



BARDA's Division of Chemical, Biological, Radiological and Nuclear Medical Countermeasures

Joe Larsen, Ph.D.
Director (Acting)

Division of CBRN Medical Countermeasures

**BARDA Industry Day
November 7 2017**



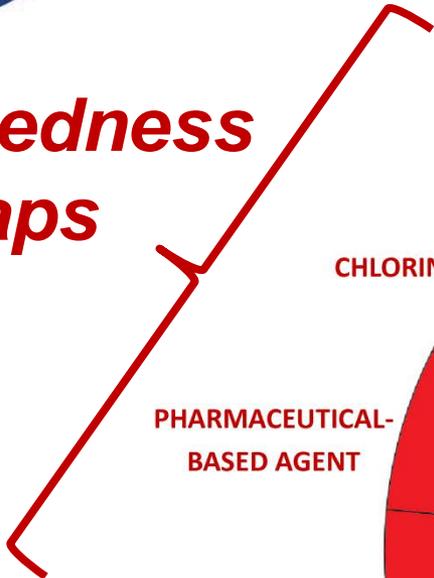
CBRN Threat Landscape



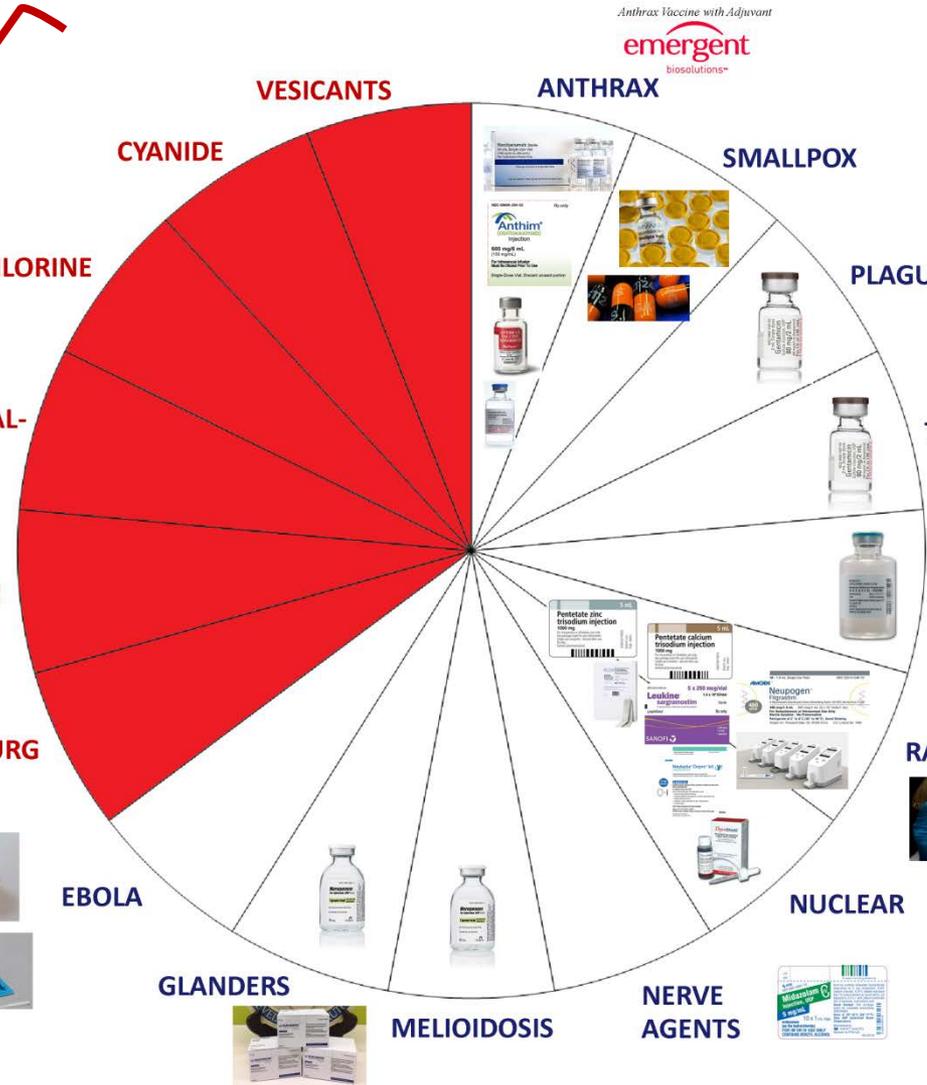


CBRN Preparedness

Preparedness Gaps



PHARMACEUTICAL-BASED AGENT





BARDA CBRN Goals

- 1. Have at least one stockpiled countermeasure by 2023 for 80% of threats that have Material Threat Determinations**
- 2. Make significant advances in all programmatic objectives by 2023**
 - Reach a point where the law of diminishing returns applies
- 3. Continue to fill operational gaps in our MCM response**



PBS Successes – 27 Products



Vaccines

Anthrax



Antitoxins



Vaccine

Smallpox



Antiviral



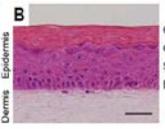
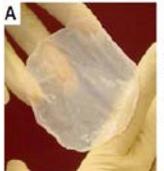
Botulism



Chemical



Burn Products – Nuclear, Radiation, Chem



Vaccines



REGENERON

Therapeutics



Nuclear/Radiation



Point of Care



High Throughput



Biodosimetry Devices



ASPR: Saving lives...Protecting America.





Advanced Research and Development (ARD) Priorities

- **Highest: addressing chemical and viral hemorrhagic fever threats**
- **Repurposing products to treat injuries from radiological and nuclear threats**
- **Sustained investment in new antibacterial agents, vaccines**
- **Continual re-evaluation: seeking more effective, sustainable solutions to address dire threats**



BARDA Highlights 2017

VABOMERE



- August 2017, Rempex Pharmaceuticals received FDA approval for Vabomere to treat complicated urinary tract infections
- This is the first BARDA-supported antibiotic to be FDA approved.





CARB-X Portfolio Powered by CARB-X

The CARB-X portfolio comprises 18 early stage R&D projects investigating 8 new classes of antibiotics, 5 non-traditional antibiotics, 10 new molecular targets and a rapid diagnostic to determine the type of drug-resistant bacteria that is causing an infection.

