

2010 Military Health System Conference

Supporting Our Installations Through CBRNE Research

Implications for Military Healthcare Providers

Sharing Knowledge: Achieving Breakthrough Performance

CAPT O. D. Hottenstein, PhD, USPHS



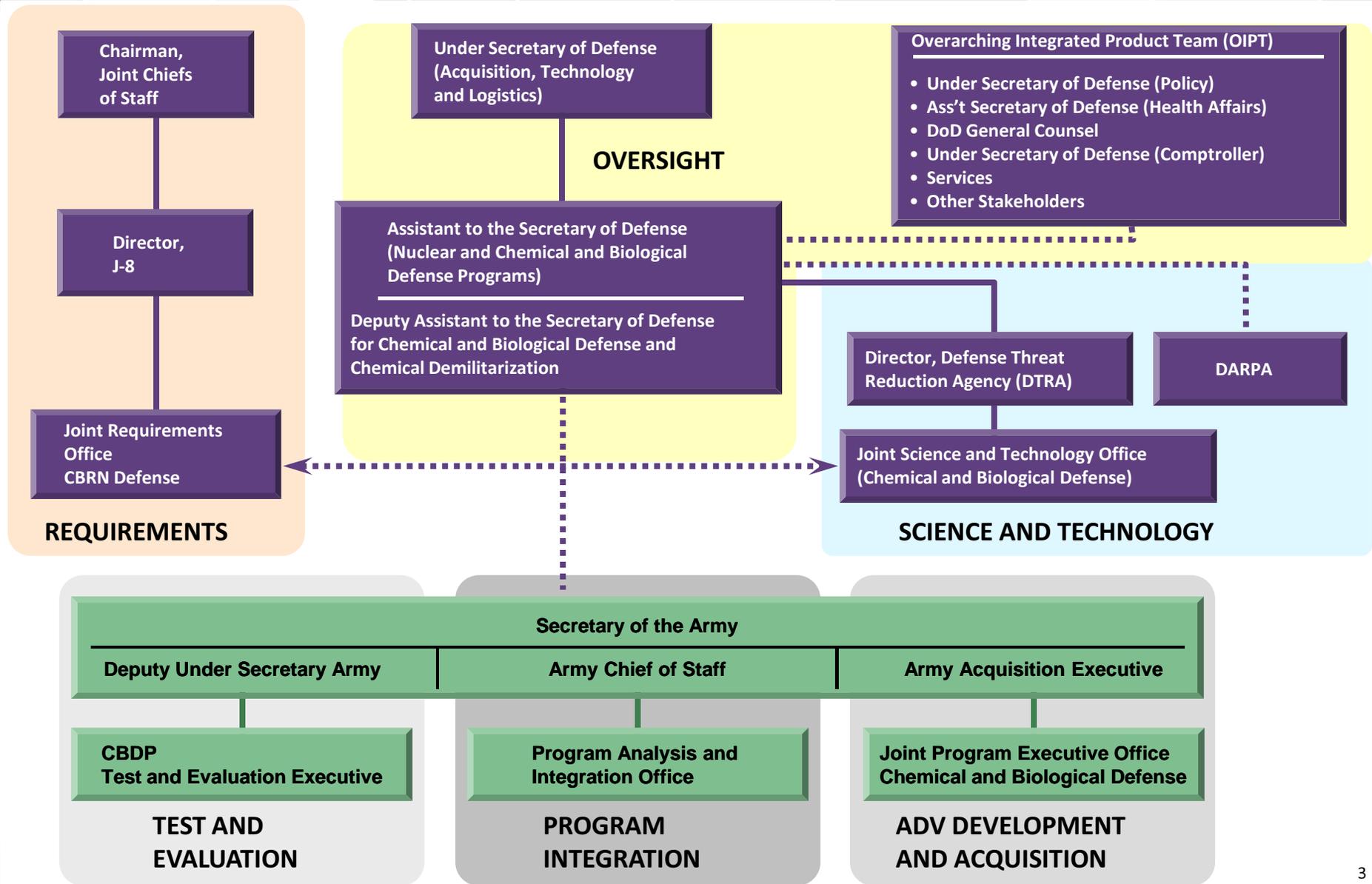
Assistant Secretary of Defense/Health
Affairs/Force Health Protection &
Readiness/Medical Countermeasures
(CBRN Office)

