

04/11/01

# **BIOLOGICAL WARFARE DEFENSE**

---

---

## **Program Overview**

**Dr. Jane A. Alexander**  
**Deputy Director, Defense Sciences Office**

DARPA/DSO, 3701 N. Fairfax Drive, Arlington, VA 22203-1714  
Phone: 703-696-2233, Fax: 703-696-3999, JALEXANDER@DARPA.MIL



# **Why is Biological Warfare Defense a Very High DARPA Priority ?**

- **Officially:**
  - **Troops, ports, airfields, supply depots, etc. are vulnerable to biological attacks**
  - **A number of countries have developed or are developing offensive biological capability**
- **Unofficially:**
  - **Most likely use will be against population centers of ours or our allies**
  - **Small demonstration and threat probably adequate to immobilize national will with panic unless reasonable defenses are available**

# Iraq - State Example

- **Iraq stockpiled, based on 5 years of sustained work:**
  - Botulinum toxin: 19,000 L (10,000 L weaponized)
  - Anthrax: 8500 L (6500 L in weapons)
  - Aflatoxin: 2200 L (1580 L in weapons)
  - Smaller amounts of ricin, mycotoxins, Haemorrhagic conjunctivitis virus, rotavirus & agents to attack crops
- **Admitted weapons**
  - 191 warheads
  - 166 bombs: 100 botulinum, 50 anthrax, 16 aflatoxin
  - 25 SCUD warheads: 13 bot, 10 anth, 2 aflatoxin
  - Aerial spray system with 2000 L of agent
- **Intent**
  - Iraq has indicated that biological and chemical weapons were deployed forward
  - Launch authority had been pre-delegated during the Gulf war, to be used if Baghdad was attacked with nuclear weapons

David Kay, "Detecting Cheating on Non-Proliferation Regimes: Lessons from the Iraqi Experience", Aspen Strategy Group Meeting, 10-15 August 1996

# Recent US Non-State Examples

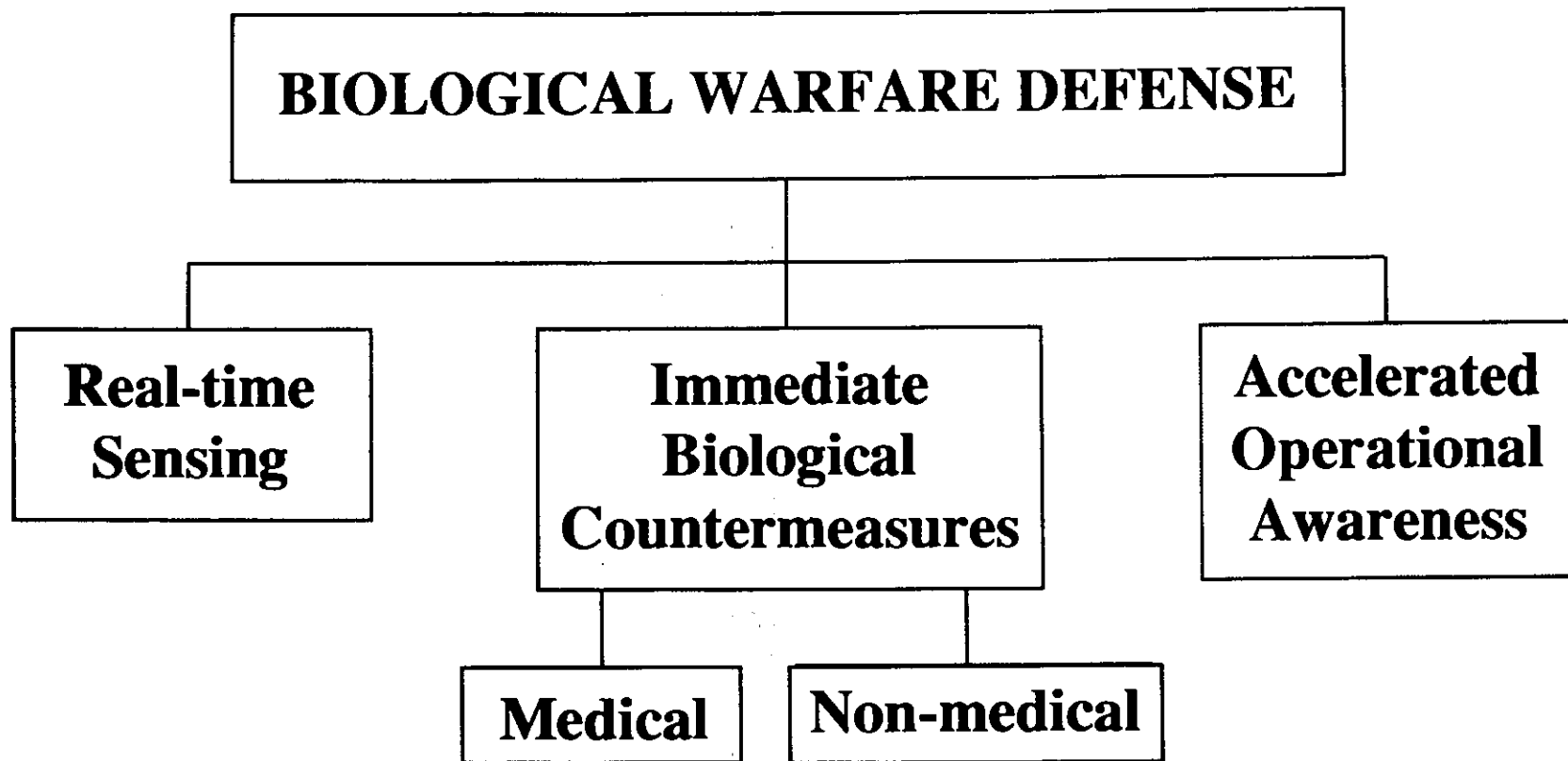
- **Dec 95:**
  - **Man (survivalist ties) charged with attempt to smuggle 130 g ricin into US to use as weapon (small amount can kill in minutes if ingested, inhaled or absorbed through skin)**
- **May 95:**
  - **White supremacist member of Aryan Nations arrested in Ohio after ordering freeze-dried bubonic plague for “research purposes”**
- **Mar 95:**
  - **Aum Shinrikyo releases deadly sarin nerve gas in Tokyo subway during rush hour, killing 12 and hospitalizing 5000**
- **Mar 95:**
  - **Two members of militia-style organization (Minnesota Patriots Council) convicted of planning to use ricin to assassinate IRS agents and other federal employees**
- **May 94:**
  - **Sentencing judge in World Trade Center case announced that defendants had placed sodium cyanide in their explosive package with the intent of creating a poisonous cyanide gas.**

