Considerations for Advanced Development of BuChE-based Countermeasures

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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
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

- **JPM ADM** (Biologics Manufacturing)
- **JPM CBMS**
  - **MEDICAL REGULATORY**
  - **MEDICAL LOGISTICS**
  - **MEDICAL ACQUISITION**
  - **BUSINESS LEGAL CONTRACTS**
  - **MEDICAL FINANCE**
- **JVAP** (VACCINES)
- **Bio-surveillance CRP** (DEVICES)
- **MITS** (DRUGS)
- **US Food & Drug Administration (FDA)**
  - **CBER** (Center for Biologics Evaluation & Research)
  - **CDRH** (Center for Devices and Radiological Health)
  - **CDER** (Center for Drug Evaluation & Research)

(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

FDA Licensure Process

Science & Technology (S&T) Development

Advanced Development

ICD
CDD
CPD

Protocols for CBRN Defense

Protecting the Warfighter

Portfolio of Safe & Effective CBRN Medical Countermeasures

CBR Threat

FDA Approved

Warfighter ➔ Requirements ➔ JRO ➔ Requirements Documents ➔ S & T ➔ JPEO-CBMS

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

Focus on PREVENTION

Prophylaxis preserves the fighting force

DIAGNOSIS

TREATMENT

Treatment preserves life
Integration of DoD Acquisition Model & FDA Regulatory Process

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- 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

**Legend:**
- DoD
- FDA

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**DoD 5000.02 Documentation**
- ICD
- TDS
- AoA

**DoD 5000.02 Documentation**
- CDD
- LCMP
- APB
- etc.

**Indication(s) for Use**
- Route(s) of Administration
- Manufacturing Process (initial)

**Phase 2 Human Trials**
(safety / dose / schedule)

**Phase 3 Human Trials**
(expanded safety)

**Pivotal Animal Efficacy Studies**

**BLA / NDA Submission**
Biologic License Agreement / New Drug Application

**FDA Review**
Licensure

**FRP Decision Review**
Full Rate Production

**Stockpile**
Full Operational Capability

**FOC**
Initial Operational Capability

**Emergency Use Authorization May Be Considered**
• 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

Max Protection of Current CMCs
1.5 - 2 X LD₅₀

Typical Protection of BSCAV*
5 - 9 X LD₅₀

* 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

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Guinea Pig
5.5 X LD$_{50}$ VX Challenge

No BSCAV (Saline Placebo)
24 hrs later gets 1.5 X LD50 VX
Dies within 35 minutes

Receives BSCAV
24 hrs after BSCAV gets 1.5 X LD50 VX
+2 hrs later 2 X LD50 VX
+2 hrs later 2 X LD50 VX
Never showed any symptoms
Bioscavenger Program Status

RFI Complete
Incorporated into LCMP (30 Sep 2011)

Draft RFP Release
(14 Oct 2011)

Industry Day
(14 Oct 2011)

Final RFP Released
(Jan 2012)

Source Selection Starts (Mar 2012)

Contract Award (3QFY12)

Contract Award (3QFY12)
Delivering Capability

Introducing new capability and then expanding the capability leveraging matured technology

“As Is”: Treatment Regimen

“To Be” Near-term: Prophylaxis for Limited Use

“To Be” Long-term: Prophylaxis for Expanded Force
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
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
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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 (2LD₅₀), 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