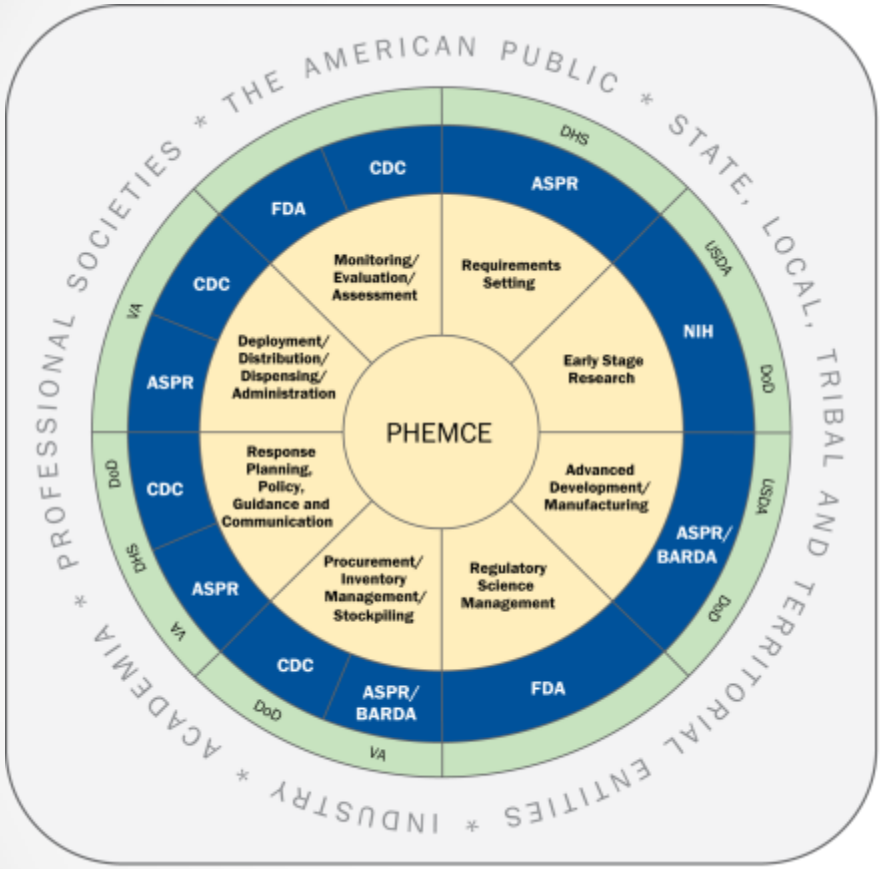
An Enterprise Approach

Strategic attributes for enterprise success:

- Products and capabilities that address clearly defined current requirements
- Multi-use technologies and platforms for future unknown threats
- Increase investment in FDA regulatory science
- Expand core services for industry partners
- More unified governance structure
- Establish a multi-year budget perspective
- Full Life Cycle Management
- Focus on “Final Mile”

ASPR
ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

PHEMCE Lead Roles



Key

- PHEMCE Mission Components
- HHS PHEMCE Agencies
- Non-HHS PHEMCE Agencies
- Non-Federal Stakeholders

Acronyms

PHEMCE: Public Health Emergency Medical Countermeasure Enterprise

DHS: Department of Homeland Security

DoD: Department of Defense

USDA: U.S. Department of Agriculture

VA: Department of Veterans' Affairs

HHS: Department of Health and Human Services

ASPR: Assistant Secretary for Preparedness and Response

BARDA: Biomedical Advanced Research & Development Authority

CDC: Centers for Disease Control and Prevention

FDA: Food and Drug Administration

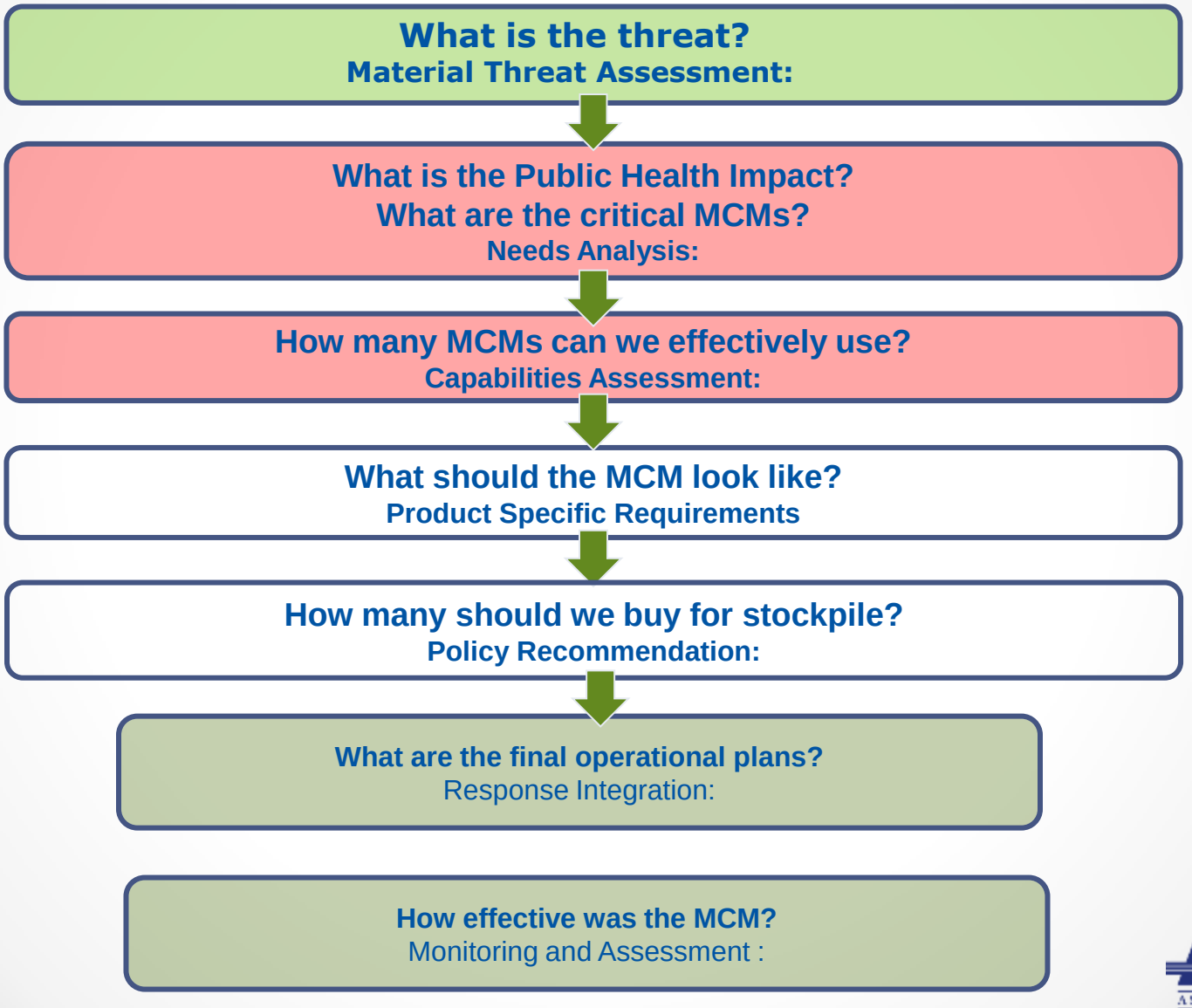
NIH: National Institutes of Health

ASPR
ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

Six Operating Principles

- Public-private partnerships
- Platform and enabling technologies
- Multipurpose products
- Control of total lifecycle costs
- Rigorous portfolio management
- Coordinated effort

PHEMCE MCM Life-cycle Architecture



ASPR
ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

Scope of SNS Inventory

- **$6.5 billion in material**
- **Approximately 900 individual line items**
- **Volume of six super WalMarts**
- **Unique kitted configurations**
- **Detailed physical location data**

A re-look at Requirements

Did we have the best approach?