# Aum Shinrikyo

- **General**
  - **Recruited scientists and technical experts from Russia, Japan and elsewhere**
  - **30,000 members in Russia alone**
  - **World-wide purchasing programs; most individual purchase appeared innocent**
  - **Own chemical manufacturing complex (sarin, VX, phosgene, sodium cyanide)**
  - **Year before subway attack (6/94), sprayed apartment complex with sarin to kill 3 judges (who lived); 7 others died and 500 injured.**
  - **After subway attack, twice attempted to release hydrogen cyanide gas in Tokyo (one disarmed within seconds of dispersing gas in crowded subway station)**
- **Experimented with biological agents**
  - **Sustained research effort to manufacture bio agents including ebola virus, anthrax and botulinum toxin for weapons use**
  - **Genetic engineering of bacillus anthracis**
  - **Cloning of botulinum genes into other bacilli**
  - **Tested dispersal techniques at least three times to assess effectiveness of their toxins on humans**
  - **One unsuccessful 8 hour dissemination of anthrax from top floor of Aum headquarters in Tokyo**
- **Apparently pretty good science but poor engineering [my observation]**

# Priority

- **Bio Warfare is a major threat**
  - It is much more than anthrax and bot-toxin usually discussed in DoD
- **US has no effective defenses**
  - Except in very limited circumstances and with optimistic assumptions
- **Most on-going work is short term and of limited effectiveness, albeit essential and the best we can do rapidly**
- **Serious long-term R&D is urgently needed if we are to achieve anything like a robust capability**



**Remove the threat of biological warfare agents (including bacterial, viral, and bioengineered organisms) as a factor in the planning and conduct of U.S. military operations**



UNCLASSIFIED

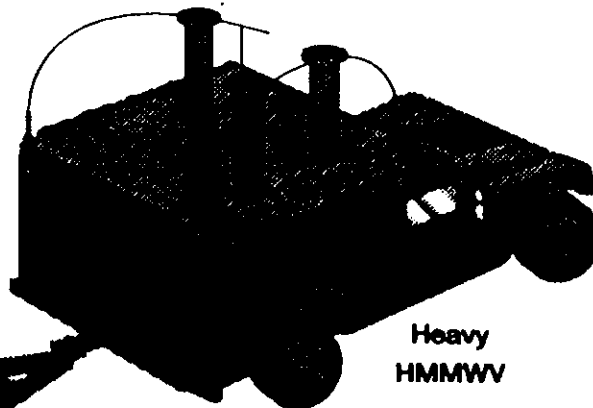


# BIDS NDI System



**Aerodynamic Particle Sizer (APS)**  
(Non-Specific Background Change)

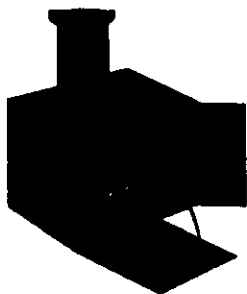
**S788 Shelter**



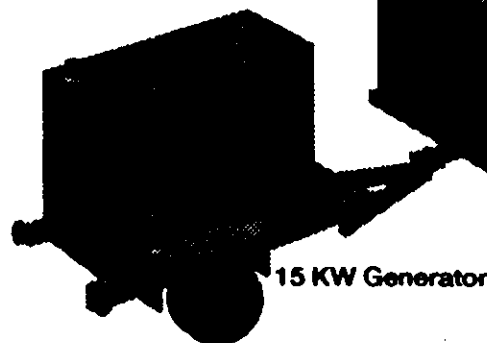
**Heavy HMMWV**



**Assay Tickets**  
(Specific Agent Identification)



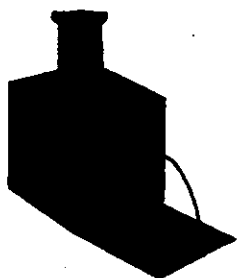
**Biological Sampler**



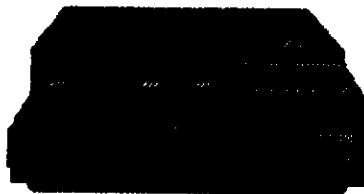
**15 KW Generator**



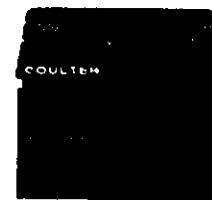
**Microluminoemeter**  
(Generic Bio/Non-Bio)