Powered by **CARB-X**
 8 new classes of antibiotics
 5 Non Traditional Approaches
 10 New Targets

Company/Research Team	Project	Novelty*			Project description	Urgency/Priority**	Bacteria Targeted / Stage of Early Development			
		New Class	Non-traditional	New Target			Hit to Lead	Lead Optimization	Pre-Clinical	Phase 1
Achaogen	AKAQ-LpxC	✓		✓	LpxC Inhibitor	✓	<i>Pseudomonas aeruginosa</i>			
Antabio	PEI		✓	✓	<i>Pseudomonas</i> Elastase inhibitor	✓	<i>Pseudomonas aeruginosa</i>			
Bugworks Research	Gyrox	✓			Gyrase-topoisomerase inhibitor	✓	Gram-negative activity			
Cidara Therapeutics	CD201		✓	✓	Bifunctional immunotherapy	✓	<i>Acinetobacter</i> + <i>P. aeruginosa</i> + Enterobacteriaceae			
ContraFect	Gram-negative lysins		✓	✓	Recombinant lysin protein	✓	<i>P. aeruginosa</i>			
Debiopharm	Debio 1453	✓		✓	Narrow-spectrum inhibitors of FabI	✓	<i>Neisseria Gonorrhoeae</i>			
Eligochem	Helical AMP	✓			Helical Antimicrobial Peptide	✓	Gram-negative activity			
Entasis Therapeutics	ETX000				Oral Gram-negative combination	✓	Gram-negative activity			
Forge Therapeutics	FG-LpxC	✓		✓	LpxC Inhibitor	✓	Gram-negative activity			
Iterum	Sulopenem				Oral and IV penem	✓	Gram-negative activity			
Microbiotix	T3SS Inhibitor		✓	✓	Virulence modifier	✓	<i>Pseudomonas aeruginosa</i>			
Oppilotech	LPS	✓		✓	Targets synthesis of LPS	✓	Gram-negative activity			
Redx Pharma	NBTI	✓			Dual-acting topoisomerase inhibitor	✓	<i>Acin.</i> + <i>P. aerug</i> + Enterobacteriaceae			
Spero Therapeutics	SPR741			✓	Potentiator	✓	Gram-negative activity			
Tetraphase Pham	TP-6076				Next-generation tetracycline	✓	<i>Acinetobacter</i> + Enterobacteriaceae			
VenatoRx	VNRX-PBP	✓			β-lactamase Resistant PBP Inhibitor	✓	Entero-bacteriaceae			
Visterra	VIS705		✓	✓	Antibody-drug conjugate	✓	<i>Pseudomonas aeruginosa</i>			