Department of Homeland Security

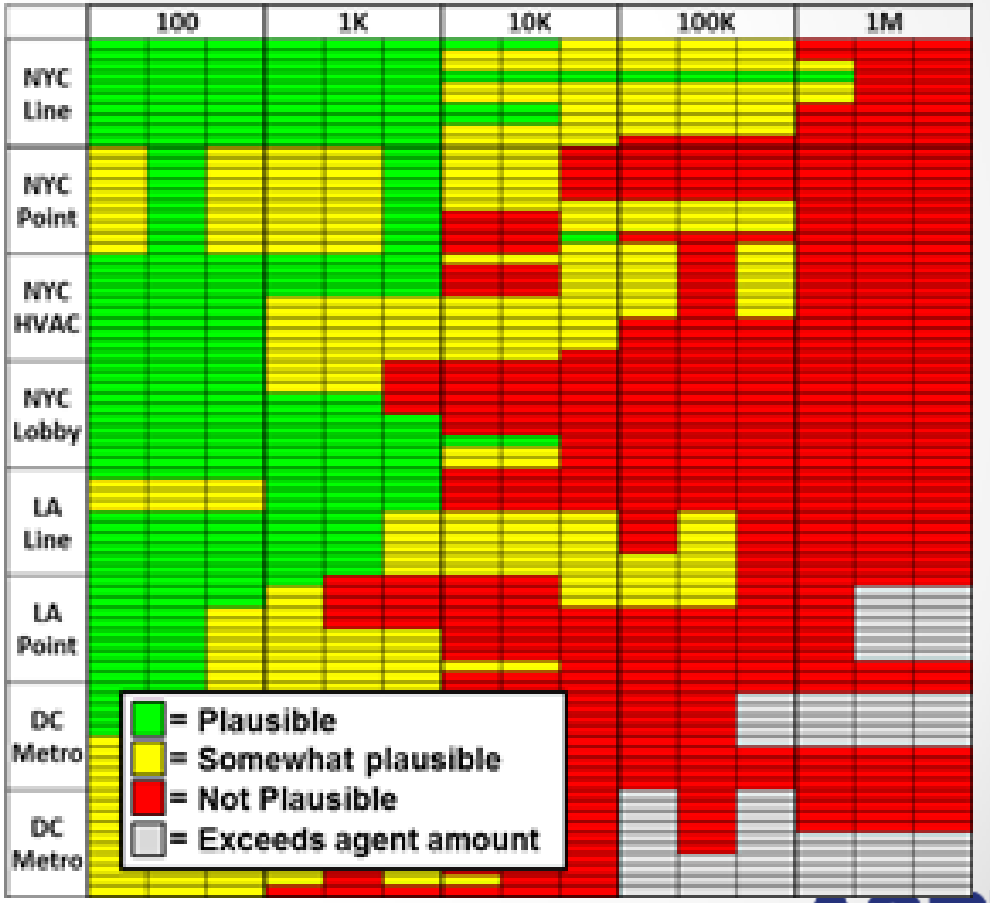
Overview of Material Threat Assessment 2.0

- MTA 2.0 provides:
  - A systematic, actor capabilities-based analyses of the plausibility of a set of scenarios
  - The unmitigated consequences of this set of scenarios
  - A smaller set of 'consensus scenarios'
    - Concurred by PHEMCE-partners
    - Includes unclassified descriptors
    - Available for preparedness and requirements planning
- MTA 2.0 does not provide:
  - Medical consequence analyses (e.g., mitigated consequences)
  - Recommendations on stockpiling
  - Answers to MCM policy questions (e.g., multiple attacks)

Main Result: MTA 2.0 Plausibility Matrices

- One matrix per adversary capability
  - Low, medium, high
- Multi-factorial output seen in one glance:
  - Scenarios of weapon use
  - Numbers of people exposed
  - Adversary capability
  - Plausibility of successful execution
- Methodology permits this matrix to be updated easily if new info arrives

NOTIONAL



Homeland Security

ASPR
ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

MTA 2.0 Status

- **Anthrax – delivery imminent**
- **Smallpox**
- **Radiological Dispersal Devices**
- **Pharmaceutical Based Agents**

Advanced Development (AD) and Procurement Priorities

Medical Countermeasure Category	AD Priorities Through FY17[1]	Current HHS Holdings[2]	Procurements Programmed Through FY13[3]	Additional Procurements Projected Through FY17[4]
Anthrax Antitoxin	X	X	SRF[5]	TBD[6]
Anthrax Vaccine	X	X	DSNS[7]	DSNS, TBD
Botulism Antitoxin	X	X		
Broad Spectrum Antimicrobials	X	X[8]	DSNS	DSNS, TBD
Cyanide Antidote	X	X		DSNS
Diagnostics – Bioassay	X			
Diagnostics – Biodosimetry	X			TBD
Diagnostics – Biological Agents	X			
Diagnostics – Pandemic Influenza	X			
Diagnostics – Volatile Nerve Agents	X			
Nerve Agent Antidote	X	X	DSNS, SRF	DSNS
Nuclear Agents – Acute Radiation Syndrome (ARS) – Gastrointestinal (GI), Skin, and/or Lung Therapeutics	X			TBD
Nuclear Agents – ARS – Hematopoietic Therapeutics	X	X	SRF	
Nuclear Agents – Thermal Burn Therapeutics	X	X	DSNS	TBD
Pandemic Influenza Antivirals	X	X	DSNS	DSNS
Pandemic and Pre-Pandemic Influenza Vaccine	X	X		
Patient (Chemical) Decontamination	X			
Radiological Agents – Decorporation/ Blocking Agents	X	X	DSNS	DSNS, TBD
Respiratory Protective Devices	X			DSNS
Smallpox Antivirals	X	X	SRF	
Smallpox Vaccine	X	X	DSNS, SRF	DSNS, TBD
Ventilators	X	X	DSNS	
Viral Hemorrhagic Fever Antivirals	X			
Viral Hemorrhagic Fever Vaccine[9]				

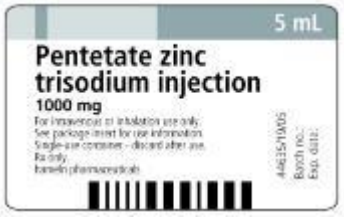
ASPR
ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

BARDA's Efforts

Stockpiled MCM's from Project BioShield

Smallpox

Anthrax

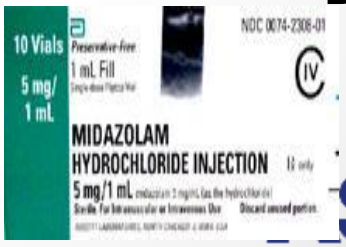


Radiation

Thermal Burns 2015

Chemical

Botulism



BARDA Supported FDA Approved Products

Cell-based Influenza Vaccine

FLUCELVAX® Influenza Virus Vaccine — *Novartis*

Influenza IV Antiviral Drug

BioCryst Pharmaceuticals, Inc.

H1N1 & H5N1 Vaccines w/ Adjuvant

GlaxoSmithKline

Next-Generation Portable Ventilators

Covidian

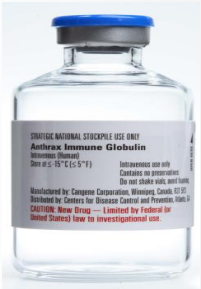
Flu/RSV POC Diagnostic

Recombinant-based Influenza Vaccine

Protein Sciences Corp.

Anthrax Antitoxins

HGS/GSK



Emergent

Botulinum Antitoxin

Cangene

Amgen

ASPR
ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

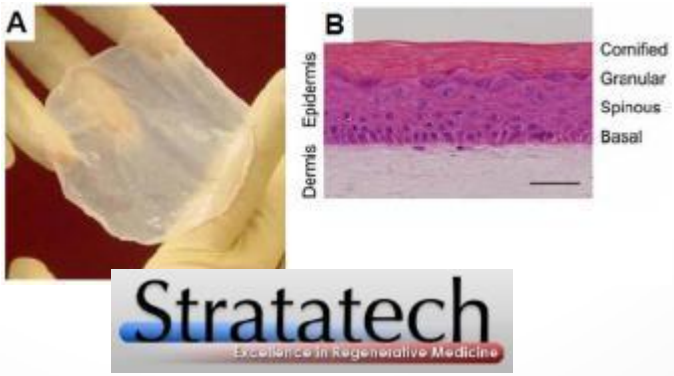
Products Stockpiled under Project BioShield – New in FY 2015

