ASPR 2018 - New Directions and Opportunities

Assistant Secretary for Preparedness and Response

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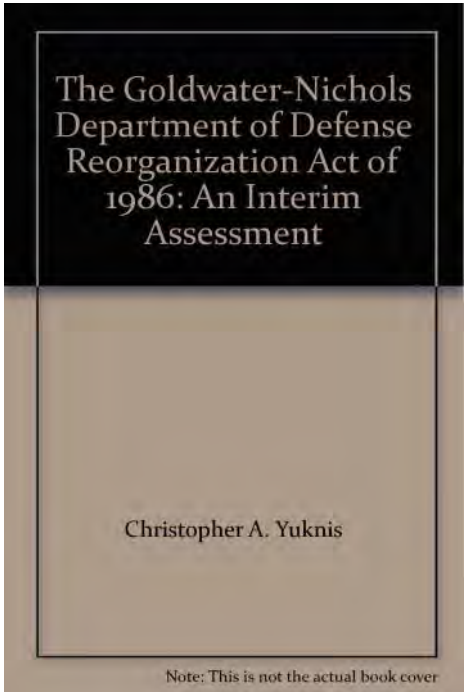
Senior Science Advisor to ASPR

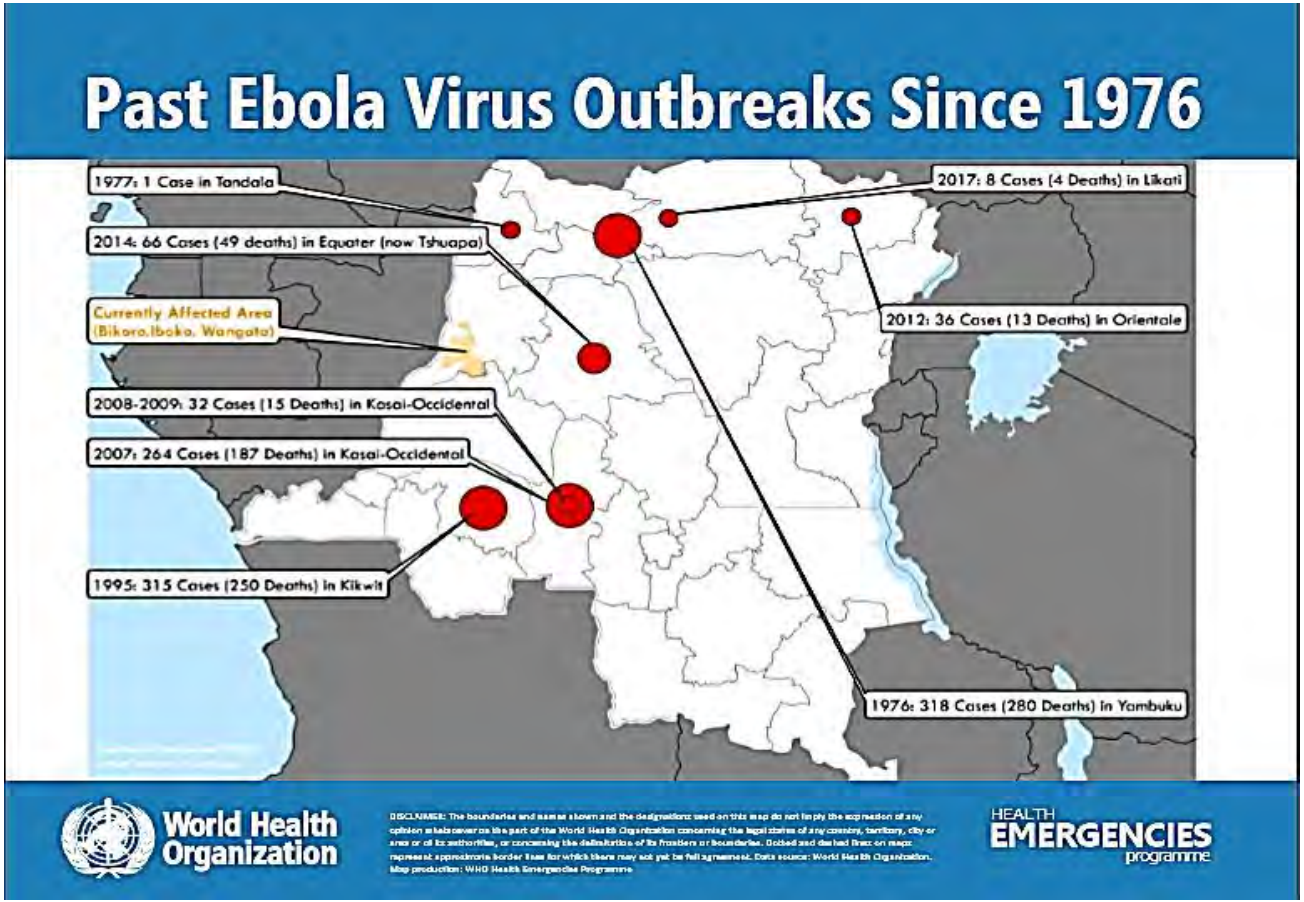
21st Century: An Increasingly Complex & Dangerous World

ASPR's Purpose: Unity of Command



ASPR's Mission

ASPR Priorities for Building Readiness for 21st Century Threats



Current Outbreak in DRC

- 38 Confirmed, 15 Probable, 29 dead
- CFR = 55%
- Locations: Iboko, Bikoro, Mbandaka
- Five healthcare workers (2 dead)
- Last detected case on 2 June
- Can be declared over after 42 days from last case
- Use of the rVSV-Ebola vaccine for ring vaccination for 1706 contacts, vaccine given to 3330 overall.