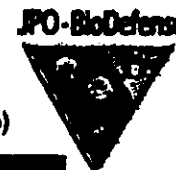
**Liquid Sampler**



**Threshold System**  
(Specific Agent Identification)



**Flow Cytometer**  
(Generic Bio/Non-Bio)



# Biological Sensors: Program Goal

---

---

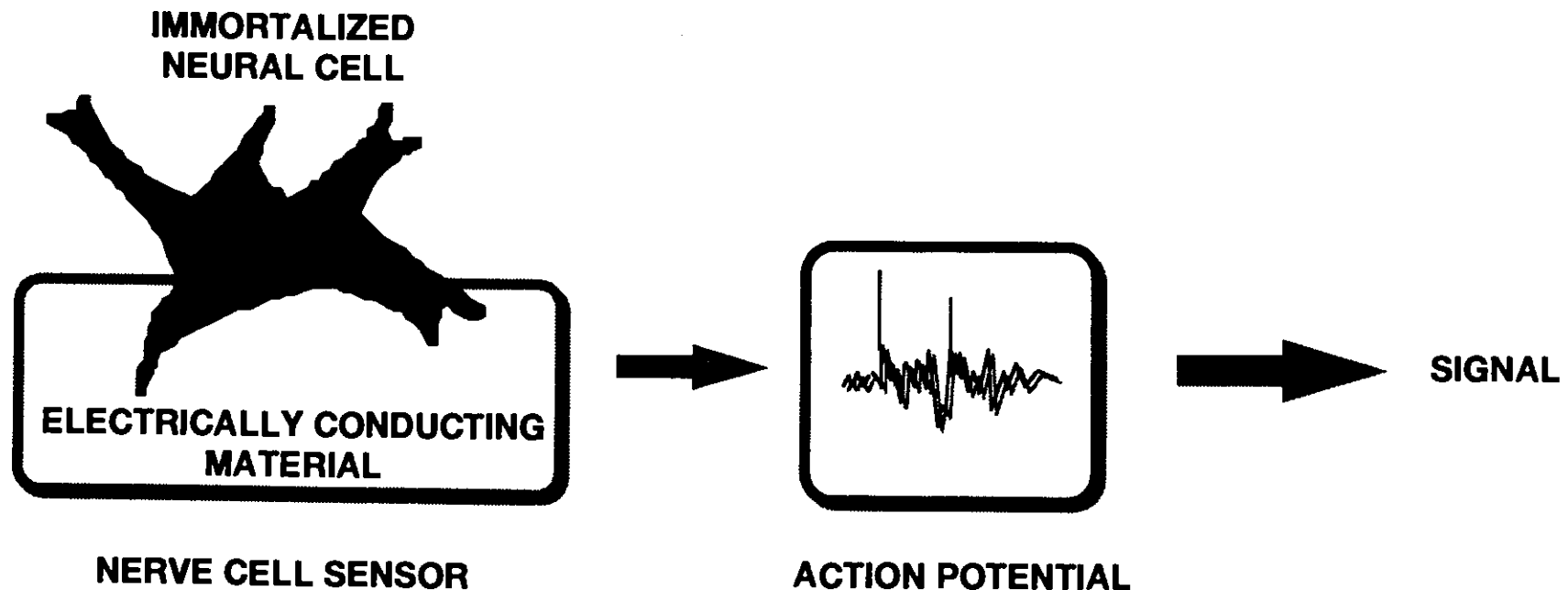
- ✦ Provide real-time, pre-exposure detection, discrimination, and identification of the threat.
- ✦ Develop robust, unattended, real-time (<2 minutes), high sensitivity (2-10 particles), multi-agent (up to 20) biological sensors that are small (<5 lbs), low cost (<\$5K) and which provide few false positives and no false negatives, even in the presence of encapsulation and contaminating and/or competing environmental biologics.