Burn MCMs

Silver Impregnated Bandages

Enzymatic Debridement

Cell-based Skin Substitutes

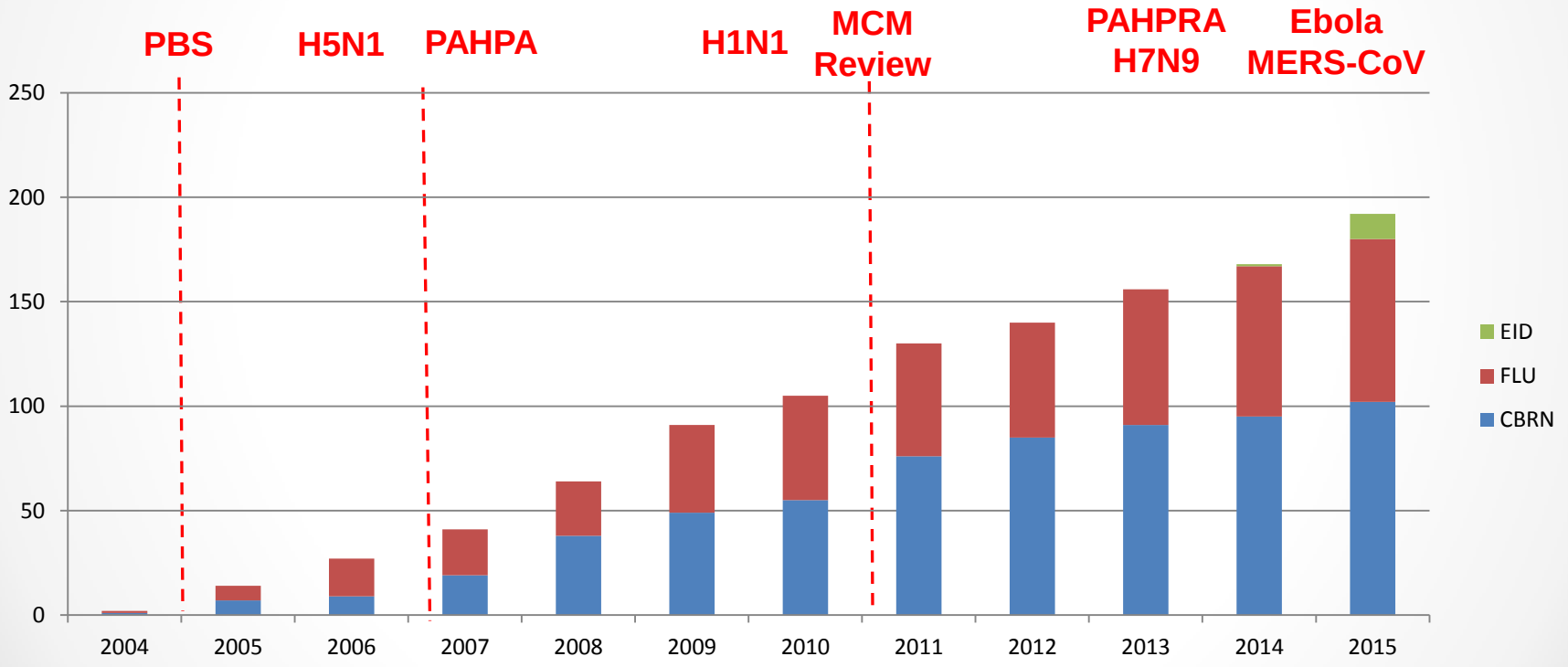


Autograft-Sparing Technologies

ASPR
ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

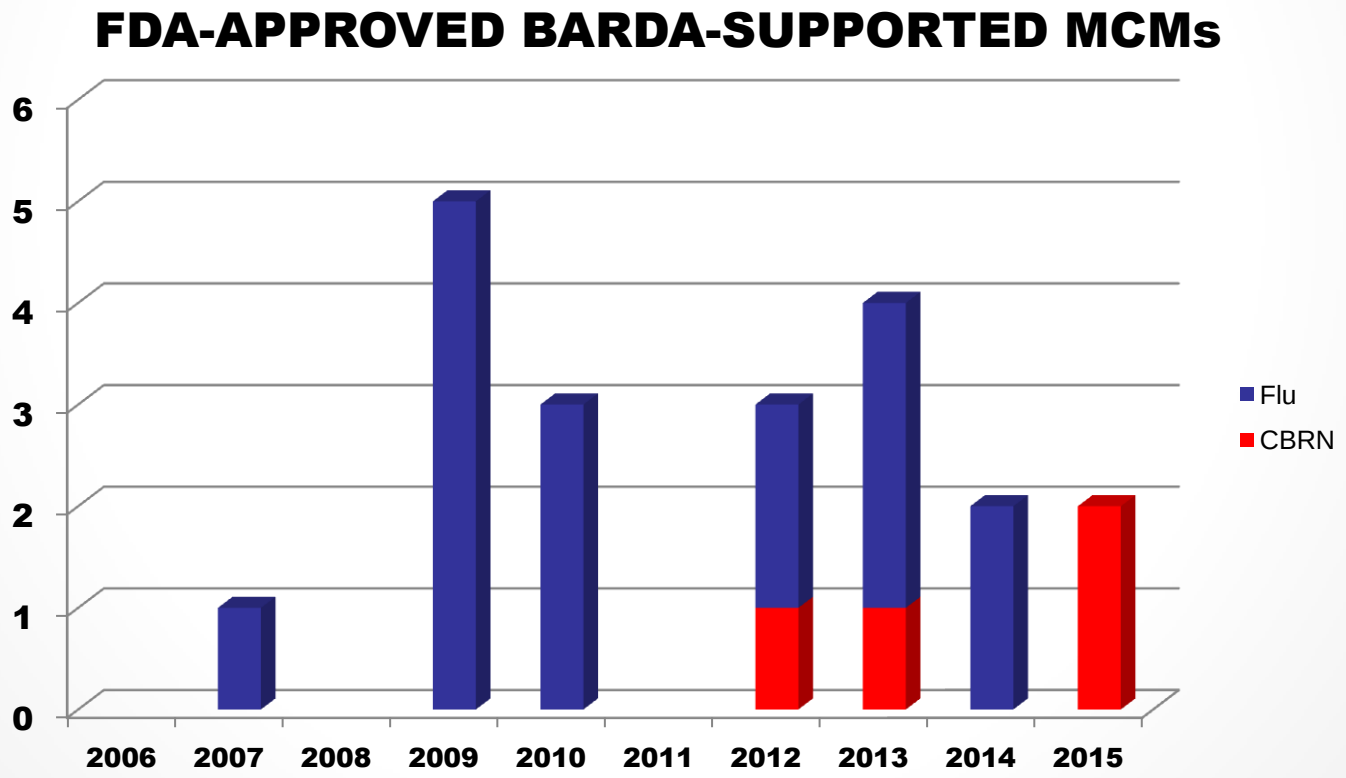
Create Robust & Innovative MCM Development Pipeline

- ~ 200 MCM product candidates in development



FDA-approved BARDA products

- **FDA has approved 15 MCMs supported by BARDA with 4-5 more approvals expected in near-future**



Major Accomplishments

- Approved nine MCM new requirements for viral hemorrhagic fevers; smallpox; chemical threats; pandemic influenza; and botulism.
- Greatly accelerated MCM's for Ebola, now Zika
- Made 2 Project BioShield Procurements for SNS (anthrax antitoxin, smallpox vaccine)
- Received FDA approval for CBRN & influenza products
  - Anthrasil, Neupogen (ARS), Cipro (plague), moxifloxicin (plague)
  - Flucelvax® and Rapivab® approved, FluBlØk® expanded indication
- Demonstrated effective reduced dose schedule for anthrax vaccine
- Data and final report submitted Neulasta for neutropenia due to radiation

New Products Projected for SNS 2016-2019

- Artificial **skin replacement therapy** for definitive care treatment of thermal and radiation burns
- Antimicrobial drug-impregnated **mesh dressings** for point-of-care treatment of thermal and radiation burns (
- Multiple **broad spectrum antibiotics** for treatment of anthrax, plague, tularemia, and other biothreats
- Gene expression- and other technology-based **biodosimetry devices** for quantitative measurement of ionizing radiation exposure in affected persons following a nuclear event
- Chemical **antidotes for cyanide poisoning and highly-volatile nerve agents**
- **Next-generation anthrax vaccine** and adjuvanted enhancement to the current anthrax vaccine
- New **lyophilized MVA smallpox vaccine** for "at-risk" individuals which will provide a significant lifecycle costs savings
- S**econd smallpox antiviral drug**
- **Therapeutics and vaccines for Ebola**
- **Zika Diagnostics and Vaccine**

ASPR
ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

Advanced Development (AD) and Procurement Priorities

	Medical Countermeasure Category	AD Priorities Through FY17[1]	Current HHS Holdings[2]	Procurements Programmed Through FY13[3]	Additional Procurements Projected Through FY17[4]
✓	Anthrax Antitoxin	X	X	SRF[5]	TBD[6]
✓	Anthrax Vaccine	X	X	DSNS[7]	DSNS, TBD
✓	Botulism Antitoxin	X	X		
✓	Broad Spectrum Antimicrobials	X	X[8]	DSNS	DSNS, TBD
✓	Cyanide Antidote	X	X		DSNS
	Diagnostics – Bioassay	X			
✓	Diagnostics – Biodosimetry	X			TBD
✓	Diagnostics – Biological Agents	X			
✓	Diagnostics – Pandemic Influenza	X			
	Diagnostics – Volatile Nerve Agents	X			
✓	Nerve Agent Antidote	X	X	DSNS, SRF	DSNS
✓	Nuclear Agents – Acute Radiation Syndrome (ARS) – Gastrointestinal (GI), Skin, and/or Lung Therapeutics	X			TBD
✓	Nuclear Agents – ARS – Hematopoietic Therapeutics	X	X	SRF	
✓	Nuclear Agents – Thermal Burn Therapeutics	X	X	DSNS	TBD
✓	Pandemic Influenza Antivirals	X	X	DSNS	DSNS
✓	Pandemic and Pre-Pandemic Influenza Vaccine	X	X		
✓	Patient (Chemical) Decontamination	X			
✓	Radiological Agents – Decorporation/ Blocking Agents	X	X	DSNS	DSNS, TBD
✓	Respiratory Protective Devices	X			DSNS
✓	Smallpox Antivirals	X	X	SRF	
✓	Smallpox Vaccine	X	X	DSNS, SRF	DSNS, TBD
✓	Ventilators	X	X	DSNS	
✓	Viral Hemorrhagic Fever Antivirals	X			
✓	Viral Hemorrhagic Fever Vaccine[9]				