Other biodefense in the news

Global Biodefense Market Growing Threat of Bioterrorism
global biodefense market to grow at a CAGR of 5.41% during the period 2017-2021.
http://www.sbwire.com/press-releases/

The Synthesis of Horsepox Virus and the Failure of Dual-Use Research Oversight

This mock, bioengineered pandemic killed 150 million people. Next time it might not be a drill

LARRY CANNER / JOHNS HOPKINS CENTER FOR HEALTH SECURITY

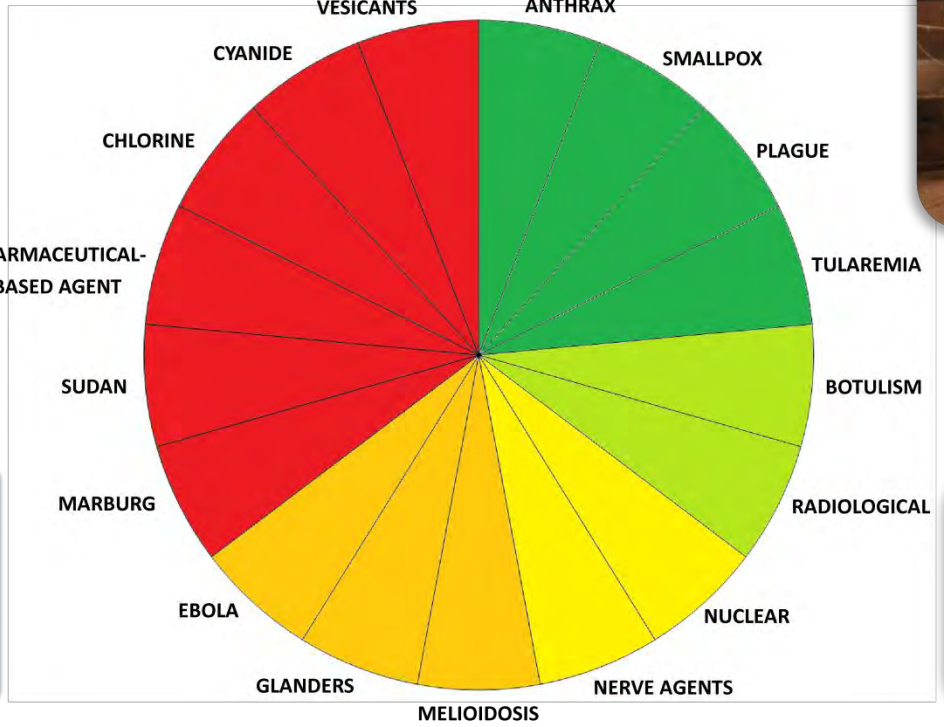
But New Advances As Well

CBS/AP *July 16, 2018, 5:34 PM*

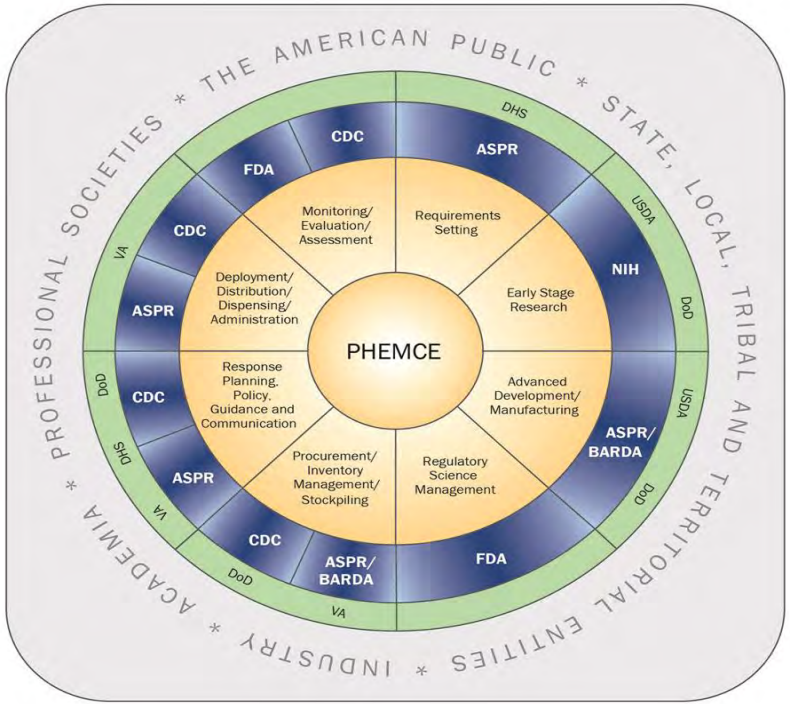
FDA approves first drug to treat smallpox, in case of terror attack

Capsules of the drug TPOXX, it was approved by the FDA in July 2018 as the first treatment for smallpox, a disease