# Neuron-based Biosensor “Canary on a Chip”

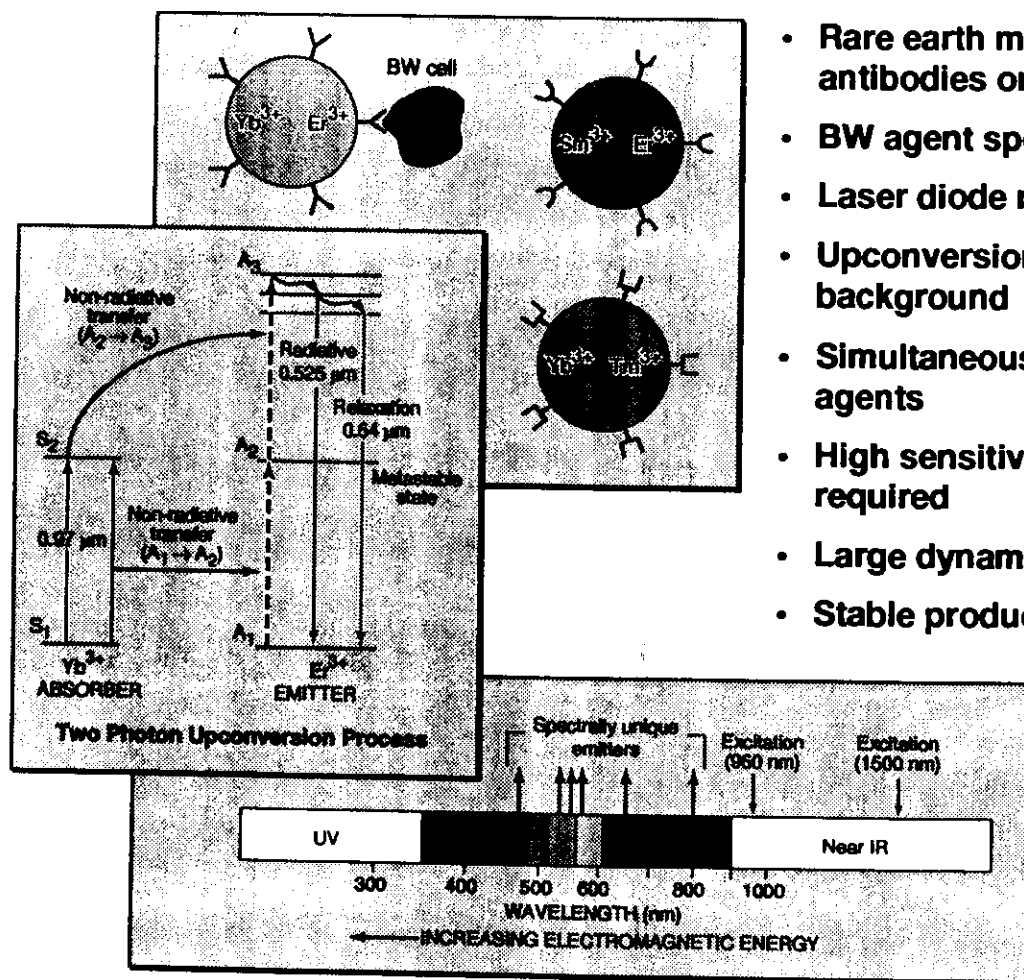
## Generic Toxic Substance Detector

- Chemical Toxins
- Biological Toxins
- WYDKCSKY\*



\* What you don't know can still kill you!

# Upconverting Phosphors for BW Agent Detection and Identification



- Rare earth microspheres attached to antibodies or DNA sequence
- BW agent specific
- Laser diode readout
- Upconversion process has very low background
- Simultaneous analysis for multiple BW agents
- High sensitivity – no amplification required
- Large dynamic range (greater than  $10^5$ )
- Stable product for storage / readout
- Applications:
  - Battlefield monitoring
  - Covert collection
  - Medical diagnostics
  - Environmental monitoring

# ***UNIQUE FEATURES OF DARPA BWD PROGRAM***

---

---

## **BIOSENSORS**

- ✦ Specific agent identification across many agents
- ✦ Dead vs. live agent identification
- ✦ Small size, lightweight, low power

## **INFORMATICS**

**BW anchor desk exploits Joint Task Force (JTF) architecture**

- ✦ Information for correct diagnosis and treatment
- ✦ Locating therapeutics - tied into logistics
- ✦ Leveraging other DARPA informatics investments



