

# Considerations for Advanced Development of BuChE-based Countermeasures

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MAJ Luis Alvarez, Ph.D.  
Assistant Joint Product Manager  
Medical Identification & Treatment Systems (MITS)  
[luis.alvarez@amedd.army.mil](mailto:luis.alvarez@amedd.army.mil)





# Purpose

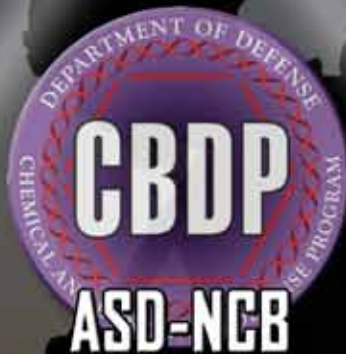


To provide general considerations for the advanced development of BuChE-based countermeasures through FDA licensure and an overview of current Bioscavenger (BSCAV) program activities





# Joint Services Chemical Biological Radiological Nuclear (CBRN) Defense



**DELIVERING JOINT WARFIGHTING CAPABILITIES**





# CBMS Program Overview



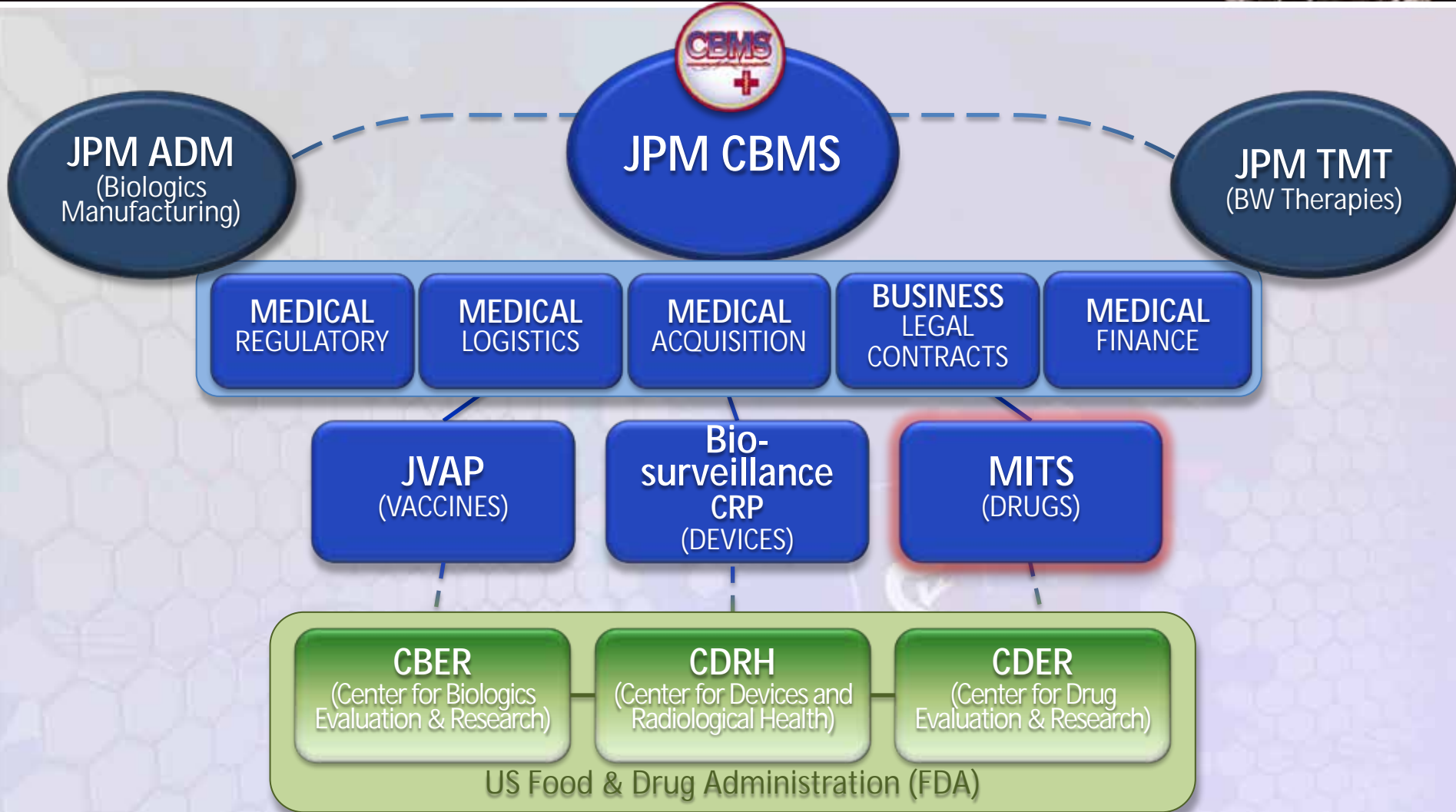
*Our Vision is to protect the Warfighter by maintaining uncontested global supremacy in CBRN medical countermeasure development and delivery*