21st Century: An Increasingly Complex & Dangerous World



Medical Countermeasures Enterprise



Key

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

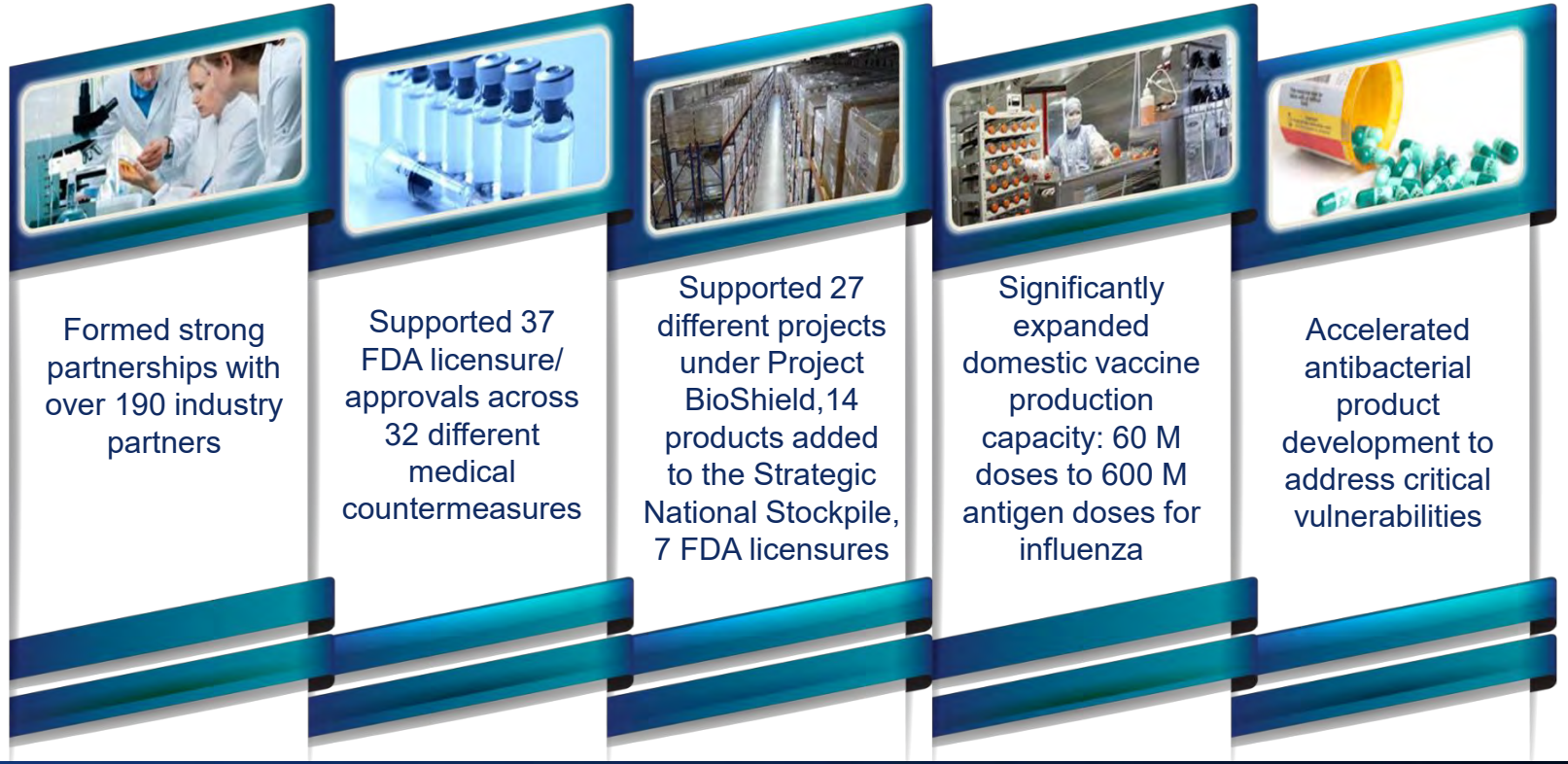
Acronyms

PHEMCE: Public Health Emergency Medical Countermeasures 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

Anthrax

Smallpox

ASPR / BARDA Has Had a Successful Decade



Formed strong partnerships with over 190 industry partners

Supported 37 FDA licensure/ approvals across 32 different medical countermeasures

Supported 27 different projects under Project BioShield,14 products added to the Strategic National Stockpile, 7 FDA licensures

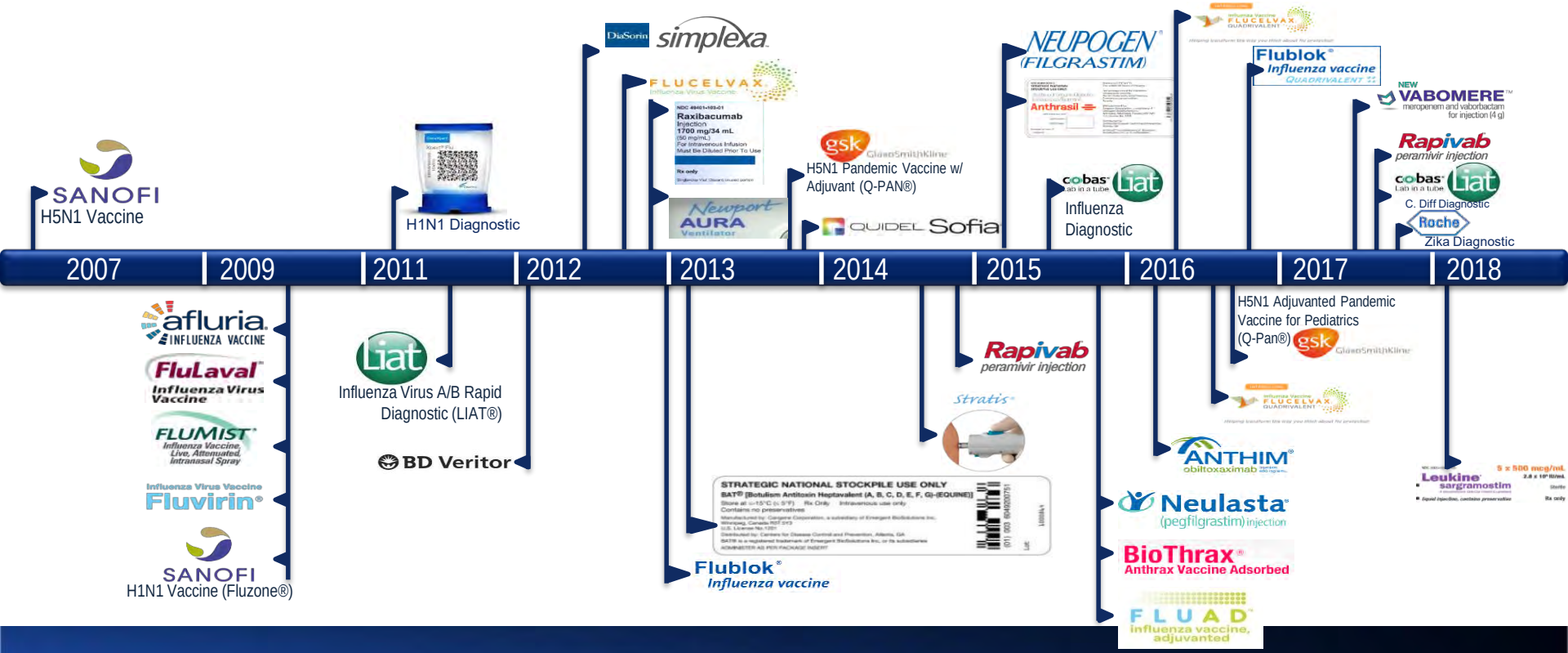
Significantly expanded domestic vaccine production capacity: 60 M doses to 600 M antigen doses for influenza

