



*United States Department of*

**Health & Human Services**

**Office of the Assistant Secretary for Preparedness and Response (ASPR)**

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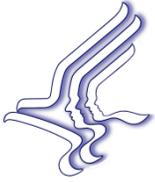


# **Chemical, Radiological and Nuclear Medical Countermeasures**

**Ron Manning, Ph.D.**

**Chief, Chemical, Radiological and Nuclear  
Division of CBRN Countermeasures**

**June 7, 2011**



# Roadmap



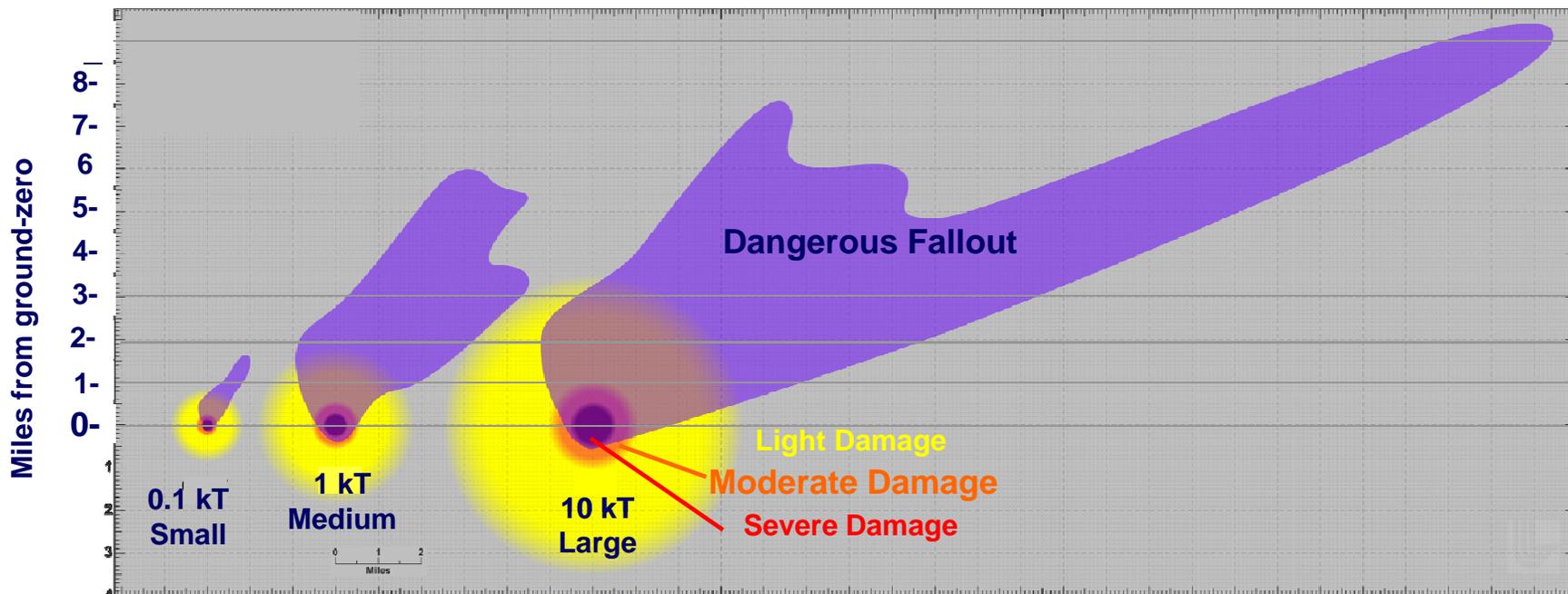
- Rad Nuc Background and the threat
- Rad Nuc Scenario considerations and Requirements development
- Areas of Rad Nuc Programmatic Interest
- Rad Nuc Portfolio Strategy
- Special Considerations for Development Efforts
- Solicitations in Fed Biz Ops
- The Chemical Threat
- Vesicants
- Chem Special Instructions
- Continuing Challenges
- Interagency Partnering
- BARDA funding



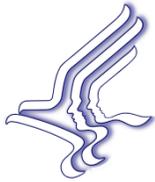
# Rad Nuc Background



- The detonation of an Improvised Nuclear Device (IND) has the potential to produce a large number of victims with multiple and mixed injuries
- Exposure to radiation induces dose-dependent injury to cells and tissue through a cascade of molecular and biochemical changes that lead to cell death or disruption