Our Mission is to rapidly provide the Warfighter with safe, robust, affordable medical countermeasures against a broad spectrum of CBRN threats. Use government and commercial best practices to acquire FDA-approved CBRN medical countermeasures and diagnostics



# JPM-CBMS Medical Program Organizational Structure



- - - (Dotted line denotes coordination)





# CBMS-Medical Identification & Treatment Systems (CBMS-MITS)



Provide the Warfighter and the Nation robust & affordable FDA-approved lifesaving medical countermeasure drug capabilities against chemical, biological, radiological and nuclear threats







# Warfighter Needs



## Requirements Identified

### Acquisition Documents

- Initial Capabilities Document (ICD)
- Capabilities Development Document (CDD)
- Capabilities Production Document (CPD)
- Key Performance Parameter = FDA Licensure





# Continuum of CBMS Medical Countermeasures



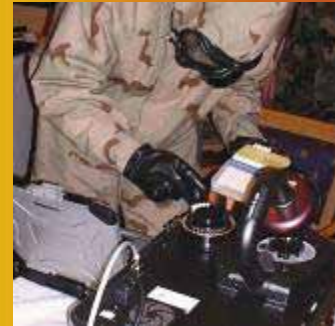
Biological Prophylaxis (vaccines) are the highest rated Medical Countermeasures (MCMs) on the "CBRN Capabilities Joint Priority List"