Company/Research Team	Project	Project description	Development Stage			
			Feasibility Demonstration	Optimization and Preparation for Development	Product Development	System Integration and Testing
Proteus	Rapid POC Diagnostic	Optical bacterial imaging	POC Diagnostic			

* Novelty characterizations of new class and new target are established by CARB-X following the Pew Trusts pipeline analysis model. Pew defines a novel chemical class as a group of antibiotics that share a new common core molecular structure. Non-traditional products include lysins and monoclonal antibodies.

** Urgent and priority drug-resistant bacteria are determined by the Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO).

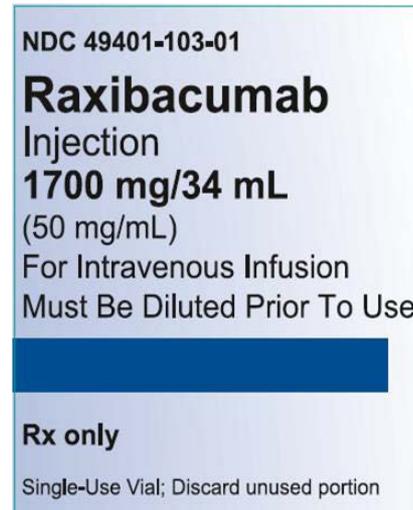
🔴 Urgent/Critical priority 🟡 Serious/High priority 🟢 Serious/Medium priority.

Stage of development is approximate as of July 2017.



MCM Status: Anthrax

- Vaccine stockpiled
- Next generation vaccine under PBS- lower cost, improved CONOPs
- Multiple antibiotics
- Multiple antitoxins
- Future: Sustainment





MCM Status: Botulism

- Emergent has performed under BARDA contract since 2006 for the development of an equine heptavalent botulism antitoxin (hBAT)
- hBAT was approved to treat confirmed or suspected botulism in adults and pediatrics in March 2013
- Product is capable of treating all seven serotypes of botulism
- Future: sustainment, need to plan for next gen solution





MCM Status: Smallpox

- Stockpiled vaccine for special populations
- Stockpiled antiviral drug for the treatment of symptomatic infections
- Need for IV formulation
- Future: 2nd antiviral drug, new formulations





MCM Status: Bacterial Threats

- Multiple generic antibiotics stockpiled for bacterial threat agents
- Support development of new antibiotics to mitigate impact of resistance on our ability to respond to ALL threats
- Future: FDA approval of late stage candidates out of ARD portfolio, graduate programs out of CARB-X



CARB-X
Xccelerating global antibacterial innovation



MCM Status: Radiation

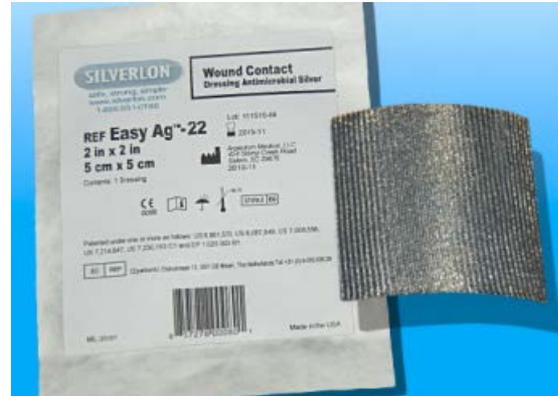
- Biodosimetry to triage patients
- Stockpiled cytokines to treat neutropenia
- Future: Thrombocytopenia, Coagulopathy, point-of-care Biodosimetry