- Acute Radiation Syndrome (ARS) is the medical consequence of approximately 2 Gy exposure
- The symptoms and progression of radiation injury occur even after the radiation exposure has ceased and there is a continuity of medical consequences from the ARS to the Delayed Effects of the Acute Exposure (DEARE) to chronic radiation damage

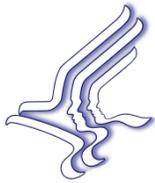


# IND Scenarios and Requirements Development



- **Hundreds of IND scenarios**
  - Developed with modeling and working groups with subject matter experts
  - Several cities modeled
  - Several radiation yields
  - 12 months (Jan - Dec): (e.g. Monthly winds and weather affect the fallout pattern)
- **Requirements established from modeling scenarios**
- **Fulfillment of requirements**
  - Acquisition of products via Project BioShield contracts
  - Development of products via Advanced Research and Development contracts
  - Review portfolio as requirements change
- **Requirements are reviewed on a regular basis and do change over time.**

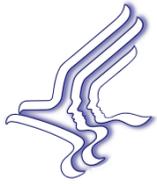




# Strategy for RAD-NUC Therapeutic Portfolio



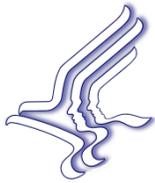
- **Short term solution: Repurpose pharmaceuticals already in use for related indications**
  - PBS/SRF Fixed Price Acquisition with cost-reimbursement support of ARS clinical indication for cytokines currently used to treat chemotherapy induced neutropenia
  - Data currently exist to support use of existing products for radiation-induced neutropenia (non-pivotal studies, about 200 NHPs)
  - Life Cycle Management (sustainability) considerations
- **Long term solution: Expand AR&D support of drugs which demonstrate efficacy**
  - Develop MCM candidates with different therapeutic approaches
  - Build in pediatric usability and CONOPS alignment from early stages
  - Target ARS all subsyndromes including those not amenable to repurposing (e.g., gastrointestinal)



# Overall Acquisition Strategy – Neutropenia Therapeutics (Short Term Solution)



- **Two Pronged Approach (in development)**
  - Stockpile set number of doses of cytokine
  - Capacity Building: for maintenance and flexibility for event-centric needs
- **Mandatory Criteria for Therapeutic:**
  - The drug is a G-CSF or GM-CSF cytokine
  - The drug product is licensed for the treatment of neutropenia by any competent/recognized regulatory authority



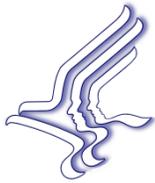
# Special Considerations for Development Efforts

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- **CONOPS and supply issues**

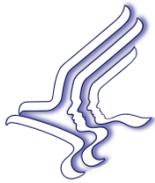
- Impact of required time to start treatment and still have efficacy
  - Limited data on delays to start treatment for 3, 5, and 7 days after exposure for radiation
- Availability of other necessary supportive care treatments (e.g. blood products, antibiotics)
- Use of VMI (current stockpile and expanded quantities), UMI, and different regional stockpile strategies
- Integration of data on local distribution resources and timelines



# Special Considerations for Development Efforts



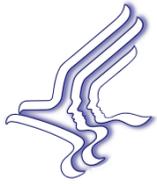
- **Licensure under the Animal Rule**
  - Pathway is complex, uncertain, and not well understood by the community
  - Radiobiology inadequate to develop models to satisfy the FDA animal rule requirements
  - Development of licensure pathways when no animal model exists -- species specificity
  - Role of cancer patient data
- **Mitigation Strategy**
  - Engage FDA in discussions at a senior management level to define how Animal Rule can be satisfied
- **Special Populations**



## CBRN “Rolling” BAA: Chem Rad Nuc Considerations



- For Chemical Radiological and Nuclear (CRN) Research Areas 4 and 5, Offerors shall propose a Statement of Work that is consistent with activities occurring at **TRL 3** or greater
- Begin research, data collection, and analysis in order to test hypothesis. Explore alternative concepts, identify and evaluate critical technologies and components, and begin characterization of candidate(s). Preliminary efficacy demonstrated *in vivo*.
  - 3A** Identify target and/or candidate.
  - 3B** Demonstrate *in vitro* activity of candidate(s) to counteract the effects of the threat agent.
  - 3C** Generate preliminary *in vivo* proof-of-concept efficacy data (non-GLP (Good Laboratory Practice)).