Focus on PREVENTION



DIAGNOSIS

TREATMENT

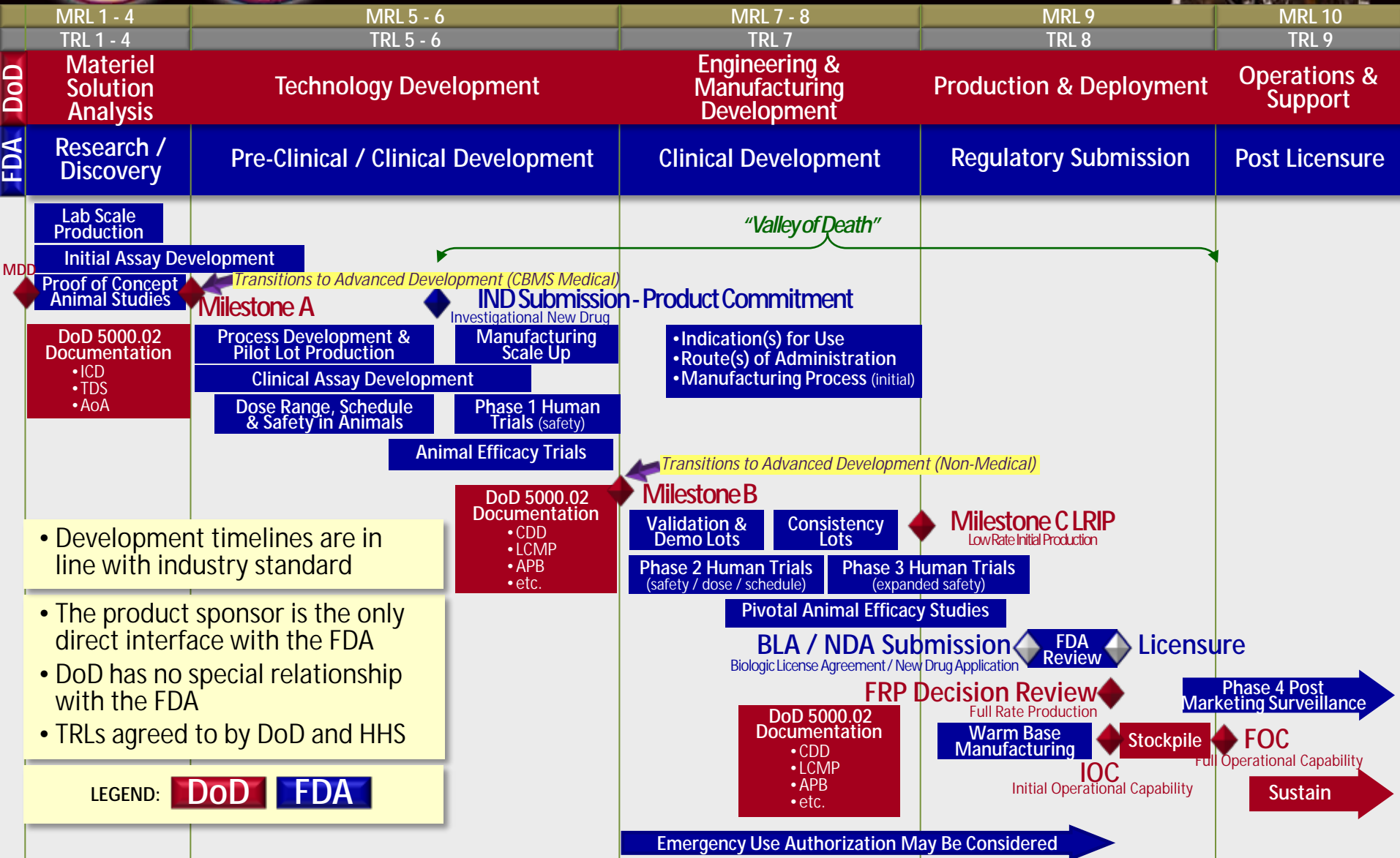


Prophylaxis preserves the fighting force

Treatment preserves life



# Integration of DoD Acquisition Model & FDA Regulatory Process



- Development timelines are in line with industry standard
- The product sponsor is the only direct interface with the FDA
- DoD has no special relationship with the FDA
- TRLs agreed to by DoD and HHS



# Program Description MITS Portfolio



- Bioscavenger is the only chemical prophylactic countermeasure in development
- Current treatment regimen has limitations; Bioscavenger fills those gaps
- It will transform how we protect Warfighters against nerve agents threats



\* With typical dose & against various agents of interest





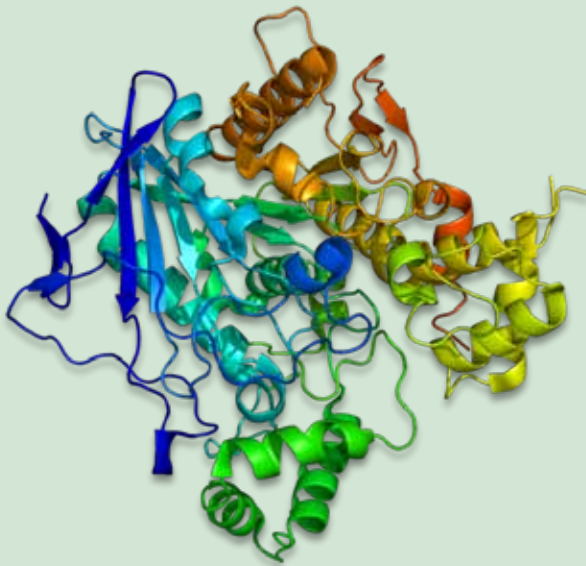
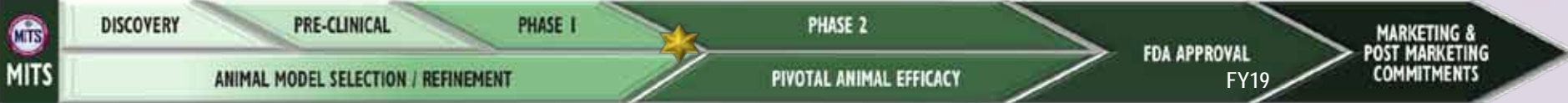
# Capability Gap



