**Biodefense MCM History**

- Pandemic & All-Hazards Preparedness Act (2006)
- Medical Countermeasure Review (2010)
- Pandemic & All-Hazards Preparedness Reauthorization Act (2013)

**BARDAs Commitment to Medical Countermeasure Development**

Support advanced development of and make available medical countermeasures for CBRN threats, pandemic influenza, and emerging infectious diseases by transitioning MCM candidates from early development across the "Valley of Death" into advanced development to regulatory approval.
Transitioning Basic Research to Advanced Development

- Basic Research / Early Develop. to Advanced Development
- Countermeasure Development
- Phase I: Discovery
- Phase II: Preclinical
- Phase III: Clinical

Chem: NIH/NINDS/CounterACT (also DTRA, industry)
Rad/Nuc: NIH/NIAID (also DTRA, industry)

BARDA
SNS

Public Health Emergency Medical Countermeasures Enterprise (PHEMCE)

- HHS Develops Requirements For each threat or requirement...
- ... a set of programs is required, each comprised of...
- ... a set of development projects to yield the required MCM

- DHS Threat Determination
- HHS Requirements

Countermeasure Program
- Innovation
- Antimicrobial
- Diagnostics
- Vaccines
- CBRN Therapeutics

PHEMCE Process

HHS: Department of Health and Human Services
DHS: Department of Homeland Security
APPR: Assistant Secretary for Preparedness and Response
DARPA: Defense Advanced Research Projects Agency
NIH: National Institutes of Health
NIAID: National Institute of Allergy and Infectious Diseases
NINDS: National Institute of Neurological Disorders and Stroke
NIH/NINDS/CounterACT
NIH/NIAID
HHS
DHS
APPR
DARPA
NIH
NIAID
NINDS/CounterACT

8/3/2016
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THE THREAT

THE SCENARIO AND REQUIREMENTS ASSUMPTIONS

RESPONSE TO A NUCLEAR DETONATION BURN-SPECIFIC ACTIVITIES

MECHANISMS OF INJURY AND DISEASE COURSE

SPECIAL REQUIREMENTS AND AT-RISK POPULATIONS

CURRENT AND DEVELOPMENTAL MEDICAL COUNTERMEASURES

MEDICAL COUNTERMEASURE REQUIREMENTS

- INTENDED USE (LABEL INDICATIONS)
- REQUIREMENTS FOR CIVILIAN AVAILABILITY
- SPECIAL CONSIDERATIONS
- LIFE-CYCLE REQUIREMENTS AND SURGE REQUIREMENTS
- FACTORS THAT AFFECT THE CIVILIAN REQUIREMENT
- ASSOCIATED REQUIREMENTS
- REQUIREMENTS FOR TRACKING MECHANISMS

TARGET PRODUCT PROFILE (TPP)

Stockpiling
CBRN MCMs under Project BioShield

More Than Just a Funding Agency
BARDA provides technical support to our contractors for all aspects of the drug development process:

- Collaborative management
- Subject Matter Experts with Pharma experience
  - Advice on experimental, non-clinical, and clinical study design
  - Regulatory experience with MCM issues including animal rule
- Integration with other government MCM-focused agencies
  - Contact with MCM-focused offices at FDA
  - Collaboration with DoD medical countermeasure programs
- BARDA Core Services
  - Critical Assistance to MCM Developers
Radiological/Nuclear Incident Considerations

Acute Radiation Injury

Cellular Damage through Many Pathways:
- ROS pathway
- Inflammatory Response
- Stem Cell Loss
- Endothelial Damage
- Bacterial Translocation
- Coagulopathy

Blood:
- (Hematopoietic)
- Decrease in blood count
- Pancytopenia (Neutropenia; Thrombocytopenia)
- Severe bone marrow damage

Intestines:
- (Gastrointestinal)
- Blistering
- Mild damage
- Moderate damage
- Severe damage

Lungs:
- (Pulmonary)
- Pneumonitis, fibrosis
- Leads to manifestation in organ systems
- Cell death & differing cell turnover rates

Response Timeline (Post-Detonation)

Goals: first 72 hrs
- Manage trauma, blood loss, burns
- Manage pain
- Biochemistry assessment
- Administer fluids and antibiotics
- Decontamination
- Begin hematopoietic syndrome MCMs

Goals: after 72 hours
- Maintain physiologic blood counts
- (CBC emphasis: neutrophils & platelets)
- Functional recovery (blood, GI, lung, skin)
- Provide fluids & nutrients
- Monitor signs/symptoms of GI syndrome
- Monitor cutaneous syndrome

Field Care Products
- Compatible w/ RTR Sites
- Ease of administration
- Typical, intramuscular, etc.
- High therapeutic index required
- Poor diagnostics, worried well patients
- Robust storage, easy deployment
- Controlled room temperature, etc.