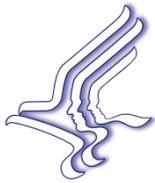


## Other Fed Biz Ops communications

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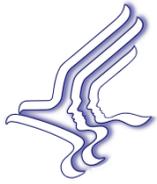
- **RFI: request for information**
- **SSN: sources sought notice**



## Sources Sought Notice, December 21, 2010



- This SSN was a request for information regarding what currently licensed and marketed G-CSF and GM-CSF medical products might be useful in the treatment of neutropenia
- Requested information regarding products that could serve all members of the U.S. population who would be in need of them
  - infants and children
  - elderly people
  - pregnant women
  - diabetics
  - individuals with mental or physical disabilities,
  - immuno-compromised people
  - hyper-allergenic people
  - other pre-existing medical conditions.

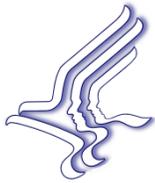


## BARDA Thermal Burn RFI, December 14, 2010



This RFI sought responses from manufacturers with products that would be useful in treating partial- and full-thickness thermal injuries resulting from the mass-casualty incidents

- Products of interest included
  - products commercially available, approved by the FDA or other regulatory authority, and demonstrated to be useful for burn care in the US and/or abroad
  - products in advanced development with data that may support their deployment in an emergency mass-casualty incident
  - products under development with supporting data demonstrating their functional value.



# Limited Clinical Capacity, Small Marketplace



- **Our nation's burn capacity is limited**
  - 125 burn centers nationwide: ~1800 burn beds total
  - Average daily availability: ~400 burn beds
- **Burn care is labor and resource intensive**
  - Frequent and timely dressing changes
  - Long hospital stays ( $\geq 1$  day for every 1% total body surface area)
- **Burn care is a relatively small (“boutique”) market**
  - 45,000 hospitalizations year (25,000 at burn centers)
  - 7,500 serious cases involving skin grafts
  - Opinions on best treatments vary significantly between experienced practitioners



# Burn Products Temporal Product Use Map



## Timeline Post Detonation

24 - 48 hr

### Primary Concerns

- Airway
- Trauma
- Burn shock

48 - 72 hr

### Primary Concerns

- Infection

Wks / Months

### Primary Concerns

- Proper wound care
- Long-term recovery

### Burn care

- Anti-infective coverings

### Others

- Tracheal
- Trauma
- Fluids
- Pain management

### Burn care

- Anti-infective coverings

### Others

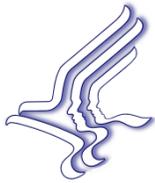
- Fluids
- Pain management

### Full-Thickness

- Autografts
- (in addition to the below)

### Partial-Thickness

- Natural Biological Products
- Mfd. Cell-Based Products
- Anti-infective Coverings
- Advanced Bandages
- Liquids & Gels



# The Chemical Threat



## *BAA Area of Interest #5: Chemical Threat Medical Countermeasures*

Specific areas of interest within Chemical Threat Medical Countermeasures include:

5.1 Nerve Agents

5.2 Pulmonary Agents

**5.3 Vesicants**

5.4 Blood/Metabolic Agents

5.5 Toxic Industrial Chemicals and Emerging Threats



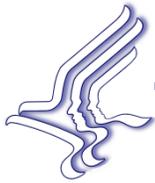
# The Threat Agent: Vesicants



There are three subclasses of vesicants:

- **Mustards (H)**
  - Sulfur mustard (HD)
  - Nitrogen mustard (HN)
  - Sesqui-mustard (Q)
  - Oxygen mustard (T)
- **Organic arsenicals or dichloroarsines**
  - Lewisite (L)
  - Methyldichloroarsine (MD)
  - Phenyldichloroarsine (PD)
  - Ethyldichloroarsine (ED)
- **Halogenated Oximes**
  - Phosgene oxime (CX)





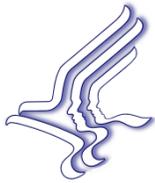
# The Threat: Potential Use for Terrorist Purposes



- **Mustard considered a potentially likely agent for terrorism purposes**
  - Persistent agents – Pose a threat for many days after release
  - Delayed effect
  - Injuries heal slowly
  - Inexpensive, easily obtainable and stockpiled
    - Large quantities (Tons) of the agent were produced for war and then dumped at sea, buried in landfills, or left for decay in storage facilities near homes