# **INFORMATION PROBLEMS**

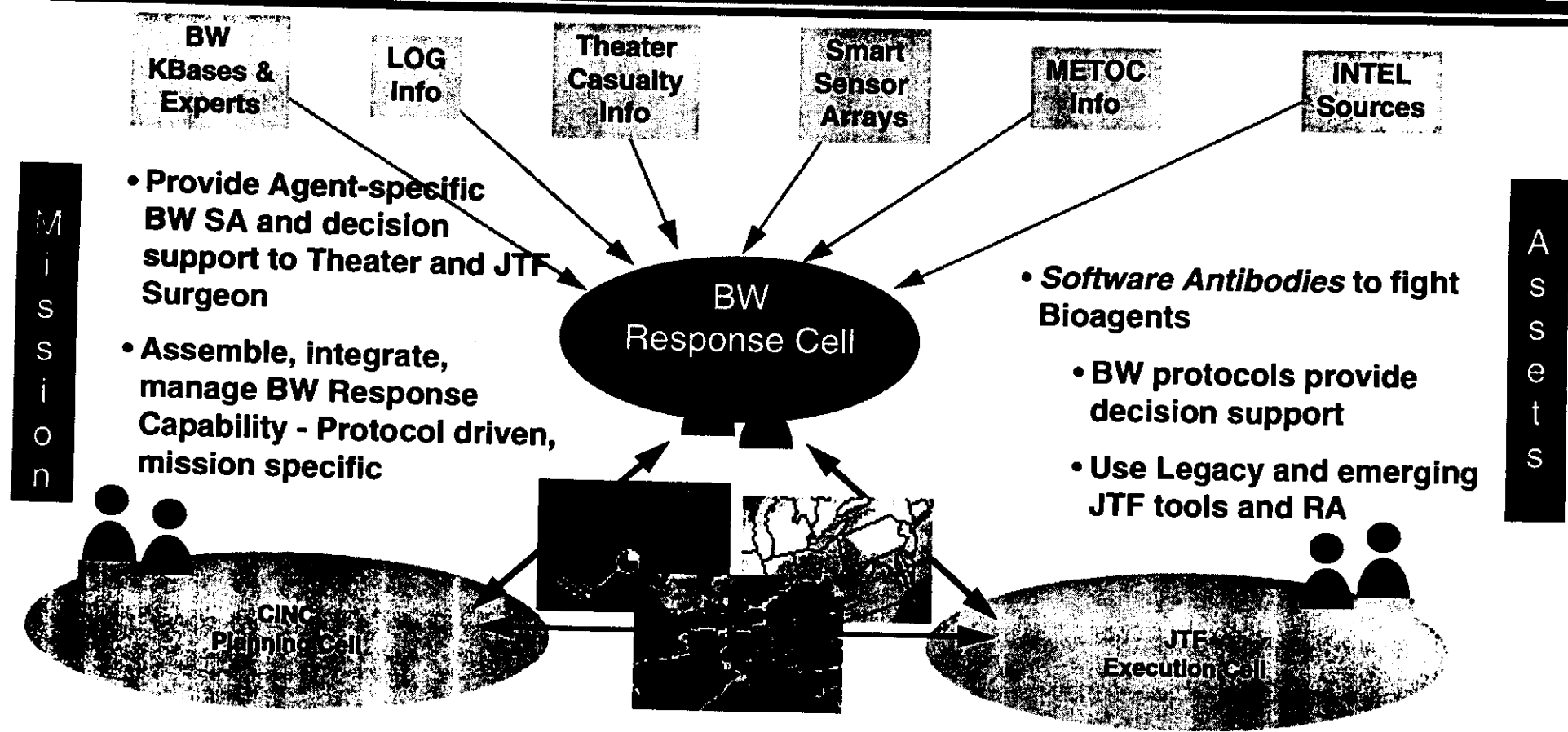
---

---

- ◆ **Managing BW attack is very complex; requiring knowledge not usually available in real-time**
- ◆ **Lack of access to the “FEW who know”**
- ◆ **Information overload when it comes, not cogent or organized to meet the need**
- ◆ **What to do is not well structured (protocols)**



# BW ANCHOR DESK CONCEPT MED-LOG PILOT



Biological Warfare Defense



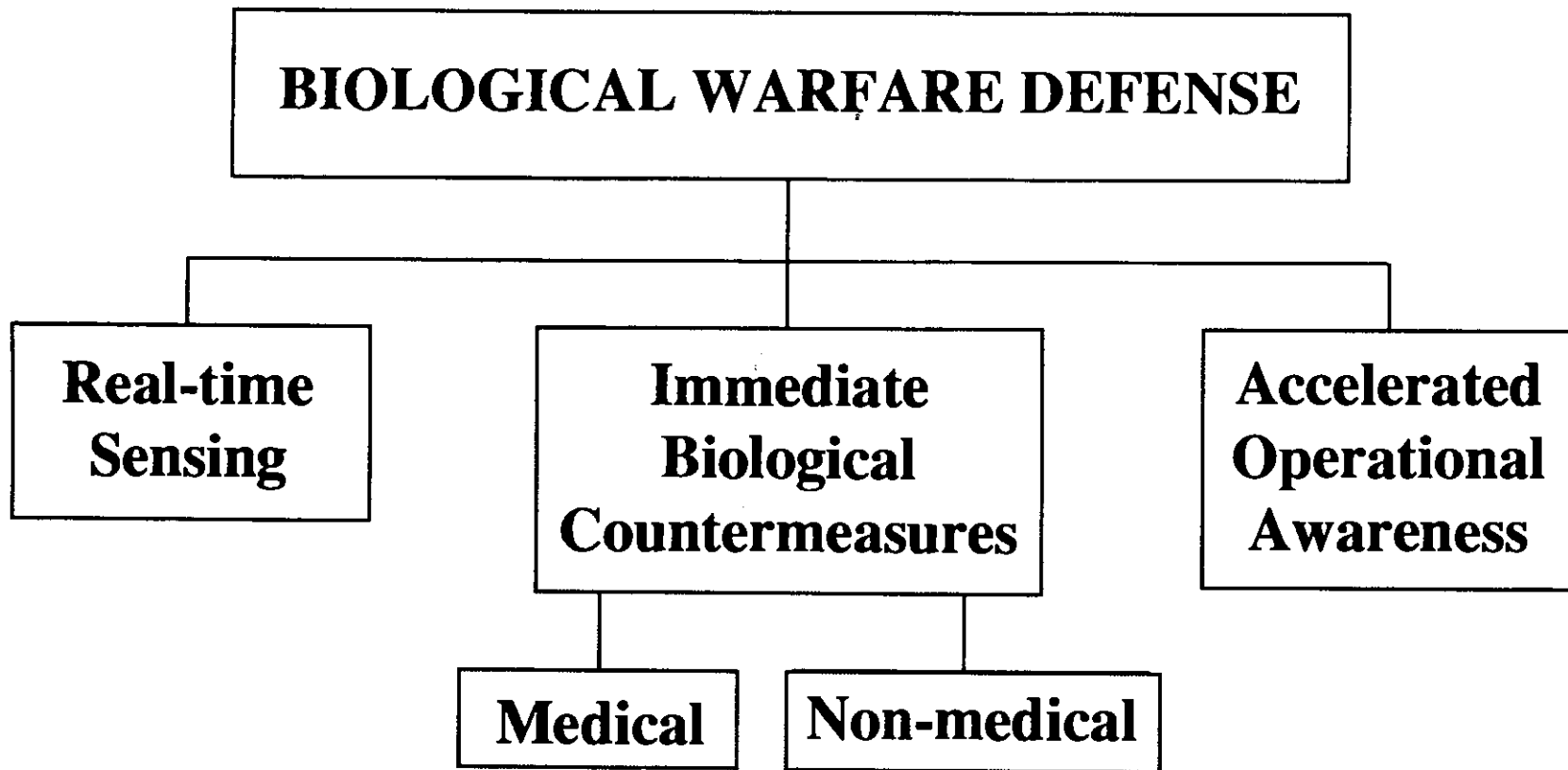
# ***Operational Impact of BWD Informatics***