Definitive Care Products
- Compatible w/ Hospital Care
- Expertise required to administer
- Intravenous, surgical grafting, etc.
- Low therapeutic index acceptable
- Better diagnostics and patient monitoring
- Low storage requirements
- Refrigeration, cryopreservation, etc.
Envisioning a Complete MCM Portfolio

**Multiple threat dimensions and timeframes**

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<th>Field Care (First 72 hours)</th>
<th>Definitive Care (After 72 hours)</th>
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Chemical Incident Considerations

- Chemical weapons have been used in war and terrorism from World War 1 to today
- Diverse Threats, Few Drugs
  - Fast onset of symptoms and rapid lethality
  - Only decontamination can stop the damage
- PHEMCE Chem IPT Top Priorities
  - Pulmonary Threat Agents
  - Cyanide
  - Nerve Agents
  - Vesicants

*For Chem, we treat the injury not the agent!*
Enabling Community Resiliency
- Improving Emergency Response
  - PRISM Guidance for Gross Decon
- New Uses for Common Medicines
  - Ensuring availability of lifesaving medicines

Our goal is to improve health outcomes for all victims of chemical exposure

Near Term Focus Areas
- Pulmonary Injury from Chlorine and Vesicants
  - Commercial Indications: Pulmonary Edema, Inflammation, Fibrosis, COPD
- Anti-seizure drugs for nerve agent victims whose seizures are refractory to treatment with benzodiazepines
  - Commercial Indications: Refractory seizure, status epilepticus, epilepsy
- Cyanide Treatments - Improved Ease of Use
- Standardized Animal Models for Efficacy Testing

Striving to Find Chemical Threat Indications for Common Drugs
- Midazolam for Nerve Agent Exposure
- Silverlon® Wound Dressing for Sulfur Mustard Burns
- Alteplase® for Sulfur Mustard Inhalation
Engaging with BARDA

- Forum for discussion about stakeholder's technologies/products and BARDA's interests and programs in seminar format at BARDA's offices in Washington
- Opportunity to receive feedback from BARDA Program and Technical staff
  - Specific direction about stakeholder's plans cannot be given
- Limitations
  - Generally cannot be held while requestor has a proposal under review by BARDA
  - Generally cannot be held to discuss topics related to an acquisition under an open RFP
  - Generally can discuss projects that may fall under an Area of Interest of an open BAA
- Allow ~6 weeks to schedule
- Please let the relevant PO/branch chief know

BARDA TechWatch Program

- Advanced Research and Development of Chemical, Biological, Radiological, and Nuclear Medical Countermeasures (CBRN)
  1. Vaccines
  2. Antitoxins and Therapeutics
  3. Antimicrobial Drugs
  4. Medical Threat Medical Countermeasures
  5. Clinical Diagnostics Tools

- Advanced Development of Medical Countermeasures for Pandemic Influenza (Flu)
  1. Personal Protective Equipment
  2. Full-Featured Continuous Ventilators
  3. Clinical Test Systems and Diagnostic Tools
  4. Influenza Therapeutics
  5. Influenza Vaccines
  6. Influenza Vaccine Manufacturing Improvement

- Science and Technology Platforms Applied to Medical Countermeasure Development (SST)*
  1. Pipeline acceleration and evaluation of candidate vaccines and therapeutics.
  2. Product improvements to enhance safety, efficacy, ease of use, and manufacturability of MCM.
  3. Product repurposing to treat novel and emerging pathogens.
  4. In vitro diagnostic platforms for the rapid diagnosis of human infection.
Questions?

www.medicalcountermeasures.gov
• Portal to BARDA
• View BAA priorities

Contact Us
Judy Laney
Chief, Chemical MCMs
202-205-8043
Judith.Laney@hhs.gov

Mary Homer
Chief, Radiological/Nuclear MCMs
202-205-8604
Mary.Homer@hhs.gov

Tom Hu
Project Officer, Chemical MCMs
202-360-2092
Tom.Hu@hhs.gov