## Recently Reported News involving Mustard Gas

Date	Reported Situation
June 2010	Two CT fishermen were sickened after discovering mustard canisters while clamming off the coast of Long Island
February 2007	Workers at Chemical Depot in UT seal a site of leaking mustard inside a storage igloo
November 2006	A military service member is injured from leaky WWI mustard gas round that washed ashore the US east coast
April 2005	Danish fishermen caught mustard gas munitions in their nets
February 2004	Chinese victims sue Japan for exposure to chemical weapons left behind during WWII
July 2003	Barrels containing mustard are found buried in Cleveland, OH
April 2001	In France, 15,000 people are evacuated from their homes as old munitions awaiting destruction begin to leak



# Chemical BAA Special Instructions, March 2010

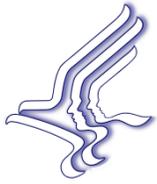


The purpose of these special instructions is to specifically solicit solutions for treating injuries resulting from exposure to the following agents.

- Nerve Agents
- Cyanide
- Pulmonary Agents: for example, phosgene, chlorine, ammonia, and diphosgene

## Goals

- Easily administered
- Rapidly effective
- Can be used by untrained persons and by first responders dealing with large numbers of exposed individuals.

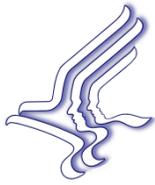


# Chem Rad Nuc Continuing Challenges

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- Immature pipeline
- Well characterized animal models
- Animal Rule
- Engaging industry (repurposing existing drugs)



# Interagency Cooperation Integrated Portfolio For CBRN Countermeasures



For each threat or requirement...

... a set of programs is required, each comprised of...

... a set of development projects to yield the required MCM



- Threat Determinations
- Consequences of Attack
- Requirements Definition



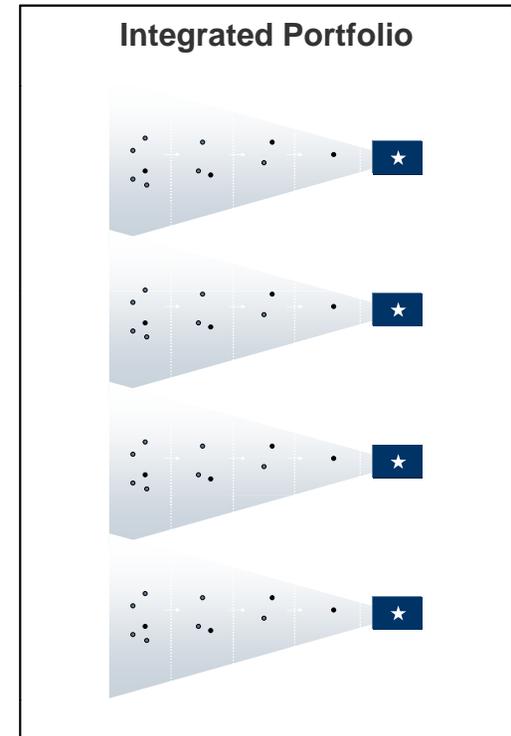
HHS Programs

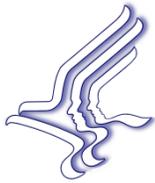


DoD Programs



DoD Requirements

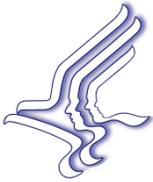




# Including BARDA in Your Development Plan



- **TechWatch** – request a meeting with program and regulatory staff at [www.medicalcountermeasures.gov](http://www.medicalcountermeasures.gov)
- **Broad Agency Announcements – Advanced Research and Development**
  - BAA open all-year round
  - Discuss with program and regulatory staff before submitting a proposal
  - Funding is typically for one year with multiple one-year options
  - Contracts are driven by well-designed development plans with go/no go milestones and decision points
- **Project BioShield**
  - Reserved for very late-stage products
  - Companies with licensed products with an interest in broadening label claims are highly encouraged to contact us



# Engaging with BARDA

- [www.phe.gov](http://www.phe.gov)
  - Program description, information, news, announcements
- [www.medicalcountermeasures.gov](http://www.medicalcountermeasures.gov)
  - Portal to BARDA
  - Register, request a meeting
  - Tech Watch
- [www.fedbizopps.gov](http://www.fedbizopps.gov)
  - Official announcements and detailed information about all government contract solicitations

