Medical Chemical and Biological Defense Research

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U.S. Army Medical Research & Materiel Command
### Medical Chemical and Biological Defense Research

#### Abstract
This article is from ADA409494 Proceedings of the 2001 ECBC Scientific Conference on Chemical and Biological Defense Research, 6-8 March, Marriott’s Hunt Valley Inn, Hunt Valley, MD. The original document contains color images.
...the threat or use of NBC weapons is “a likely condition of future warfare.” Quadrennial Defense Review (May 1997)

Direct payoff of chemical/biological defense R&D: Reduction, even elimination, of casualties which would otherwise follow a CW/BW attack.

Indirect payoffs: Effective products against CW/BW deter employment and proliferation of CW/BW capabilities.

Efforts address Joint Service/CINC requirements
Provide medical solutions for military requirements to protect and sustain the force in a Chemical and/or Biological Warfare environment.
MCBDRP Vision

To Preserve Total Warfighter Effectiveness on a CW/BW Battlefield

- Prevent casualties
- Provide effective treatment of casualties for rapid return to duty
- Provide rapid, far-forward diagnosis of CW/BW disease
Protecting Warfighters Through Integration and Teamwork

**Intelligence**
- Agent
- Delivery System
- Organization
- Time

**Medical Countermeasures**
- Vaccines & Prophylaxes
- Diagnostics
- Therapeutics

**Chem/Bio Defense Doctrine**

**Education & Training**
- Military and Civilian Health Care Providers
- Electronic Communication
- Distance Learning

**Physical Countermeasures**
- Detection
- Physical Protection
- Decontamination
Product Development Overview

Acquisition of Products for Future Warfighters
Soldier, Biological and Chemical Command
JPO-BD/JVAP
Other Commodity Area Managers

Medical Products for Chemical Agents
USAMMDA

6.4 - 6.5 Advanced Development

Medical Products for Biological Agents
JPO-JVAP

6.3 Concept Exploration
6.2 Applied Research
6.1 Basic Research

U.S. Army Medical Research & Materiel Command
The “Tech Base” Products

- Basic Research Discoveries (Scientific Knowledge)
- Model Development for Agents of DoD Interest
- Vaccine/pretreatment Candidates
- Therapeutic Candidates
- Diagnostic Tests and Reagents
- Information
- Education
- Expertise & Consultation
- Technology Watch

Tech Base

Our Readiness Posture For Meeting Future Threats And Avoiding Technological Surprise
Medical Biological Defense

Technical Approach:

- Identify mechanisms involved in disease process.
- Develop and evaluate products (vaccines or drugs) to prevent or counter effects of biological toxins, bacteria, and viruses.
- Develop methods to measure effectiveness of medical countermeasures in animal models which are predictive of human response.
- Develop diagnostic systems and reagents.
Medical Biological Defense Organizational Taxonomy

Medical Countermeasures (MC) against BW Agents

- CB.24 MC for Encephalitis Viruses
- CB.25 Multiagent Vaccines for Biological Threat Agents
- CB.26 Common Diagnostic Systems
- CB.31 MC for Brucellae
- CB.32 Needleless Delivery Methods for Recombinant Protein Vaccines
- CB.33 Recombinant Protective Antigen (rPA) Vaccine Candidate
- CB.34 Recombinant Plague Vaccine Candidate
Medical Biological Defense Transitions

- **FY99/00**
  - Multivalent (A,B,C,E,F) Recombinant Botulinum Vaccine - MS I
  - Plague (F1-V) Antigen Vaccine - MS 0
  - Recombinant VEE Vaccine - MS 0

- **FY01**
  - Next Generation Anthrax Vaccine - MS I
  - Plague (F1-V) Antigen Vaccine - MS I
  - Common Diagnostics - MS 0
  - Multiagent Vaccine - MS 0
  - Brucella Vaccine - MS 0
  - Marburg (Filovirus) Vaccine - MS 0
Medical Biological Defense
Products in Development
(Projected Fielding)

- Q-Fever Vaccine – 2004 ?
- Smallpox Vaccine (Cell Culture Derived) - 2005
- Recombinant Plague Vaccine - 2006
- Venezuelan Equine Encephalitis Vaccine - 2008
- Tularemia Vaccine - 2008
- Recombinant Botulinum Vaccine - 2009
- Brucella Vaccine - 2010
Emerging Medical BD Products