MCM Status: Thermal Burns

- Stockpiling 4 products awarded under PBS
- Working towards transforming the continuum of care for burn patients
- Future: Studies in pediatric populations, Temporizing matrix, enhanced imaging devices





MCM Status: Ebola/VHFs

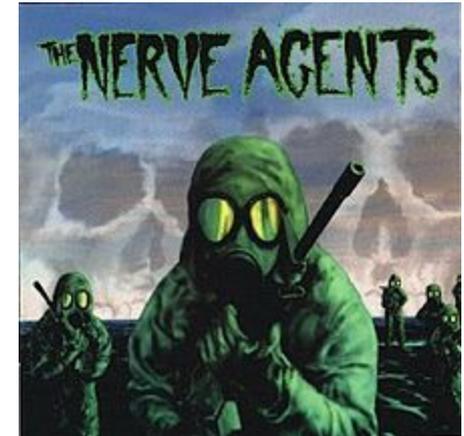
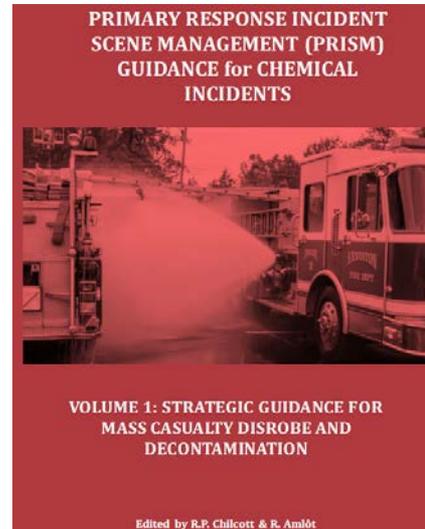
- PBS awards for late stage development and stockpiling of Ebola Zaire vaccine(s) therapeutic(s) completed in FY2017
- Goal will be licensure/approval of those products
- Future: Transition support to Ebola Sudan and Marburg MCMs





MCM Status: Nerve Agents

- Published decontamination guidance
- In process of stockpiling midazolam as anti-seizure therapy
- Future: Therapies to treat seizures refractory to midazolam treatment





MCM Status: Mustard/Chlorine

- We need MCMs for these threat agents
- Advanced Research and Development efforts focused on treating the injury
- Focus on repurposing where possible
- Future: Heavy investment, transition to PBS





MCM Status: Cyanide

- Need for improved antidotes
- Focus on more rapid delivery, ease of administration-intranasal formulations
- Future: Transition programs to PBS

Hydrogen Cyanide

Colorless gas; faint bitter almond odor. Poison. Irritating to respiratory tract.

Also causes: headache, weakness, confusion, rapid/difficult breathing, convulsions, coma, death. Chronic: enlarged thyroid, fatigue, nervous instability, colic. Flammable.



CAS No. 74-90-8





Overarching Challenges

- **Sustainment**
- **Maintaining an industry base**
- **Thin MCM Pipeline (chemical and radiological and nuclear)**
- **Limited BSL-4 space**



CBRN Initiatives

- **Develop animal models to support licensure of Ebola/VHF MCMs**
- **Develop animal models to support the FDA approval of chemical and radiological and nuclear MCMs**
- **Invest in technologies to enhance sustainment, improve response operations, lower life cycle costs**



Summary

- **BARDA has successfully developed and stockpiled MCMs against multiple threats**
- **Significant threats remain unaddressed**
- **Sustainability is a challenge**
- **BARDA seeks to partner with industry to address the remaining gaps with flexible, nimble public private partnerships**



BARDA's ORISE Fellowship

- **BARDA initiated the ORISE fellow program at BARDA to attract early career scientists**
- **Anticipating hosting 3-5 fellows/per year for a 2 year fellowship**

To apply:

www.zintellect.com and search BARDA

Please send questions by email to:

**Joseph Larsen, CBRN Director (Acting) & BARDA
ORISE Sponsor
Joseph.larsen@hhs.gov**

**Pamela Payne, BARDA ORISE Coordinator
Pamela.Payne@hhs.gov**



OAK RIDGE INSTITUTE FOR SCIENCE AND EDUCATION



Questions?

joseph.larsen@hhs.gov

202-260-0050