Accelerated antibacterial product development to address critical vulnerabilities

BARDA Priorities

- Sustainment of products developed under PBS and re-establishing the market guarantee provided under the original SRF
- CBRN ARD – addressing gaps in preparedness; chemical agents, Sudan, Marburg, drug resistant pathogens
- CARB-X – to address all threats, CBRN, PI, and public health
- Better, faster, flu vaccines
- Maintaining and expanding domestic manufacturing capacity for non-egg based influenza vaccines (seasonal and pre-pandemic)
- Launch DRIVe

FDA Approvals, Licensures, and Clearances



The BARDA Model

BARDA develops and makes available medical countermeasures **(MCMs)** by forming unique public-private partnerships with industry partners

Our Industry Partners

Our Government Partners

HHS.gov
National Vaccine Program Office
Office of the Assistant Secretary for Health
Division of Veterinary Resources
Office of Intramural Research

Office of Infectious Diseases
Office of Public Health Preparedness and Response
National Center for Immunization and Respiratory Diseases (NCIRD)
CDC Immunization Safety Office
National Center for Environmental Health
National Center for Emerging and Zoonotic Infectious Diseases

National Heart
Lung and Blood Institute

NATIONAL CANCER INSTITUTE
Technology Transfer Center

National Institute
of Allergy and
Infectious Diseases

Project BioShield

A commitment

27 products supported

14 products added to the Strategic National Stockpile

7 products taken to FDA approval/licensure/clearance

Project BioShield Successes

Anthrax Antitoxins

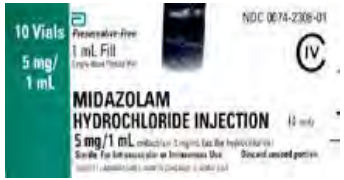
Anthrax Vaccines

Smallpox

Vaccine

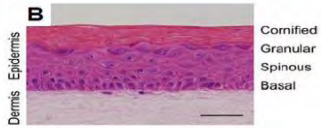
ST-246 Antiviral

Burn Products – Nuclear, Radiation



Chemical

Botulism



BARDA Pandemic Influenza Preparedness

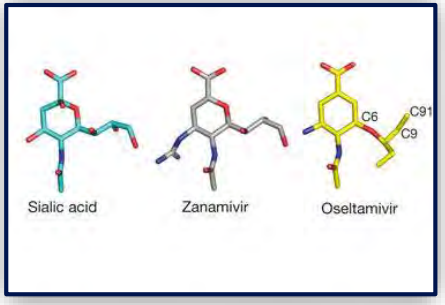
Early Detection → Early Response → Saving Lives

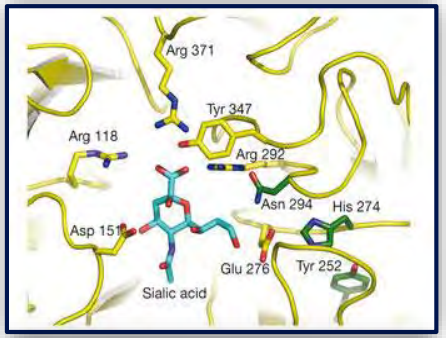
Best, Faster Flu Vaccines Now: Strategy

- Expand domestic capacity of cell and recombinant vaccines;
- Enhance their effectiveness, with the addition of adjuvants and higher doses;
- Conduct clinical trials to expand their use in all ages; and,
- Modernize vaccine production for speed and flexibility.