---

---

- ✦ Medical protocols down to appropriate echelon of care
- ✦ Reach back to experts and useful information
- ✦ Identify BW attack from scattered illness reports
- ✦ Readiness information to military commanders of present BWD casualties and projected casualties over time
- ✦ Tie in to logistics to get needed treatment/supplies
- ✦ Effective BWD training tools for medical personnel

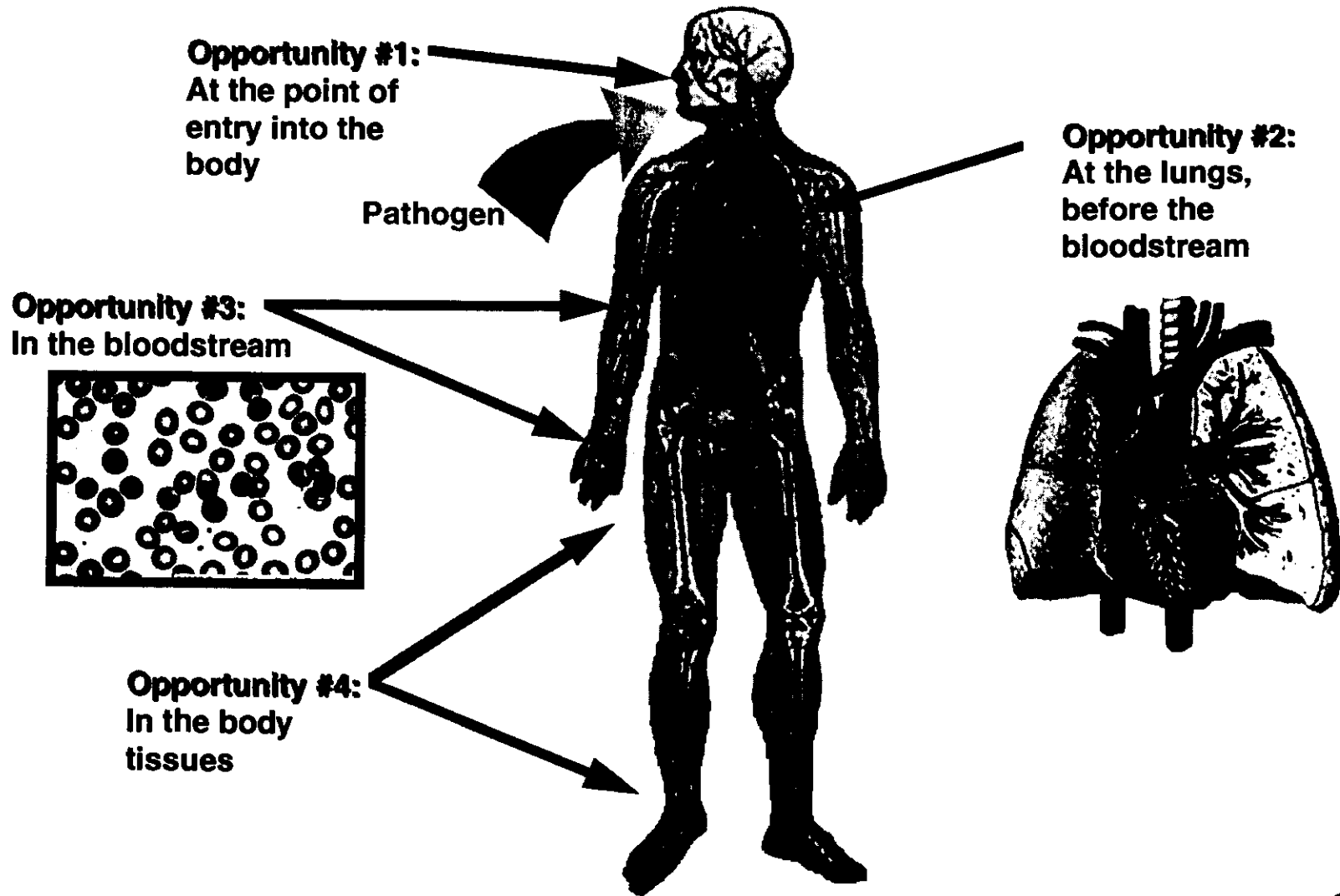




**Remove the threat of biological warfare agents (including bacterial, viral, and bioengineered organisms) as a factor in the planning and conduct of U.S. military operations**



# DEFENSE OPPORTUNITIES



# BIOLOGICAL/TOXIN WARFARE AGENTS

## Bacteria

Bacillus anthracis  
 Brucella abortus  
 Brucella melitensis  
 Brucella suis  
 Chlamydia psittaci  
 Clostridium botulinum  
 Clostridium perfringens  
 Clostridium tetani  
 Enterohemorrhagic Escherichia coli serotype O157 and other verotoxin producing serotypes  
 Francisella tularensis  
 Legionella pneumophila  
 Pseudomonas mallei  
 Pseudomonas pseudomallei  
 Salmonella typhi  
 Shigella dysenteriae  
 Vibrio cholerae  
 Yersinia pestis  
 Yersinia pseudotuberculosis

## Toxins

Abrin  
 Botulinum toxins  
 Cholera toxin  
 Clostridium perfringens toxins  
 Conotoxin  
 Microcystins (Cyanoginsins)  
 Ricin  
 Saxitoxin  
 Shigatoxin  
 Staphylococcus aureus toxins  
 Tetanus toxin

Tetrodotoxin  
 Trichothecene mycotoxin  
 Verotoxin

## Rickettsiae

Coxiella burnetii  
 Rickettsia prowasecki  
 Rickettsia rickettsia  
 Rochalimaea quintans

## Viruses

Chikungunya virus  
 Congo-Crimean hemorrhagic fever virus  
 Dengue fever virus  
 Eastern equine encephalitis virus  
 Ebola virus  
 Hantaan virus  
 Japanese encephalitis virus  
 Junin virus  
 Kyasanur Forest virus  
 Lassa fever virus  
 Louping ill virus  
 Lymphocytic choriomeningitis virus  
 Machupo virus  
 Marburg virus  
 Monkey pox virus  
 Murray Valley encephalitis virus  
 Omsk hemorrhagic fever virus  