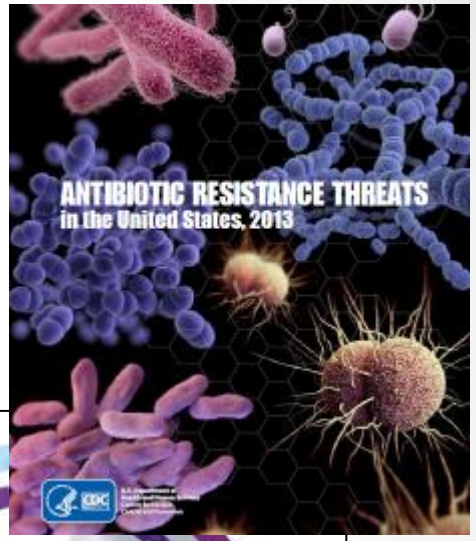
ASPR
ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

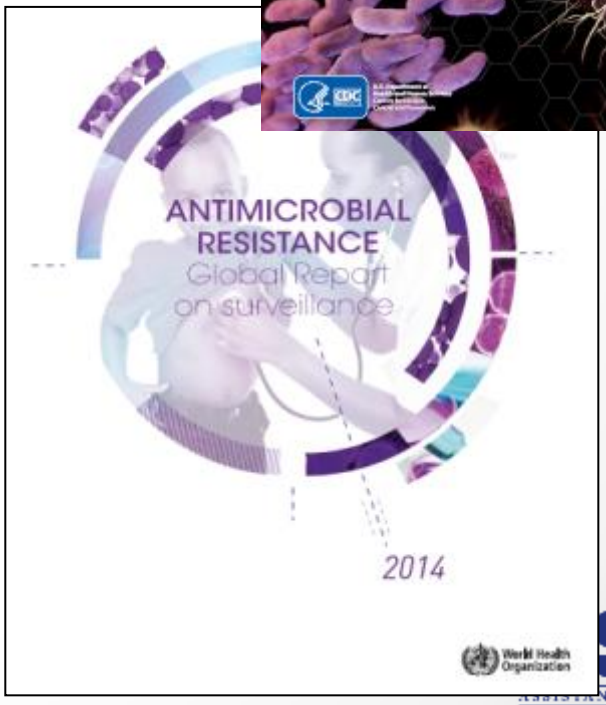
More Major Accomplishments

- CDC published four Guidance Documents
  - Expert Panel Meetings on Prevention and Treatment of Anthrax in Adults" (*Emerging Infectious Dis*eases)
  - "Special Considerations for Prophylaxis and Treatment of Anthrax in Pregnant and Postpartum Women" (*Emerging Infectious Diseases*)
  - "Pediatric Anthrax Clinical Management" (*Pediatrics*)
  - "Clinical Guidance for Smallpox Vaccine Use in a Postevent Vaccination Program" (*MMWR*)

Antimicrobial Resistance Threat

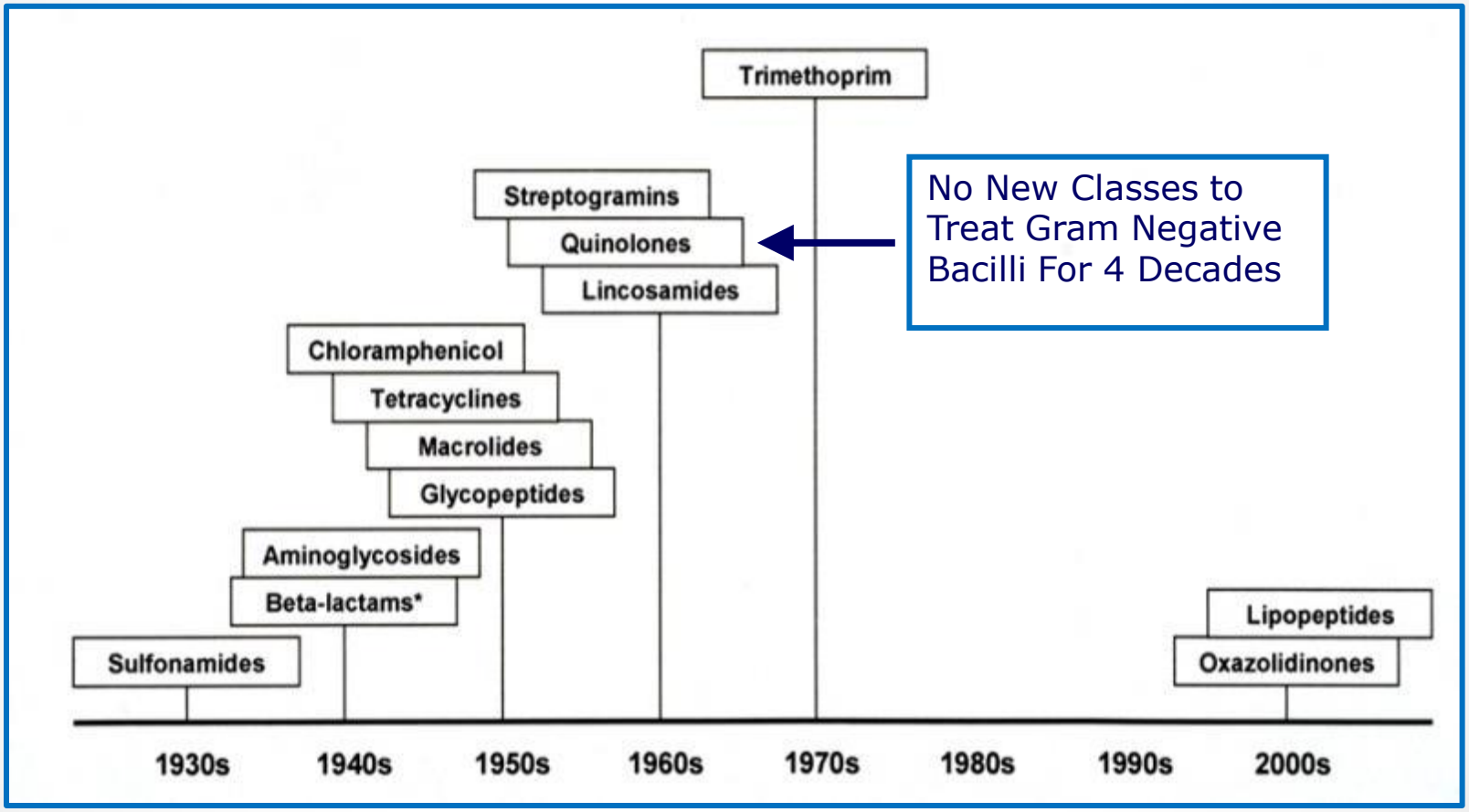
- 2M infections per year caused by AMR pathogens
- 23,000 deaths annually in US
- Estimated economic burden of $20-35B annually
- Categorizes AMR pathogens in terms of public health threat: Urgent, Serious, or Concerning
- FQ resistance in *E. coli* now greater than 50%, untreatable GC now detected in 11 countries.





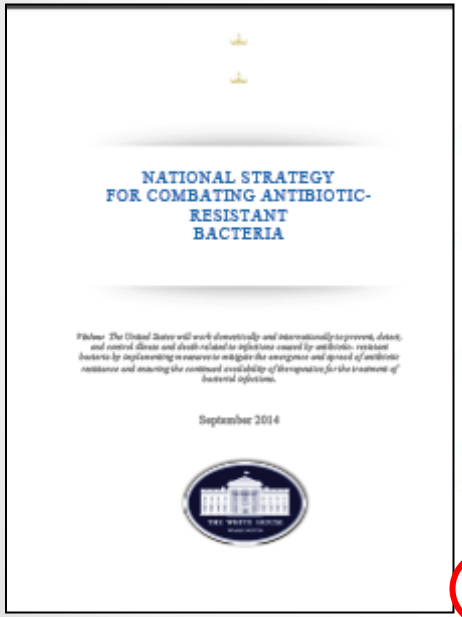
SPR
ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

The Antibiotic Development Gap



Combatting Antibiotic Resistant Bacteria (CARB) National Strategy

- GOAL 4: Accelerate Basic and Applied Research and Development for New Antibiotics, Other Therapeutics, and Vaccines



4.1 Conduct research to enhance understanding of environmental factors that facilitate the development of antibiotic resistance and the spread of resistance genes that are common to animals and humans.