- There are insufficient medical products to adequately protect the operational force in all nerve agent threat environments
- Current FDA-approved pretreatments fail to provide comprehensive protection against the adverse effects of exposure to nerve agents



# Bioscavenger (BSCAV)



- First ever nerve agent prophylactic that prevents incapacitation and death from exposure to a broad spectrum of nerve agent
  - Provides an extra layer of protection to Individual Protection Equipment
  - Prevents performance degradation
- Based on human butyrylcholinesterase (HuBChE), a blood or plasma protein that binds and inactivates nerve agents
- Plasma-derived BChE, when administered via IV, can provide protection in less than 10 minutes and remain effective for over 10 days

## Team Members

Dr. Kristen Herring	DTRA/JSTO
Dr. Doug Cerasoli	USAMRICD
Dr. Judith Laney	BARDA
Dr. David Yeung	NINDS
Dr. (COL) Alan Magill	DARPA

**MAJ Luis Alvarez**  
 Pharmaceutical Manager  
 luis.alvarez@us.army.mil  
 301.619.8429





# Guinea Pig 5.5 X LD<sub>50</sub> VX Challenge



### No BSCAV (Saline Placebo)

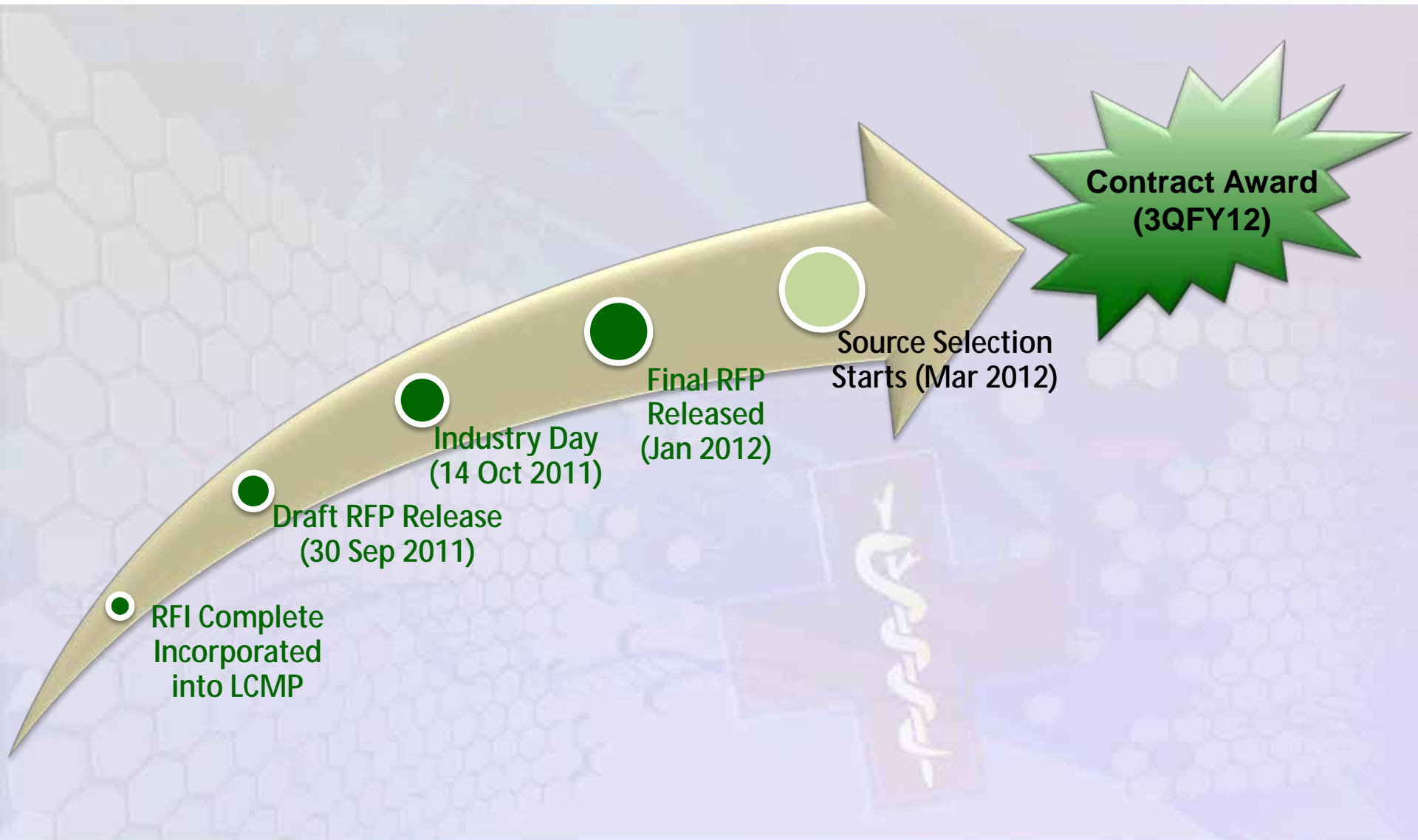
24 hrs later gets 1.5 X LD<sub>50</sub> VX  
Dies within 35 minutes