 Oropouche virus  
 Powassan virus  
 Rift Valley fever virus  
 Rocio virus  
 St Louis encephalitis virus

Tick-borne encephalitis virus (Russian Spring-Summer encephalitis virus)  
 Variola virus  
 Venezuelan equine encephalitis virus  
 Western equine encephalitis virus  
 White pox  
 Yellow fever virus

## Genetically Modified Micro-organisms

Genetically modified micro-organisms or genetic elements that contain nucleic acid sequences associated with pathogenicity and are derived from organisms in the core list.  
 Genetically modified micro-organisms or genetic elements that contain nucleic acid sequences coding for any of the toxins in the core list.

## Plant Pathogens

**Bacteria**  
 Xanthomonas campestris pv. citri  
 Xanthomonas albilineans

**Fungi**  
 Cochliobolus miyabeanus (Helminthosporium oryzae)  
 Colletotrichum coffeanum var. virulans  
 Microcyclus ulei (syn. Dothidella ulei)  
 Puccinia graminis (syn. Puccinia graminis f. sp. tritici)  
 Puccinia striiformis (syn. Puccinia glumarum)  
 Pyricularia grisea/Pyricularia oryzae

**Genetically Modified Micro-organisms:**  
 Genetically modified micro-organisms or genetic elements that contain nucleic acid sequences associated with pathogenicity derived from the plant pathogens identified on the export control list.

## Animal Pathogens

### Viruses:

African swine fever virus  
 Avian influenza virus  
 Bluetongue virus  
 Foot and mouth disease virus  
 Goat pox virus  
 Hog cholera virus  
 Lyssa virus  
 Newcastle disease virus  
 Peste des petits ruminants virus  
 Porcine enterovirus type 9  
 Porcine herpes virus (Aujeszky's disease)  
 Rinderpest virus  
 Sheep pox virus  
 Teschen disease virus  
 Vesicular stomatitis virus

### Bacteria:

Mycoplasma mycoides

### Genetically Modified Micro-organisms:

Genetically modified micro-organisms or genetic elements that contain nucleic acid sequences associated with pathogenicity and are derived from organisms in the list.