4.2 Increase research focused on understanding the nature of microbial communities, how antibiotics affect them, and how they can be harnessed to prevent disease.

4.3 Intensify research and development of new therapeutics and vaccines, first-in-class drugs, and new combination therapies for treatment of bacterial infections.

4.4 Develop non-traditional therapeutics and innovative strategies to minimize outbreaks caused by resistant bacteria in human and animal populations.

4.5 Expand ongoing efforts to provide key data and materials to support the development of promising antibacterial drug candidates.

4.6 Enhance opportunities for public-private partnerships to accelerate research on new antibiotics and other tools to combat resistant bacteria.

4.7 Create a biopharmaceutical incubator—a consortium of academic, biotechnology and pharmaceutical industry partners—to promote innovation and increase the number of antibiotics in the drug-development pipeline.

DEPARTMENT OF HEALTH & HUMAN SERVICES · USA

ASPR
ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

BARDA's Antimicrobial Portfolio

BARDA's BSA Supported Product Pipeline

	Sponsor	Compound	Development			
			Preclinical	Phase I	Phase II	Phase III
Antibiotics	Achaogen	Plazomicin (ACHN-490)	**Next-generation aminoglycoside: Broad Spectrum** plague, tularemia and carbapenem resistant Enterobacteriaceae (CRE)			
	CUBRC/ Tetraphase	Eravacycline (TP-434)	**A novel fully synthetic tetracycline: Broad Spectrum** plague, tularemia, complicated intra-abdominal and urinary tract infections (cIAI, cUTI)			
	Cempra	Solithromycin (CEM-101)	**Next-generation fluoroketolide: Broad Spectrum** anthrax, tularemia , gonorrhea and community-acquired bacterial pneumonia (CABP)			
	Rempex	Carbavance™ (meropenem/ RPX7009	**Carbapenem/β-lactamase inhibitor: Broad Spectrum** CRE, cUTI, hospital-acquired pneumonia /ventilator-associated pneumonia (HAP)/(VAP), melioidosis, glanders			
	GSK	A portfolio approach	**Broad Spectrum Antibiotic Portfolio** A partnership to fund multiple compounds to combat antibiotic resistance at various stages of development			
	Astra Zeneca	A portfolio approach	**Broad Spectrum Antibiotic Portfolio** A partnership to fund multiple compounds to combat antibiotic resistance at various stages of development			

Disclaimer: The above projects are supported by BARDA's BSA Program utilizing non-dilutive funding via a contract and/or agreement. The stage of development is approximate as of July 2015 (please refer to the sponsors site for updated information). The table represents the compounds most advanced commercial indication being pursued by the developer.

Partnership for Antibacterial Drug Development

Use of Other Transactional Authorities

- Five year $200M public:private partnership in May 2013
- Development of multiple antibiotic candidates
- Fluidity in activities and resources to adapt to technical risk and programmatic priorities
- Governance is through a BARDA:GSK Joint Oversight Committee
- Allows for external partnerships through co-development or in-licensing agreements

More Success

- 2nd Other Transaction Authority Use Negotiated
- Portfolio of antibacterial candidates, the lead of which is aztreonam-avibactam (ATM-AVI)
- Strategic decisions will be made by a BARDA-AZ Joint Oversight Committee
- Fulfills requirement in CARB National Plan for ASPR/BARDA
  - Create at least one additional portfolio partnership with a pharmaceutical or biotechnology company by March 2016 to accelerate development of new antibacterial drugs
- Establishes international collaboration between BARDA and the EU's Innovative Medicines Initiative (IMI)
  - Both entities will provide support for ATM-AVI pivotal trials

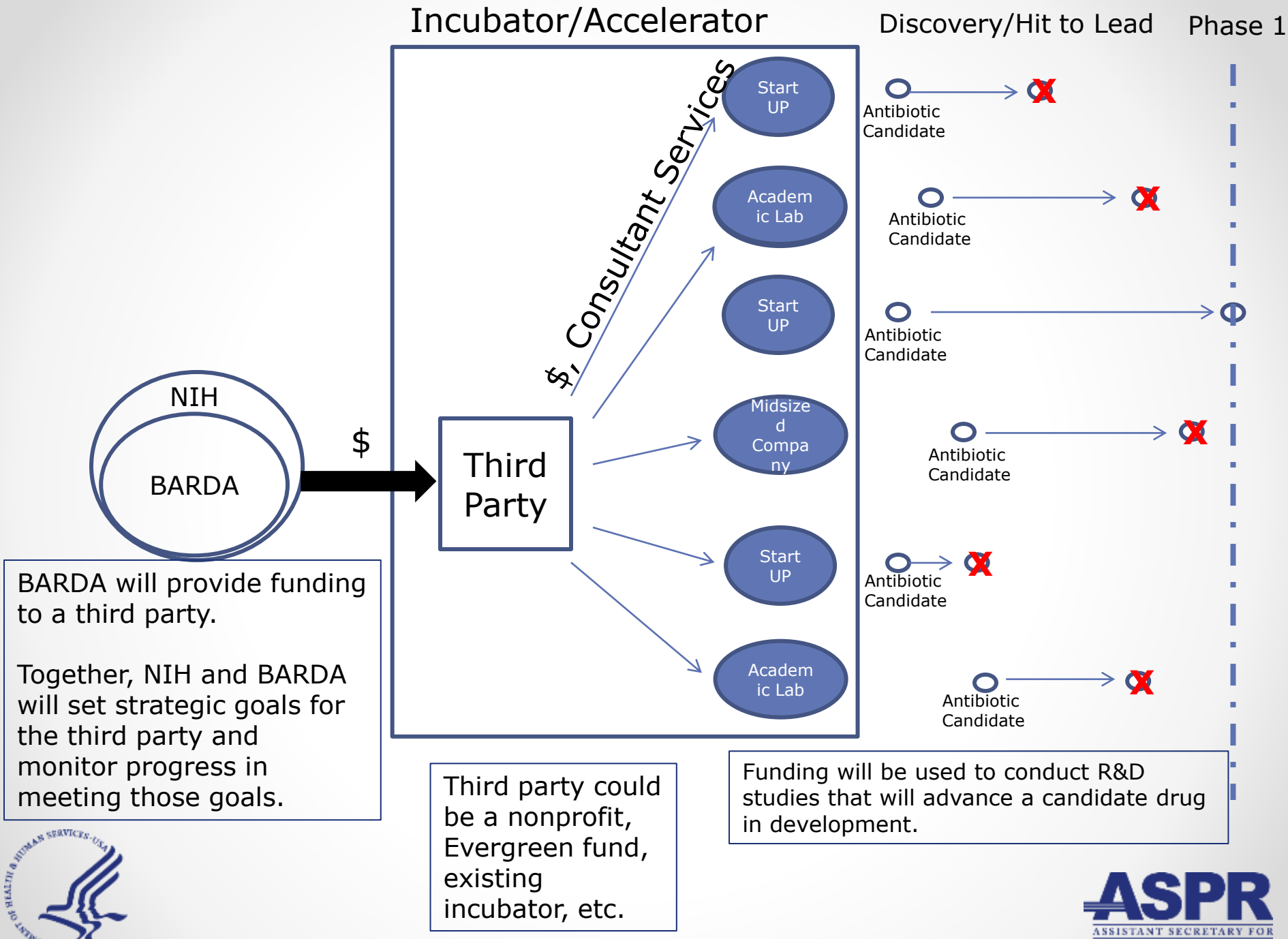
CARB Accelerator (CARB-X)

- Robust early stage R&D environment and pipeline of antimicrobial products to counter the increasing threat of antimicrobial resistant infections
  - rapidly develop and commercialize new antibacterial products

- NIAID and BARDA collaboration to fund a Biopharmaceutical Accelerators (s) to identify, assemble, and accelerate a portfolio of innovative early antibacterial products
- Formally Announced on July 28th

Award Information

- Cooperative Agreement
- Anticipated # of awards: 1
- Anticipated Project Period: 5 years
- Five one (1) year budget periods
- First Year Anticipated Budget Funding(FY16): $30M
- Total Anticipated Project Funding (subject to availability of funds): $250M
- Total Anticipated Match: $275M