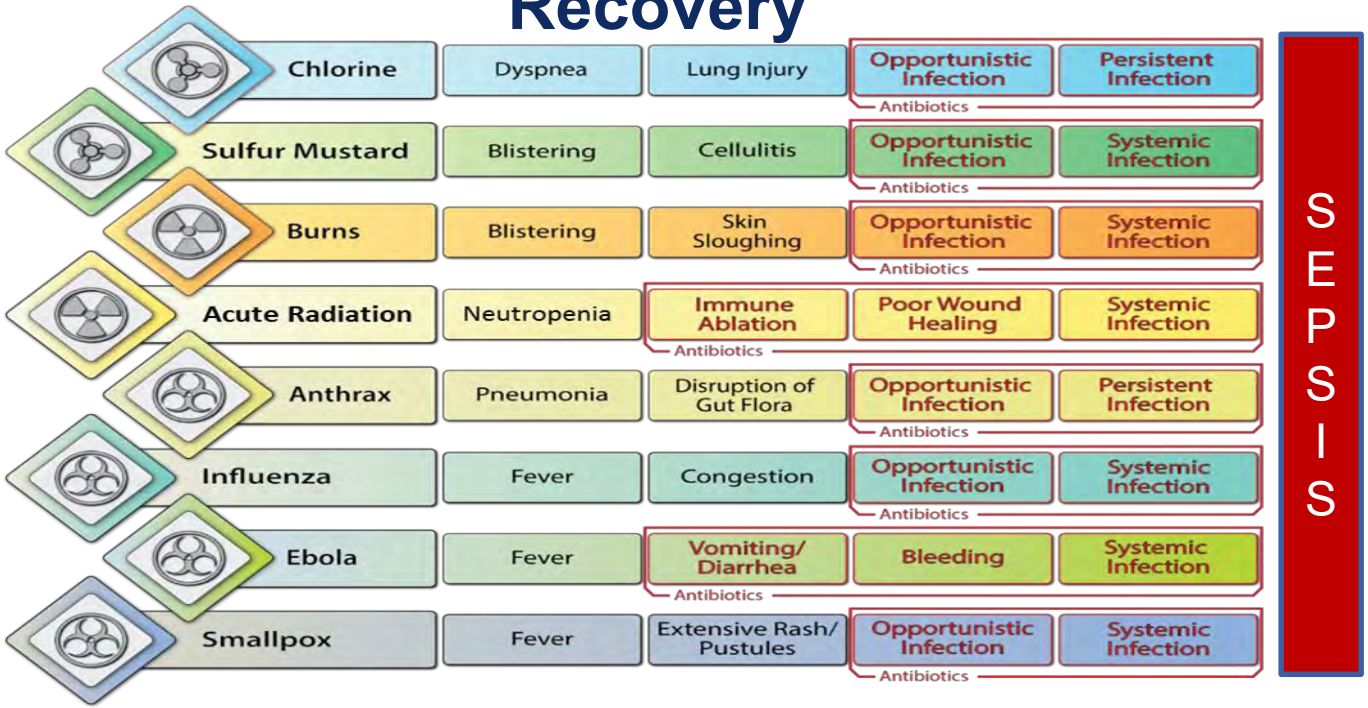
New Therapeutics

- Only one class of antivirals currently approved in the US
  - Significant public health risk if resistance develops
- Multiple BARDA funded clinical trials of new therapeutics ongoing
- Antiviral with novel mechanism of action recently approved in Japan
  - BARDA discussing how to support US licensure





Addressing the Continuum of Care from Exposure to Recovery



Novel antibiotics ensure that *no patient is left behind*

BARDA's Antibiotic AR&D Portfolio

Sponsor	Antibacterial	Development Phase	Biodefense Profile	Commercial Indication
Medicines Company	**Vabomere**	Approved	Burkholderia	cUTI, CRE
Achaogen	**Plazomicin**	NDA Submitted	Plague, Tularemia, Anthrax	cUTI, CRE
CUBRC/Tetraphase	**Eravacycline**	NDA Submitted	Plague, Tularemia, Anthrax	cIAI, MDR bacteria
Basilea	**Ceftobiprole**	Phase 3	Plague, Tularemia	ABSSSI, SAB, CABP
Summit	**Ridinilazole**	Phase 3	Anthrax (adjunct)	C. diff
Pfizer	**Aztreonam-Avibactam**	Phase 3	Burkholderia, Plague	cIAI, HABP/VABP, cUTI, BSI
GlaxoSmithKline	**Gepotidacin**	Phase 3	Plague, Tularemia, Anthrax	CABP, GC, cUTI
GlaxoSmithKline	**GSK--680**	Phase 1	TBD	TBD
Hoffman-La Roche	**RG6080**	Phase 3	Burkholderia	cUTI, cIAI, HABP/VABP
Achaogen	**C-Scape**	Phase 3	Plague, Tularemia	cUTI

CARB-X Progress – 2 Years In

By the numbers:

- *28 projects targeting MDR bacteria*
- *$76.3M invested to date*
- *7 countries*
- *8 new classes of antibiotics*
- *11 new molecular targets*
- *10 non traditional candidates*
- *4 rapid diagnostics*
- *1 vaccine*
- *5 candidates advanced into clinic*
- *For every $1 CARB-X invested, $7.2 secured from private sector*
- *For every $1 BARDA invested, $11.9 secured from private sector*

As of April, 2018

BARDA Division of Research, Innovation, and Ventures (DRIVe)

DRIVe Mission: Transforming Health Security

Accelerate the research, development, and availability of transformative countermeasures to protect Americans from natural and intentional health security threats.

BIOMEDICAL ADVANCED RESEARCH AND DEVELOPMENT AUTHORITY
BARDA

DRIVe
Transforming Health Security

Response Framework

Situational Awareness/Recognize
How do we know something is happening, an agent has entered the community ENACT, Opioids

Design
How do we stop the spread of the disease? Drugs, vaccines, PPE, social distancing? UniRx

Produce
On demand manufacturing of X PoD

Administration
everyone who needs X is provided X Opioids, Solving Sepsis

Identification/Characterize
What is it, is it drug resistant, are certain subpopulations more susceptible, will it become an epidemic? ENACT, Opioids

Validate
Methods under design are evaluated, clinical trials, non-clinical trials, epidemiology, surveillance eRAT

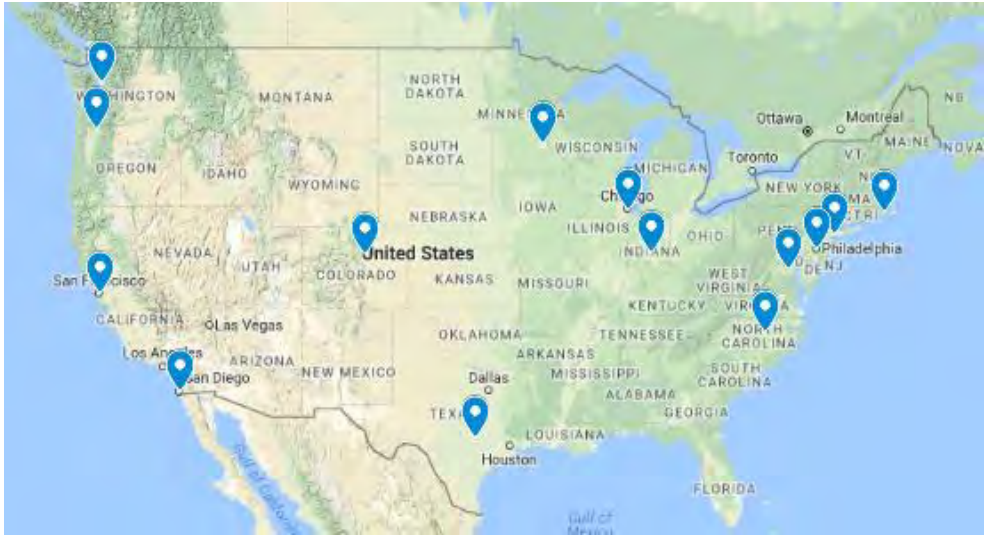
Distribute
novel ways to get product/information to those who need it. PoD