### Receives BSCAV

24 hrs after BSCAV gets 1.5 X LD<sub>50</sub> VX  
+2 hrs later 2 X LD<sub>50</sub> VX  
+2 hrs later 2 X LD<sub>50</sub> VX  
Never showed any symptoms



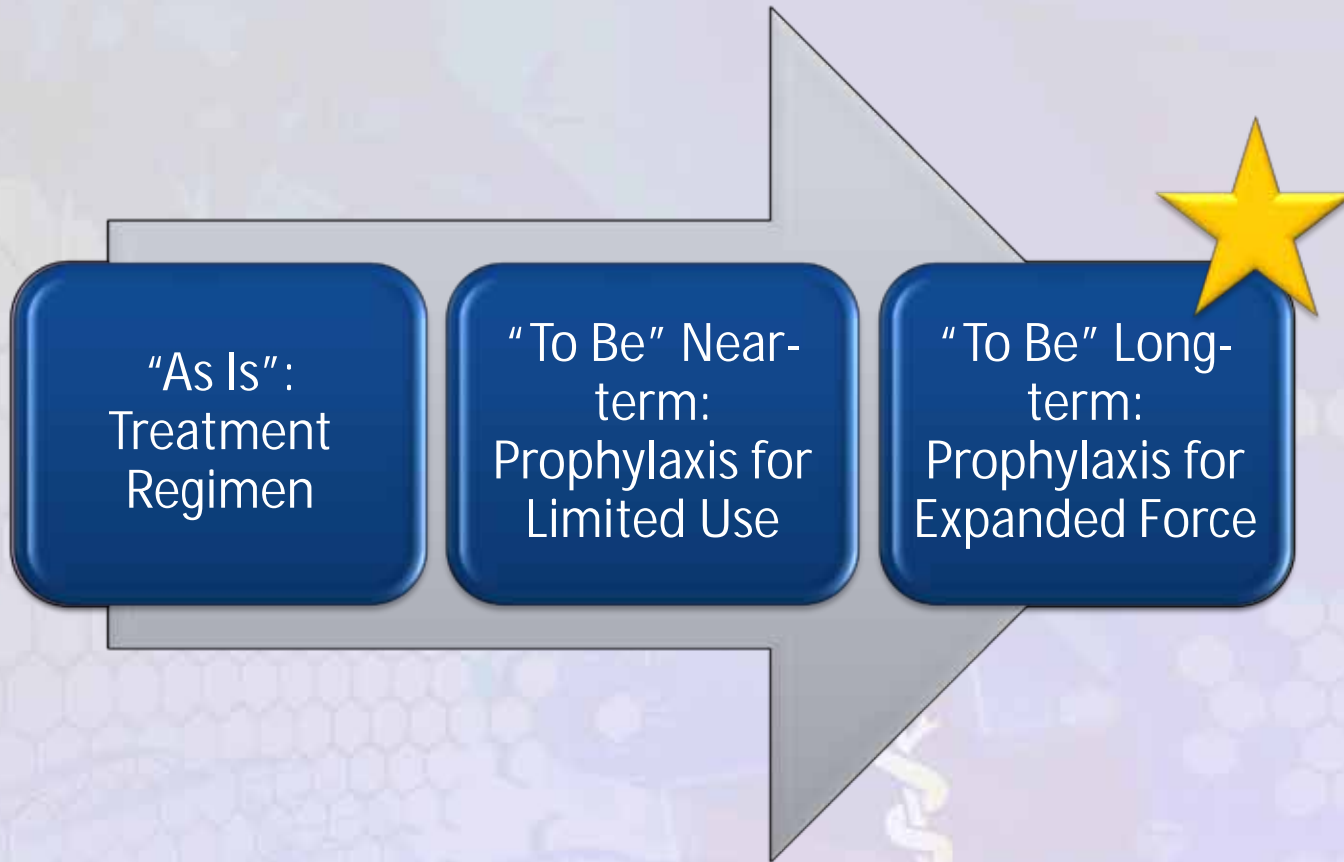
# Bioscavenger Program Status







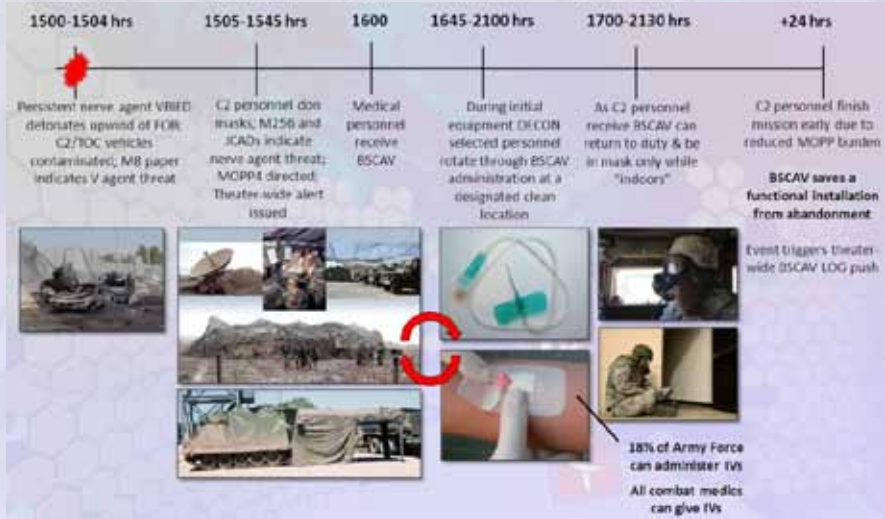
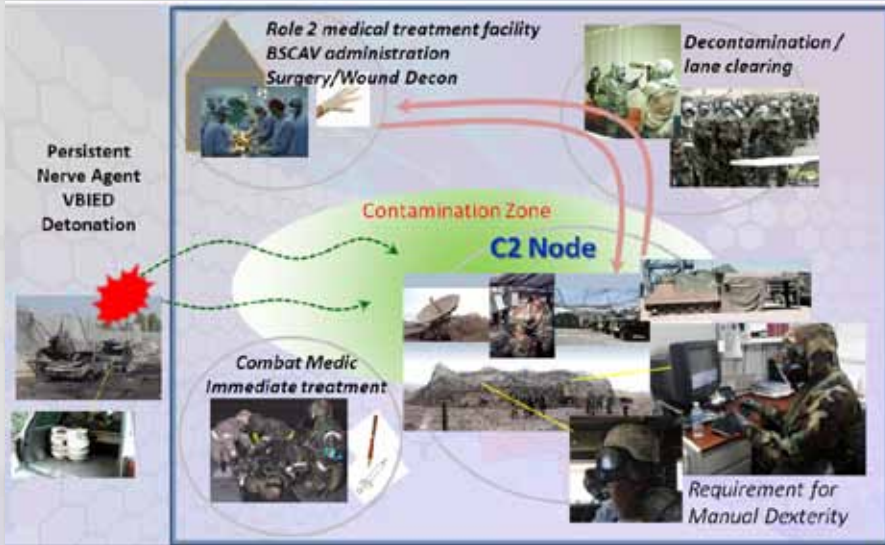
# Delivering Capability