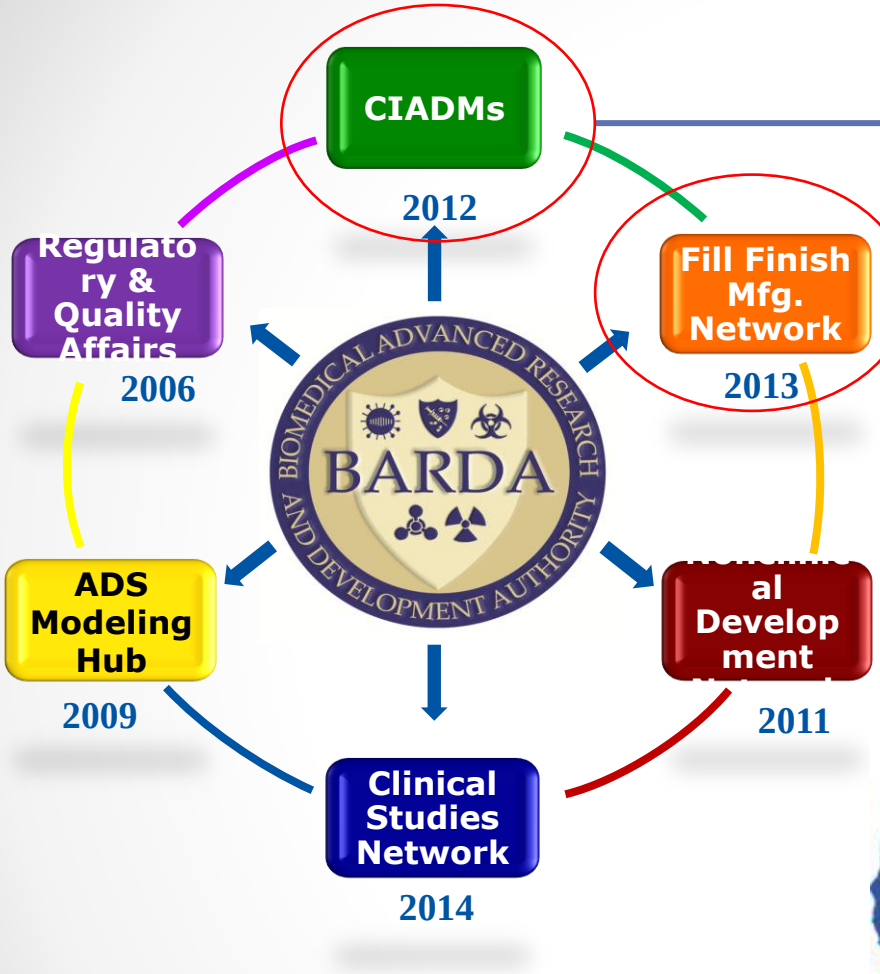

Incubator/Accelerator
Discovery/Hit to Lead
Phase 1
NIH
BARDA
$
Third Party
$, Consultant Services
Start UP
Academic Lab
Start UP
Midsized Company
Start UP
Academic Lab
Antibiotic Candidate
Antibiotic Candidate
Antibiotic Candidate
Antibiotic Candidate
Antibiotic Candidate
Antibiotic Candidate
BARDA will provide funding to a third party.
Together, NIH and BARDA will set strategic goals for the third party and monitor progress in meeting those goals.
Third party could be a nonprofit, Evergreen fund, existing incubator, etc.
Funding will be used to conduct R&D studies that will advance a candidate drug in development.
ASPR
ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

Building Advanced Research and Development **Capacity** for the Future

Change from Threat to Capability Focus

- Build facilities and strategy to adapt to rapidly identified threats
- Centers for innovative Advanced Development and Manufacturing (BARDA)
- Fill and Finish network (BARDA)
- Animal Model Network and Services (BARDA, NIH)
- Clinical Trials Network and Training Programs (BARDA and NIH)
- NIH diagnostics, sequencing facilities, reagent manufacturing, epitope mapping, biosafety lab support, and computational biology.

BARDA Core Services Assistance Program



Focus on Manufacturing capabilities

National Center for Therapeutics Manufacturing (NCTM)

TAMUS managed, privately-operated, biopharmaceutical process development and manufacturing facility

- ***Flexible-by-design, multi-product, multi-technology architecture***
- ***Accommodate all "best of breed" flexible bioprocess technologies***
- Personalized therapeutics to moderate scale bioreactors (1,000 L)
- Lower initial capital outlay by ~5X and reduces operational costs
- Focus: Phase 1, Phase 2, and Phase 3 transition studies
- Supports workforce training with dedicated mock cGMP lab space
- Multiple projects conducted simultaneously in fully contained modular clean rooms (MCRs)
- Conducting work on Process Development & Validation Plans
- Originally funded by a $50 million competitive award from the State of Texas Emerging Technology Fund (January 27, 2009)

The NCTM is a fully operational flexible, multi-product, multi-technology biopharmaceutical facility using modular technology with the ability to rapidly surge in response to national threat.

Flexing the "Capability Muscle" Ebola & International Efforts

2014-15: Worst Ebola Epidemic in History

Ebola Epidemic Therapeutic Programs

Discovery | Preclinical | Phase I | Phase II | Phase III

Other Ebola mAbs

GS-5734

TKM -100802

Convalescent Sera

Pichia platform

AVI-7530

Zmab mAbs

ZMapp™ mAbs

BCX4430

Brincidofovir for CMV/Adno

Favipiravir for influenza

REGN3477-70-71

hZMapp mAbs

Trichoderma platform

Mil-77

Current Snapshot November 2015

Ebola Epidemic
Vaccine Programs

USAMRIID
VRP

USAMRIID
VLP

Profectus BioSciences, Inc.
rVSVN4CT1

gsk
ChAd3 EBOV

NewLink GENETICS
MERCK
Be well
xΔG EBOV

NOVARTIS
RNA vaccine

Russian Flu
ΔNS1 Vector

VAXART
HuAd6
EBOV

NOVAVAX
Creating Tomorrow's Vaccines
EBOV GP
Nanoparticle

Crucell
BAVARIAN NORDIC
Ad26/MVA-Filo

Protein Sciences CORPORATION
Protein
Sciences

emergent biosolutions™
MVA for boost

Jefferson.
Rabies EBOV

Current Snapshot
November 2015

FOR OFFICIAL USE ONLY

ASPR
ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

Moving Fast from Bench to Bedside

- Successful rapid testing for Phase I safety (NIH, DOD)
- Accelerated development of Common Master Protocol for adaptive randomized clinical trial design (NIH and others)
- Accelerated Manufacturing Schedule for vaccines (BARDA and Industry)
- Vaccines
  - Clinical Trial Designs
    - ChAd3 EBOV Vaccine (NIH/VRC & GSK) – RCT in Liberia
    - rVSV-ZEBOV GP vaccine (CDC, Merck) – Randomized clustered step wedge in Sierra Leone
  - Providing CRO, logistical plans, & clinical oversight for clinical trial in W. Africa
    - rVSV-ZEBOV GP vaccine (CDC, BARDA) – Randomized clustered step wedge in Sierra Leone
- Therapeutics
  - ZMapp monoclonal antibody therapeutic (BARDA and Industry)
  - Clinical Trial Design
  - Partnership with WHO – on-site liaison on clinical studies for Ebola therapeutics