DRIVe-Ready

Capture
- Sets research agenda
- Coordinates across USG, academia, industry and other stakeholders

Solution Mapping
- Accelerator network across the US has been awarded

US Hubs of Innovation



DRIVe-X

Initial Emphasis:

- Prevent illness from infectious exposures through early identification and action
- Save lives by solving sepsis

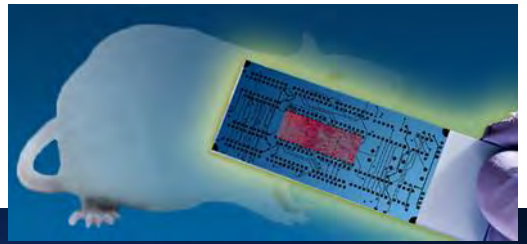
SOLVING SePSIS

ENACT
Early Notification to Act, Control, and Treat

Future Areas:

- *Create universal treatment options for broad classes of pathogens*
- *Ensure access to life-saving medical countermeasures for all Americans*
- *Transform the process by which medical countermeasures are developed (non-animal testing)*

- Viral
- Bacterial
- Fungal



The General Problem

Enormous healthcare impact to the US public and growing each year…

Lives Lost

- **Morbidity - 1.5 Million people each year in US**
- **Mortality - >250,000 people die each year**
  - **~80,000 are discharged to hospice**
- **Management - 1:3 patients who die in hospital have sepsis** CDC

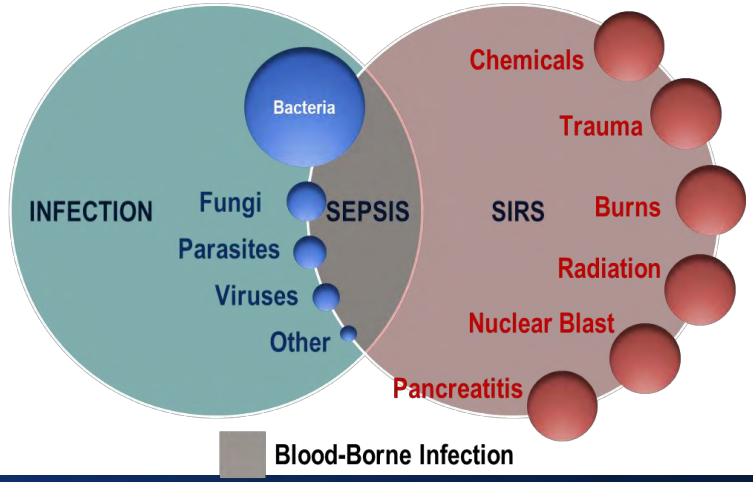
Growing Cost

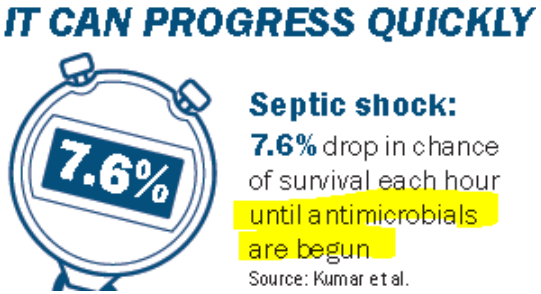
Responsible for nearly $24 billion annually
(6.2% of hospital costs)

https://www.hcup-us.ahrq.gov/reports/statbriefs/sb204-Most-Expensive-Hospital-Conditions.pdf
(2016 report, 2013 data)