Introducing new capability and then expanding the capability leveraging matured technology



# Limited Use Operational Scenarios



- BSCAV significantly reduces the risk of injury from OP exposure & **complements** the system-of-systems approach in countering nerve agent threats

- BSCAV provides immediate “chemical immunity” against all OP agents in the operationally relevant exposure range of 2-9 X LD50s

- BSCAV will provide protection against all known and **future** organophosphate cholinesterase inhibitors

- BSCAV will **reduce numbers of casualties** and **minimize disruption** to Warfighter mission readiness

- BSCAV **gives commanders flexibility** in determining courses of action for mission execution in nerve agent contaminated operational environments

- MOPP flexibility enhances mission performance and further reduces risk by speeding completion of mission essential tasks

- BSCAV provides an **extra later of protection** in the event of MOPP equipment failure





# Limited Use Scenario 2 – Civilian Preparedness Credible INTEL Threat



0 hrs

+24 hrs

+36 hrs

+48 hrs

+52 hrs

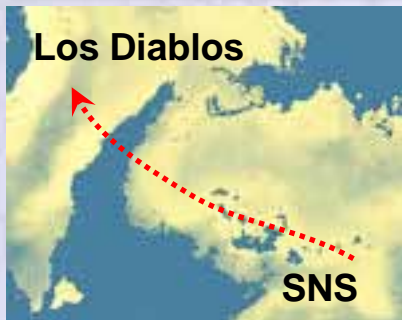
Credible INTEL indicates high likelihood of an OP pesticide attack on a dense urban target in the next 48-72 hrs in the city of Los Diablos

500 units of BSCAV are moved from the Strategic National Stockpile (SNS) and prepositioned in Los Diablos; CBIRF Casualty Search & Extraction and Medical teams prepare for possible event

Three major trauma centers & five EMS units in selected Los Diablos precincts receive BSCAV; protocols are in place for healthcare providers and first responders to take BSCAV in the event of a confirmed attack

Parathion release occurs at an open market; 45 people suffer OP effects; reports of people exhibiting NA symptoms; CBIRF and EMS teams take BSCAV prior to responding

First responders & CBIRF are able to perform duties with greater confidence and lower impediment from protective gear under certain conditions







# CBMS Government Points of Contact



- LTC Nanette Patton      Joint Product Manager (JPM), MITS  
nanette.patton@amedd.army.mil
- Dr. Renae Malek      Chief Technical Officer, MITS  
renae.malek@amedd.army.mil
- MAJ Luis Alvarez      BSCAV Pharmaceutical Manager  
luis.alvarez@amedd.army.mil
- Mr. Brett Peterson      BSCAV Senior Science Manager  
brett.peterson3@amedd.army.mil
- Ms. Mona Atkinson      BSCAV Science Manager  
mona.atkinson@amedd.army.mil

***MAJ Luis M. Alvarez, Ph.D.***

Pharmaceutical Manager,  
CBMS-MITS

301-619-8429

[luis.alvarez@amedd.army.mil](mailto:luis.alvarez@amedd.army.mil)





# Backup







# Improvement over Existing Treatment Regimen



- **Treatment regimen (post-exposure, post-symptomatic administration)**
  - Suite of products required, especially to achieve broad spectrum
  - SNAPP – pre-treatment in case of GD threat ( $2LD_{50}$ ), requires subsequent treatment with ATR (atropine) / oxime (2-PAM) [ATNAA]
  - ATNAA and anticonvulsant (CANA: diazepam) – treatment initiated upon symptoms, within minutes of nerve agent exposure
  - Servicemember is a casualty; may suffer performance decrements and long term sequelae
- **Prophylactic regimen (pre-exposure administration)**
  - Stand alone product administered prior to nerve agent exposure
  - Broad spectrum protection against a broad range of organophosphorus nerve agents
  - Prevents nerve agent intoxication or extends lead time to react before becoming symptomatic
  - Protects central nervous system (CNS) by sequestering agent in blood
  - Prevents performance decrement
  - Long term sequelae averted