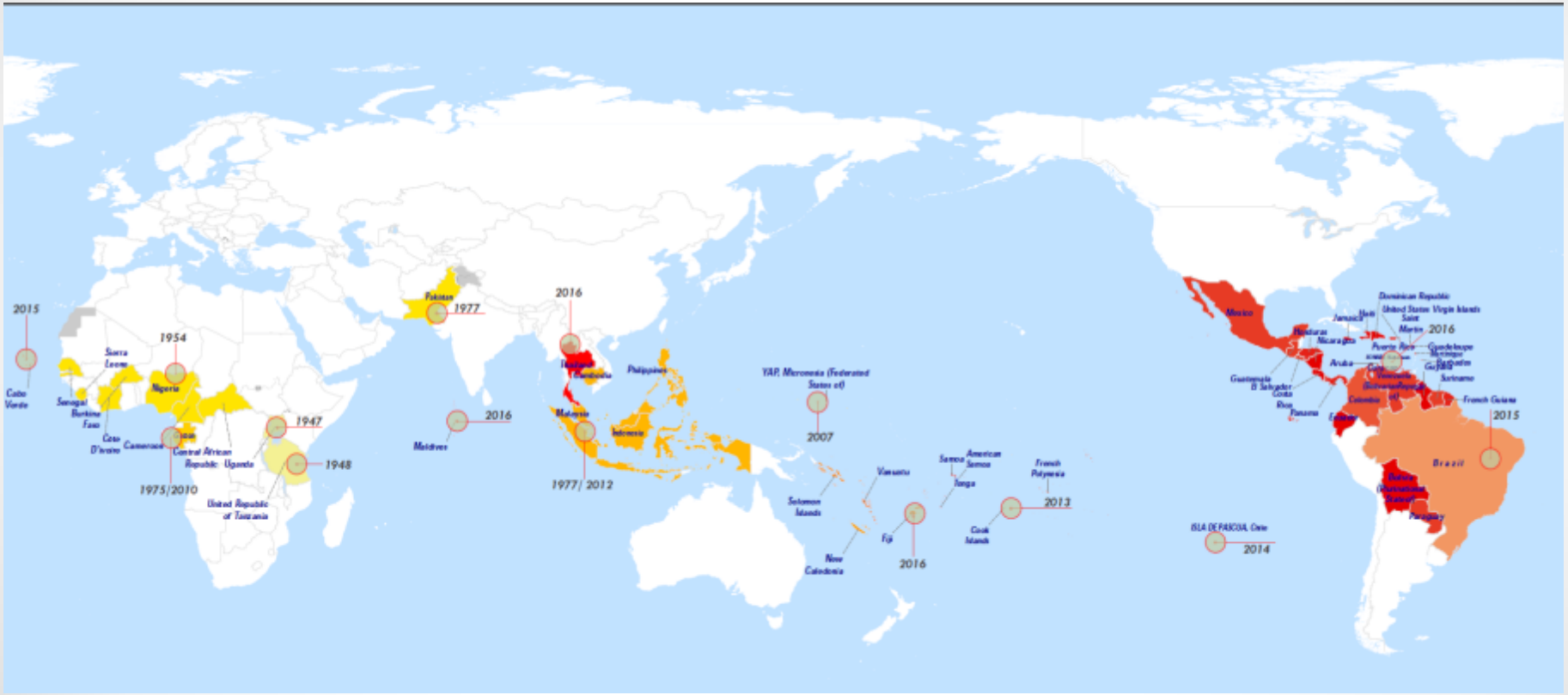
Results for STRIVE

- 7 clinical sites
- 3 data entry hubs
- Web based data system
- 8678 participants enrolled
- 453 safety sub-study participants enrolled
- 527 immunogenicity study participants enrolled

What we have we learned from the PHEMCE can be leveraged for new diseases

- Epidemiology and clinical characterization of the disease are foundational for informed choices about MCM development
- Diagnostics need to move closer to the patient
- Governments have key roles in supporting developers—especially for novel diseases
  - e.g access to samples, development of validation panels
- Consider the full scope of possible countermeasures including diagnostics, vaccines, therapeutics, and other approaches
  - Prioritizing most appropriate candidates for development and testing requires early engagement across MCM Enterprise and with end users
- Distribution and acceptability are critical factors to address up front

Spread of ZIKA Virus 1947-2016



PREPAREDNESS AND RESPONSE

Addressing the Zika Virus Epidemic
ASPR/BARDA Priorities

BARDA will work with PHEMCE partners to address medical countermeasure needs for the Zika response both domestically and globally.

Prevent Zika virus infection through new vaccines

Detect acute and previous Zika virus infections through new rapid diagnostics

Ensure a blood supply safe from Zika virus through use of screening tests for donated blood and virus inactivation in blood products

Activate our National Medical Countermeasure Response Infrastructure to help medical countermeasure developers

ASPR
ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

US Vaccine Priorities

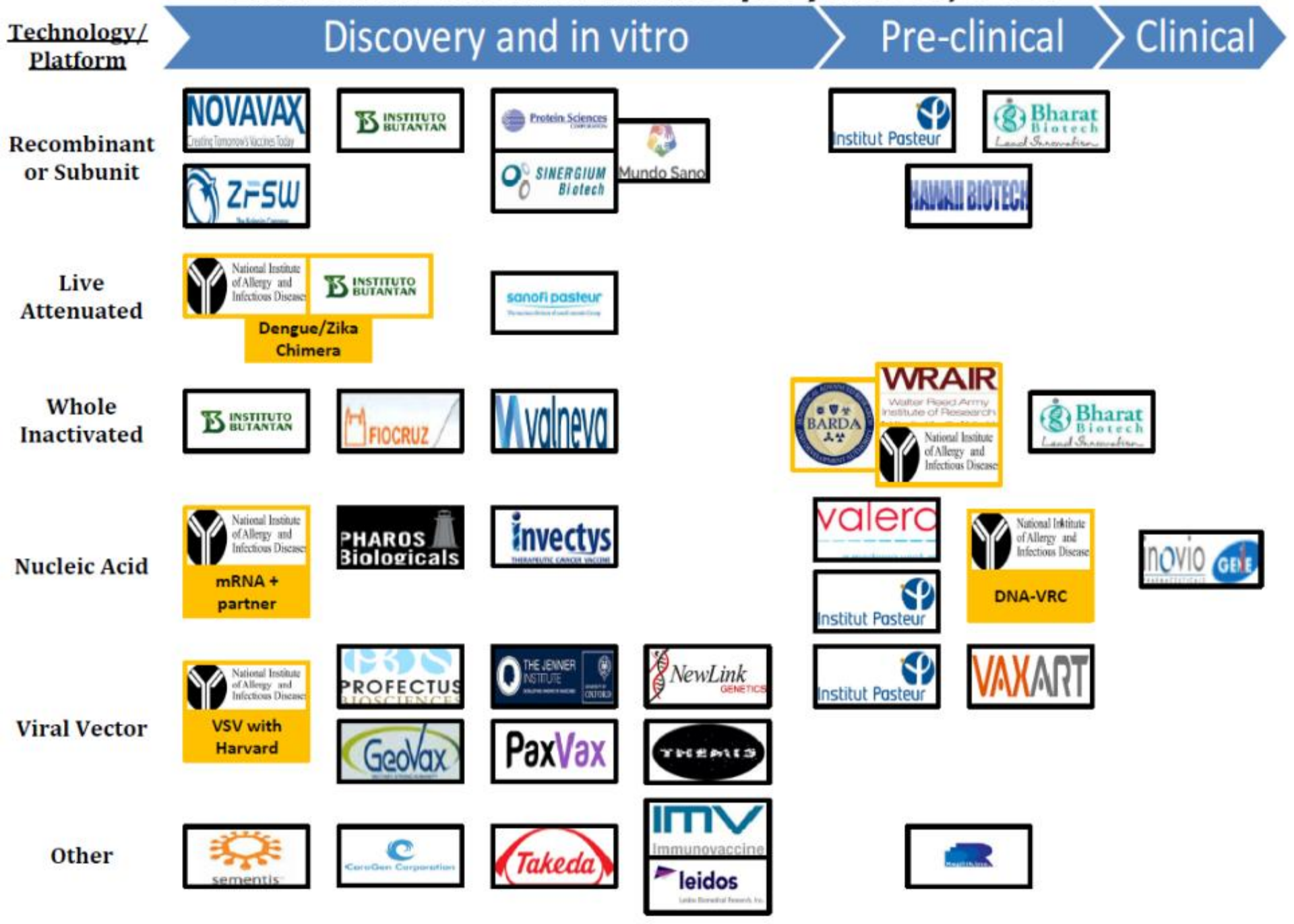
Prevent Zika Infection

- NIH/DOD/BARDA collaboration for USG-developed, manufactured, and evaluated Zika virus vaccine
- NIH and BARDA to support private sector development of vaccine through federal funding opportunities
- HHS to support international collaborations, including vaccine production at the Butantan Institute in Brazil

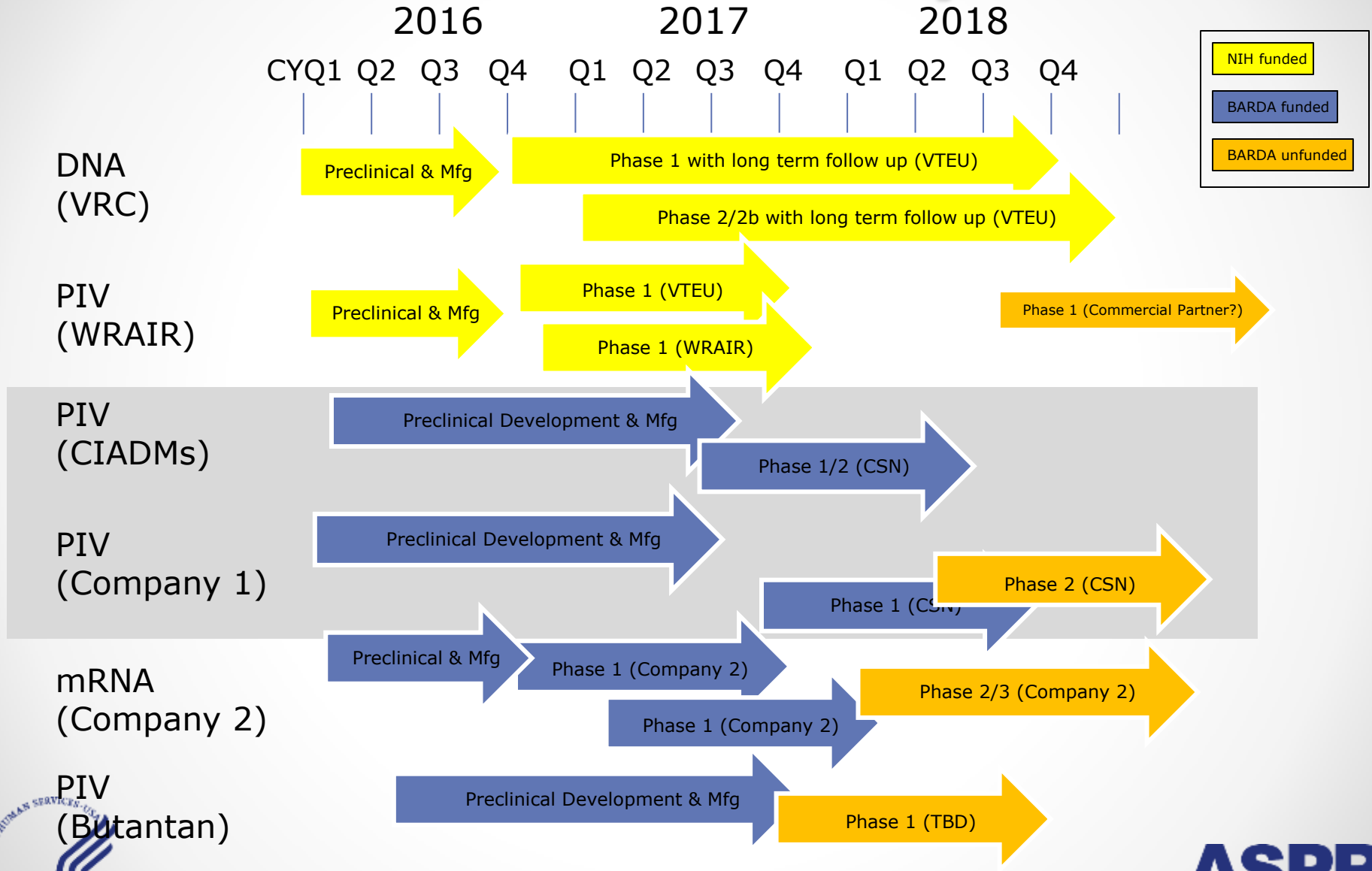
Zika Virus Vaccine Landscape: 1 February 2016