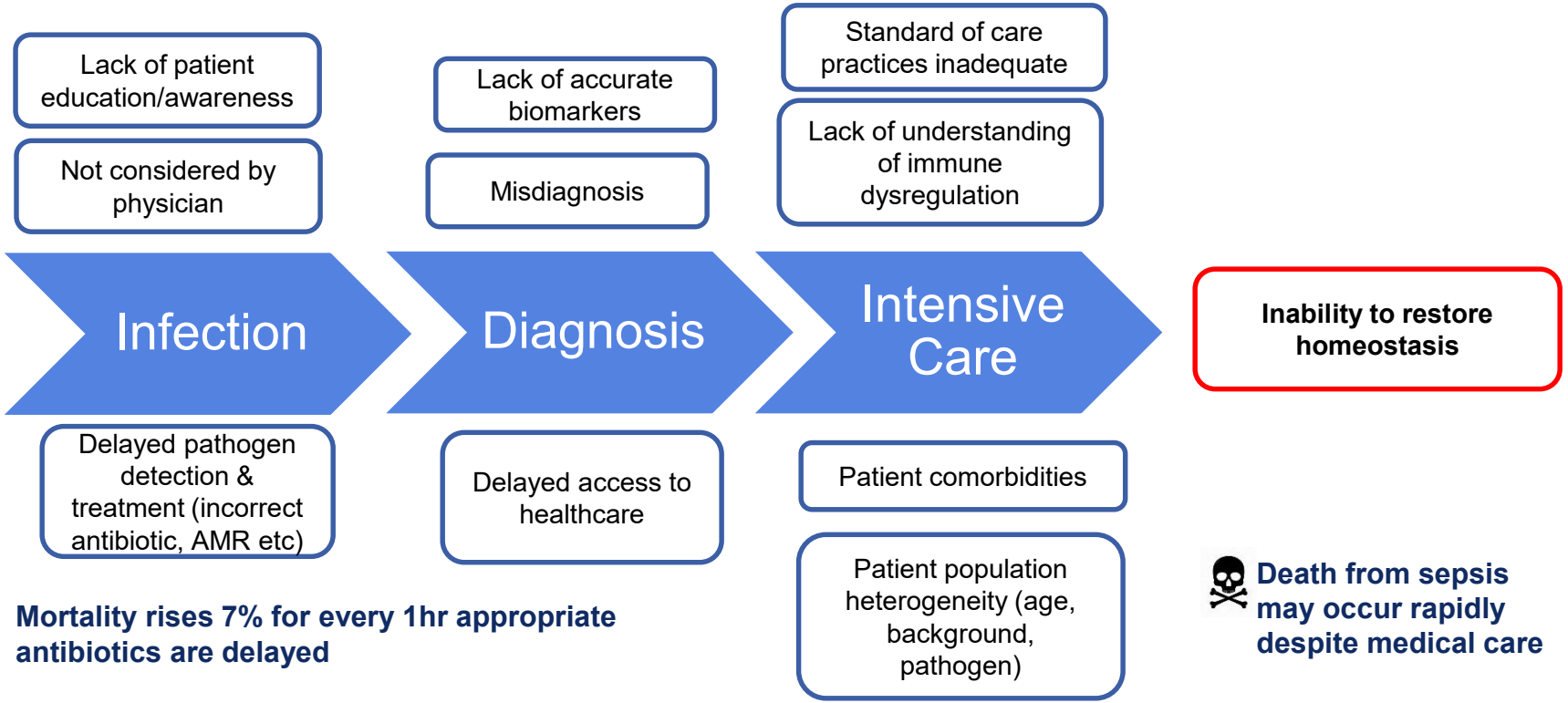
Solving Sepsis in Our Lifetime

- **The problem:** The downstream effects of a Chemical, Biologic, Radiologic or Nuclear (CBRN) attack will create a major surge in sepsis cases overwhelming critical care centers and hospitals.
- **The solution:** Multi-disciplinary, comprehensive approach for a breakthrough in decreasing mortality and improving post-sepsis outcomes, including:



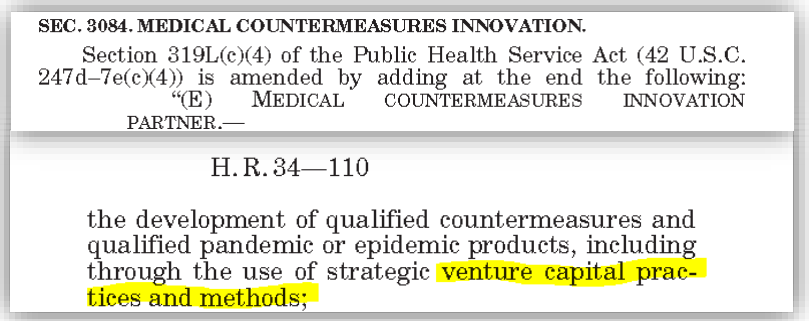


Failure Points in Current Practices



DRIVe-Launch

- **Model:** Angel/Early Investor
  - Seed funding [3rd Party Entity]
  - Accelerator, Capture and Sprint
- **Investment Horizon:** 18 months to Next Phase



SEC. 3084. MEDICAL COUNTERMEASURES INNOVATION.

Section 319L(c)(4) of the Public Health Service Act (42 U.S.C. 247d–7e(c)(4)) is amended by adding at the end the following:

"(E) MEDICAL COUNTERMEASURES INNOVATION PARTNER.—

H. R. 34—110

the development of qualified countermeasures and qualified pandemic or epidemic products, including through the use of strategic venture capital practices and methods;

MCIP

Medical Countermeasure Innovation Partnership

DRIVe VENTURES

Investing in National Health Security

- **Model:** Product specific investments leveraging corporate venture practices
- **Investment Horizon:** Evolve to Evergreen
  - Re-prioritize and sustain investments across the BARDA portfolio in performance-based fashion;
  - Cull what does not make the cut and re-invest

What the future holds…

DRIVe VENTURES Portfolio Overview

Panacea Clinic · Emerge Medical Spa at Bridgeport · pharmaSTRATEGIES · calematix · iba · CASAMED · Hospital Veterinário das Travessas · RajeshMahara · Angel MedFlight · PROMISES

Pharmacy on Demand (PoD)