# **PATHOGEN COUNTERMEASURES TECHNICAL DEVELOPMENT**

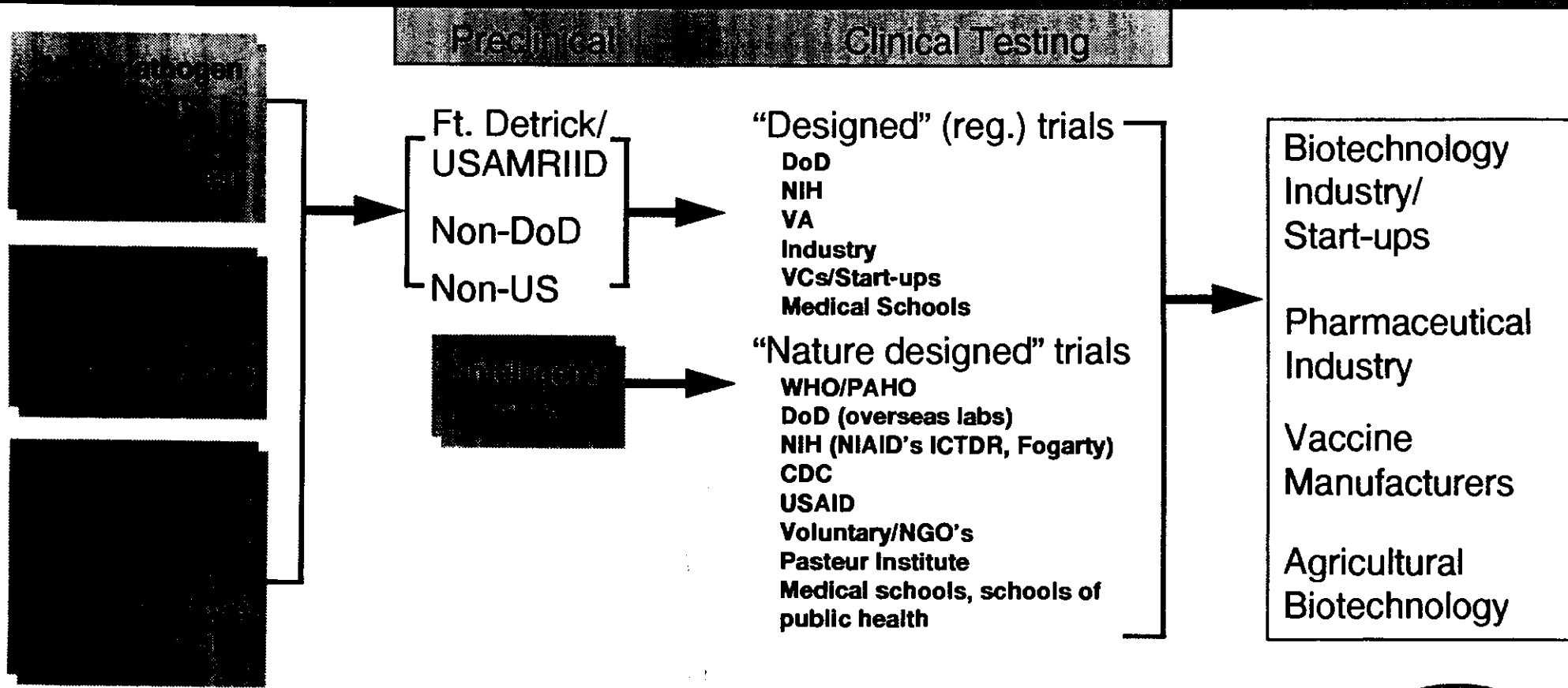
---

---

- ① Targeting common mechanisms of pathogenesis and functions or structures shared by groups of pathogens**
- ② Modulating the human biological response to pathogens**



# PROGRAM STRATEGY



# ***UNIQUE FEATURES OF DARPA BWD PROGRAM***

---

## **THERAPEUTICS**

- ◆ **Common virulence approach to get broad classes of pathogens**
  - **Broader coverage for both known and unknown threats**
  - **Makes much more difficult to circumvent through bioengineering**
- ◆ **Drugs which prevent disease after exposure**
  - **Purge pathogens from the body**
  - **Modified cells to synthesize and release therapeutics automatically into the body**
- ◆ **Working with pharmaceutical and biotechnology industry**



# DARPA Advanced Biological and Medical Technologies Program Managers

---

- ◆ Mildred A. Donlon, Ph.D.
  - » Program Manager for BWD Detector thrust
  - » 703-696-2289, mildonlon@darpa.mil
- ◆ CDR Shaun B. Jones, M.D., USN
  - » Program Manager for Unconventional Pathogen Countermeasures
  - » 703-696-4427, sjones@darpa.mil
- ◆ Stephen S. Morse, Ph.D.
  - » Program Manager for Unconventional Pathogen Countermeasures
  - » 703-696-7489, smorse@darpa.mil
- ◆ COL Richard Satava, M.D., USA
  - » Program Manager for Combat Casualty Care Program
  - » 703-696-2265, rsatava@darpa.mil
- ◆ Col John Silva, M.D., USAF
  - » Program Manager for BWD Informatics thrust
  - » 703-696-2221, jsilva@darpa.mil



# Future Thrusts

---

---

- **BW Medical Diagnostics**
  - » Field portable system for rapid differential diagnosis
- **Mathematics Applied to BW Countermeasures**
  - » Methods to mine pathogen genomic information
  - » Mathematical methods and models applied to rational drug design