Technology/ Platform	Discovery and *in vitro*	Preclinical	Clinical
Recombinant or Subunit	NOVAVAX; HAWAII BIOTECH		
Live Attenuated	National Institute of Allergy and Infectious Diseases: Dengue/Zika Chimera		
Nucleic Acid	National Institute of Allergy and Infectious Diseases: DNA-VRC		
Viral Vector	PROFECTUS BIOSCIENCES		

Zika Virus Vaccine Landscape: June 20, 2016



Vaccines in Development



ASPR
ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

Where might a global MCM development effort have a role?

Neglected Diseases of Public Health Significance

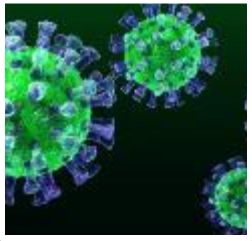
- For neglected diseases with sporadic outbreaks, global coordination and prioritization of MCMs makes sense

Emerging/Re-Emerging Diseases

- Emerging and re-emerging diseases require global collaboration in to speed MCM development.

Combatting Antibiotic Resistance

- Global coordination on prioritization, clinical research networks, and regulatory policy could help develop new antimicrobials faster



Science Preparedness

- We must ensure that we learn and institutionalize the important clinical, public health, and research lessons during international public health emergencies so we are better prepared next time

ASPR
ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

Key MCM R&D Challenges

Ebola

- **Licensure of vaccines(s), Rx clinical studies, & Survivor transmission**

Pandemic and Seasonal Influenza

- **Antigenic drift & and seasonal influenza vaccine mismatch**

Antibiotic Drug Resistance

- **New drug R&D: conventional & unconventional**
- **Global networks for clinical studies**

MERS-CoV

- **Complete the MERS-CoV basic and translational R&D towards MCM development & approval & clinical study infrastructure in Middle East**
- **Rx & vaccine licensure pathways? Mass vaccination campaigns occur? Stockpiles? What about camel vaccines?**

Zika Virus

- **Diagnostics for Pregnant Population, Vector Control, Vaccines**

Assuring State/Local Readiness CDC's Commitment

- **Measures state/local ability to plan and execute a large-scale MCM response (2015/2016 initiative)**
  - Baseline data for 433 jurisdictions by July 2016
- **Identifies operational gaps and develops solutions**
- **Aligns with PHEMCE methodology for assessing federal operational readiness for an MCM event**
- **GOAL: By 2022, all 62 PHEP jurisdictions will have achieved a "satisfactory" status level on the CDC MCM assessment**

ASPR
ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

Prioritizing Work for Full Preparedness

Determinant	Initiatives
Research and Development	• Develop pre-Emergency Use Authorization (EUA) packages • Evaluate data collection strategies during a public health emergency response • Continue R&D for novel next-generation therapeutics • Provide coverage for additional populations (e.g., under 2 years)
Manufacturing	• Assess production surge capacity and/or market availability for "just in time" procurements
Procurement and Stockpiling	• Procure new and additional MCMs for the Strategic National Stockpile (SNS) • Evaluate options for extending lifecycle of MCMs in the SNS
Response Planning and Guidance	• Develop MCM response strategies • Develop and publish clinical and medical management guidelines • Develop tiered response strategies
Operational Capacity	• Explore alternatives to expand national ability to utilize IV products in an emergency setting • Continue efforts to plan for federal resource support to jurisdictions • Better leverage CDC/DSLR's Operational Readiness Review evaluation process

Special Populations

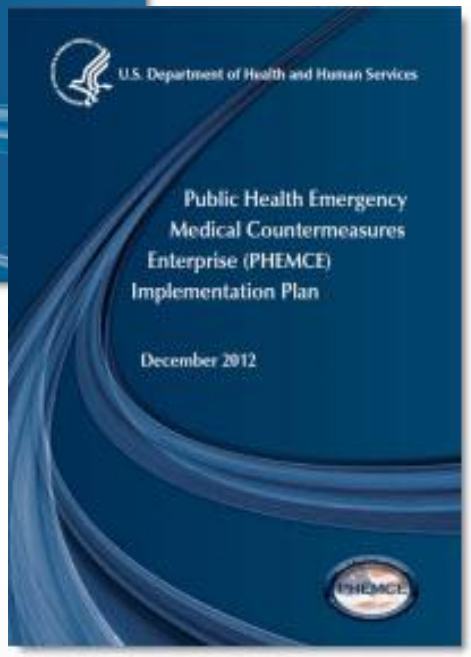
- Pediatric
- Geriatric
- Pregnant/Lactating
- Immunocompromised
- Disabled
- Institutionalized
- Transportation Disadvantaged
- Chronic Illness
- Pharmacological Dependency
- Obesity
- Communication (non-English)

The Evolution of PHEMCE Planning and Capabilities

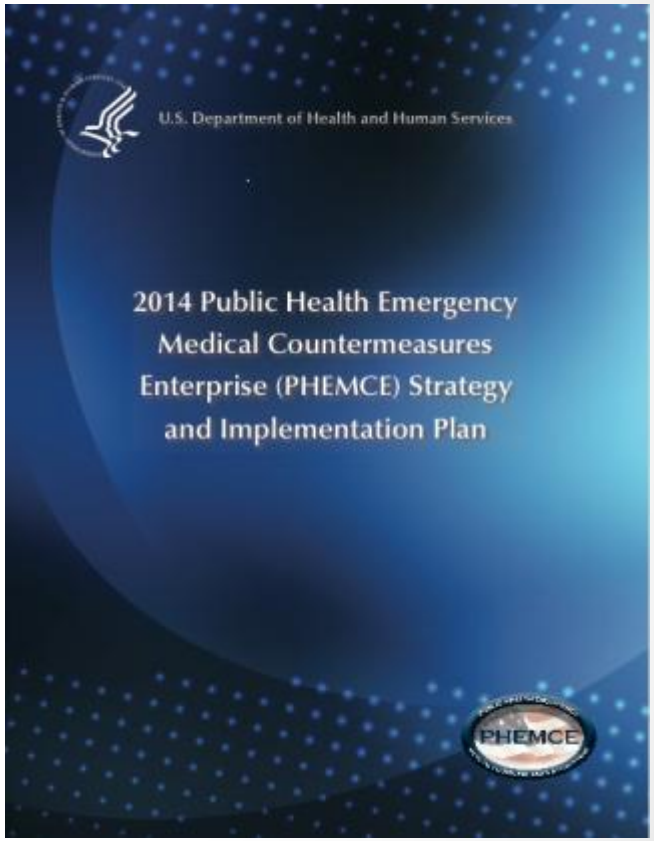
2010

2012

2012



2014



ASPR
ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

Looking Forward

- Greater emphasis needed on Operational Capacity
- "Right-sizing" the portfolio
- Needed attention to SNS Sustainability
- Need continued regulatory research investments
- Better communication with External Stakeholders
- Re-looking at the approaches to unidentified future threats via basic research initiatives