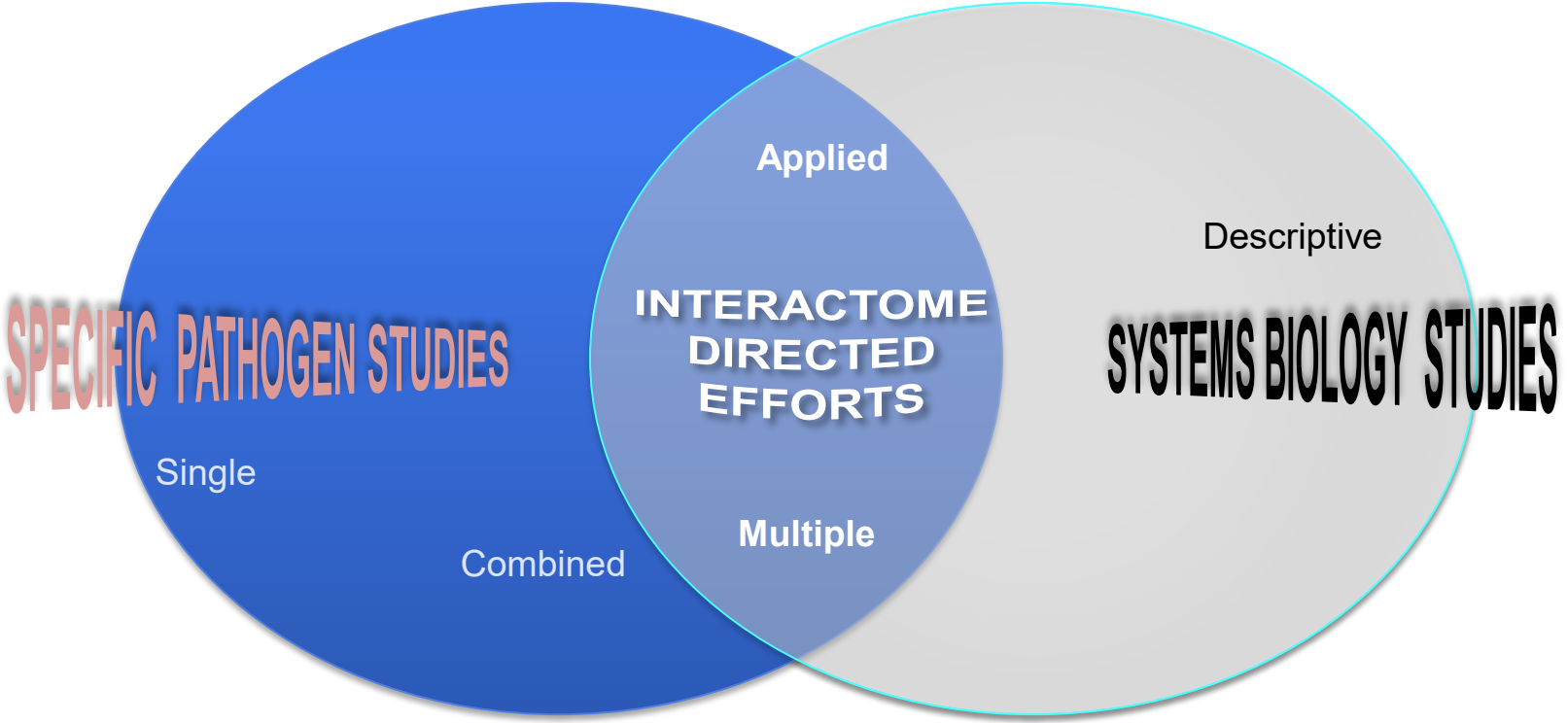
- **The Problem:** Access to medicines requires visits to health care professionals, stocks of drugs in pharmacies, and delays in receiving therapies especially in events where healthcare infrastructure is limited or under peak demand (e.g., influenza outbreaks).
- **The Solution:** Medicines are available in areas frequented by all and/or can be shipped rapidly through emerging technologies. On demand production and supply.

Patient engagement via telehealth

Meds delivered to home

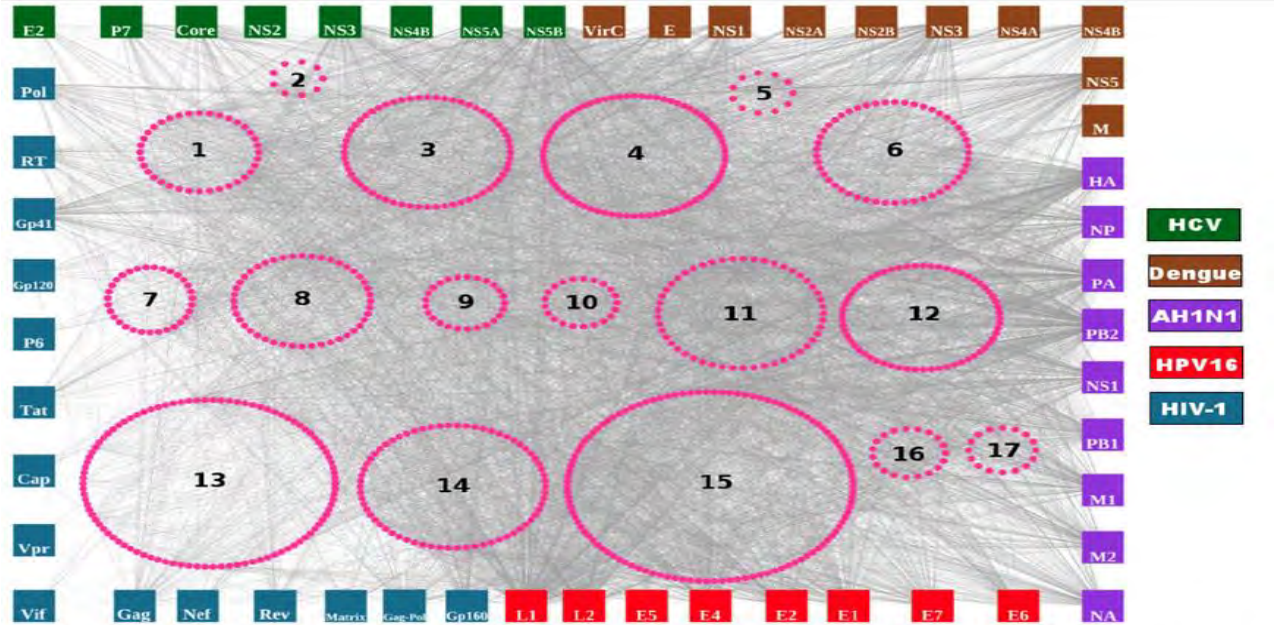
Booth that dispenses meds via smartphone eScript

CURRENT INVESTMENT MODELS IN INFECTIOUS DISEASES



Example of the Interactome

Functional Human Host Domains Targeted by Diverse Viruses –



Cabrera et al 2013 PLoS ONE

Examples - Broad Spectrum Approaches (host-based and pathogen-based)

- Apoptosis Induction Domains
  - Rider et al 2011 – Double Stranded RNA Activated Caspase Oligomerizer (NIAID funded)
- Innate Defense Regulator Peptides
  - Soligenix – Dusquetide (anti-inflammatory)
- Sirtuins - Host cell metabolic regulators
  - Forge Life Sciences
- Histidine Kinase Targets (fungal)
  - UW-Madison – WARF
- Inflammasome Inhibitors
  - Olatec
- AR-12 antiviral, antifungal

2018 Priorities

Sustain	• Industry Partnerships • Capabilities • Capacity
Streamline	• Single BARDA BAA • BARDA Contracting • Communications
Foster Consortia & Partnerships	• Other Transaction Agreements • Strengthen alignment with DoD
Promote Innovation	• End-to-End Focus • Last Mile

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