- VEE/EEE/WEE Combined Vaccine
- Staphylococcal Enterotoxins Vaccine
- Ricin Vaccine
- Common Diagnostic System for BD Threats and ID Diseases
- Next Generation Anthrax Vaccine
Medical Biological Defense
Investment in the Future

- **Countermeasures for Genetically Engineered Microbes**
  - Genomic sequencing of BW threat agents to identify and understand virulence factors, toxins and drug resistance genes

- **Immunomodulators and Therapies**
  - Alternatives to agent-specific vaccines or therapies

- **Multiagent Vaccines**
  - Alternative to one vaccine for one BW threat agent
Strategic Challenges
Medical Chemical and Biological Defense RDT&E

- Acquisition Model
- FDA Regulations
- Multiplicity of Threats
Acquisition Model - Linear
- Old DoD 5000
- New DoD 5000
- Technology Readiness Levels
- Risk Reduction

Biologicals/Pharmaceuticals – Recursive
- Iterative testing of numerous candidates
- Kill products early
- Finite lifetime
# Integration of DoD Milestones and FDA Licensure Process

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**Basic Research**
- Identify Threat Agent
- Characterize Threat Agent
- Identify Vaccine Antigens

**Applied Research**
- Define Animal Models
- Evaluate Vaccine Candidates
- Determine Effectiveness
- Develop Assays and Reagents

**Concept Exploration**
- Manufacture Small Scale Pilot Lots
- Characterize Vaccine Candidates
- Animal Testing
- Design Surrogate Endpoint of Clinical Efficacy

**PRE-IND MEETING**
- Prepare Pre-IND Read Ahead
- Sponsor Pre-IND Meeting

**JVAP/Prime Systems Contractor**
- Program Definition and Risk Reduction
- Engineering and Manufacturing Development
- Production

**Manufacture Pilot Lots**
- Non-Clinical Testing
- Prepare and Submit IND Application to FDA
- Formulate Multivalent Vaccine (if required)
- Conduct Phase 1 and Phase 2a Clinical Trials
- Perform Surrogate Efficacy Tests

**Consistency Lots**
- Post Marketing Surveillance

**BLA to FDA**
- Produce Vaccine
- Store and Maintain Vaccine Stockpile

**TECHNOLOGY DEFINED**

**U.S. Army Medical Research & Materiel Command**
**Defense Acquisition Management Framework**

- **Technology Opportunities & User Needs**
  - Concept Exploration
  - Component Advanced Development
  - System Integration
  - System Demonstration
  - LRIP
  - System Development & Demonstration
  - Production & Deployment

- **Pre-Systems Acquisition**
  - Concept & Tech Development
  - Decision Review

- **Systems Acquisition**
  - (Demonstration, Engineering Development, LRIP & Production)
  - Interim Progress Review
  - FRP Decision Review

- **Sustainment**
  - Operations & Support
  - Sustainment
  - Sustainment Disposal

- **Disposal**
  - MNS
  - ORD

**Relationship to Requirements Process**

- U.S. Army Medical Research & Materiel Command
- Validated & approved by operational validation authority

- **Single Step or Evolution to Full Capability**
- Enter process at Milestones A, B, or C (or within phases)
- Program outyear funding when it makes sense, but no later than Milestone B
Strategic Challenges

- FDA Regulatory Requirements
  - Products must be safe
    - Demonstrate in animals
    - Demonstrate in humans
  - Products must be effective
    - Demonstrate in animals
    - Demonstrate in human clinical studies and field trials

- Medical Chem/Bio Products – we can:
  - Demonstrate safety in animals and humans
  - Demonstrate efficacy in animals
  - Estimate efficacy in humans
Proposed new FDA Rule

- Allows consideration of animal efficacy studies in support of licensure request
- Additional requirements
  - Understand mechanisms of action of the disease-causing agent
  - Understand basis of action of the vaccine or drug
  - Demonstrate efficacy in two relevant animal models
  - Identify surrogate markers of efficacy
Strategic Challenges

- Multiplicity of Threats
  - Chemical Warfare Agents
    - Nerve agents
    - Mustards
    - Blood/Choking agents
  - Biological Warfare Agents
    - Viruses
    - Bacteria
    - Toxins
  - Emerging Threats
Medical chemical and biological defense research presents unique challenges
- Chemical threat agents
- Biological threat agents
- Medical regulatory compliance and DoD acquisition

We need cutting edge technologies to develop medical countermeasures for the warfighter
- Biotechnology
- Informatics
- Genomics and Proteomics

Partnerships with the science community & industry are essential
- CRADAs
- Contracts