Overview and Objectives



- Overview: DoD CBRN Research supports warfighting capability with the best technology at the right time and right place. MTFs and Military Healthcare Providers must be prepared to support installation and beneficiary CBRN healthcare needs.
- Objectives:
 - #1 - Learners will understand CBRN successes and how they support warfighting capability and prepare MTFs to protect beneficiaries during a CBRN Event. Medical CBRN countermeasures will be incorporated into MTF initial response and disease containment plans to provide effective consequence management.
 - #2 – Learners will understand MTF roles in emergency health and mass prophylaxis planning and use this knowledge to improve their MTF’s initial response capability for the initial 48 hours after a CBRN event.
- Support for the MHS “Quadruple Aim” – DoD CBRN R&D supports three of four components of the Quadruple Aim: Readiness, Population Health, and Cost of Care (by preventing illness that would be time consuming and costly to treat).

DoD Chem-Bio Defense Program (CBDP) and PEO-CBD (Program Executive Office-CBD)



Joint Staff/Joint Requirements Office



As of 13 Jan 10

Prophylaxes	
Joint Medical Biological Warfare Agent Prophylaxes ICD	Approved – 14 Sep 04
Joint Medical Chemical, Radiological, and Nuclear Prophylaxes ICD	Approved – 31 Jul 09
Joint Medical Biological Warfare Agent Prophylaxes Vaccine Increment CDD	Approved – 22 May 06
Joint Medical Biological Warfare Agent Prophylaxes Vaccinia Immune Globulin - Intravenous (VIG-IV) Increment CPD	Approved – 5 Jul 05
Joint Medical Biological Warfare Agent Prophylactic Pharmaceutical: Filovirus Vaccine Increment CDD	Pending – Pre-KMDS Draft
Joint Medical Chemical Warfare Agent Prophylactic and Pretreatment Pharmaceuticals: Advanced Nerve Agent Increment CDD	Pending – Pre-KMDS Draft
Joint Medical Biological Warfare Agent Prophylactic Pharmaceutical: Botulinum Toxin Vaccine Inc CPD	TBD
Joint Medical Biological Warfare Agent Prophylactic Pharmaceutical: Plague Vaccine Inc CPD	TBD

KEY:

ORD – Operational Requirements Document
CDD – Capability Development Document

ICD – Initial Capabilities Document
CPD – Capability Production Document

Joint Staff/Joint Requirements Office



As of 13 Jan 10

Therapeutics	
Chemical, Biological, Radiological and Nuclear (CBRN) Therapeutic Pharmaceuticals ICD	Approved – 18 Jul 05
Joint Medical CBRN Therapeutic Pharmaceuticals Advanced Nerve Agent Countermeasure Increment CDD	Approved – 24 Aug 07
Joint Medical Radiation Therapeutic Pharmaceuticals: Gastrointestinal and Hematopoietic Increment CDD	Pending – Pre-KMDS Draft
Joint Medical Chemical Therapeutic Pharmaceuticals: Improved Nerve Agent Treatment System (INATS) Increment CPD	TBD
Joint Medical Chemical Therapeutic Pharmaceuticals: Advanced Anticonvulsant System (AAS) Increment CPD	TBD
Joint Medical Chemical Therapeutic Pharmaceuticals: Inhalational Atropine Increment CDD	Draft
Joint Medical Biological Therapeutic Pharmaceuticals: Hemorrhagic Fever Virus (HFV) Increment CDD	Draft
Joint Medical Biological Therapeutic Pharmaceuticals: Intracellular Bacterial Pathogen (IBP) Increment CDD	TBD
Field Analytics	
Joint Biological Agent Identification and Diagnostic System (JBAIDS) ORD	Approved – 6 May 03
CBRN Field Analytics ICD	Approved – 12 Jan 10
Next Generation Diagnostic Systems (NGDS) CDD	TBD
Common Analytical Laboratory System (CALS) CDD	Draft

KEY:

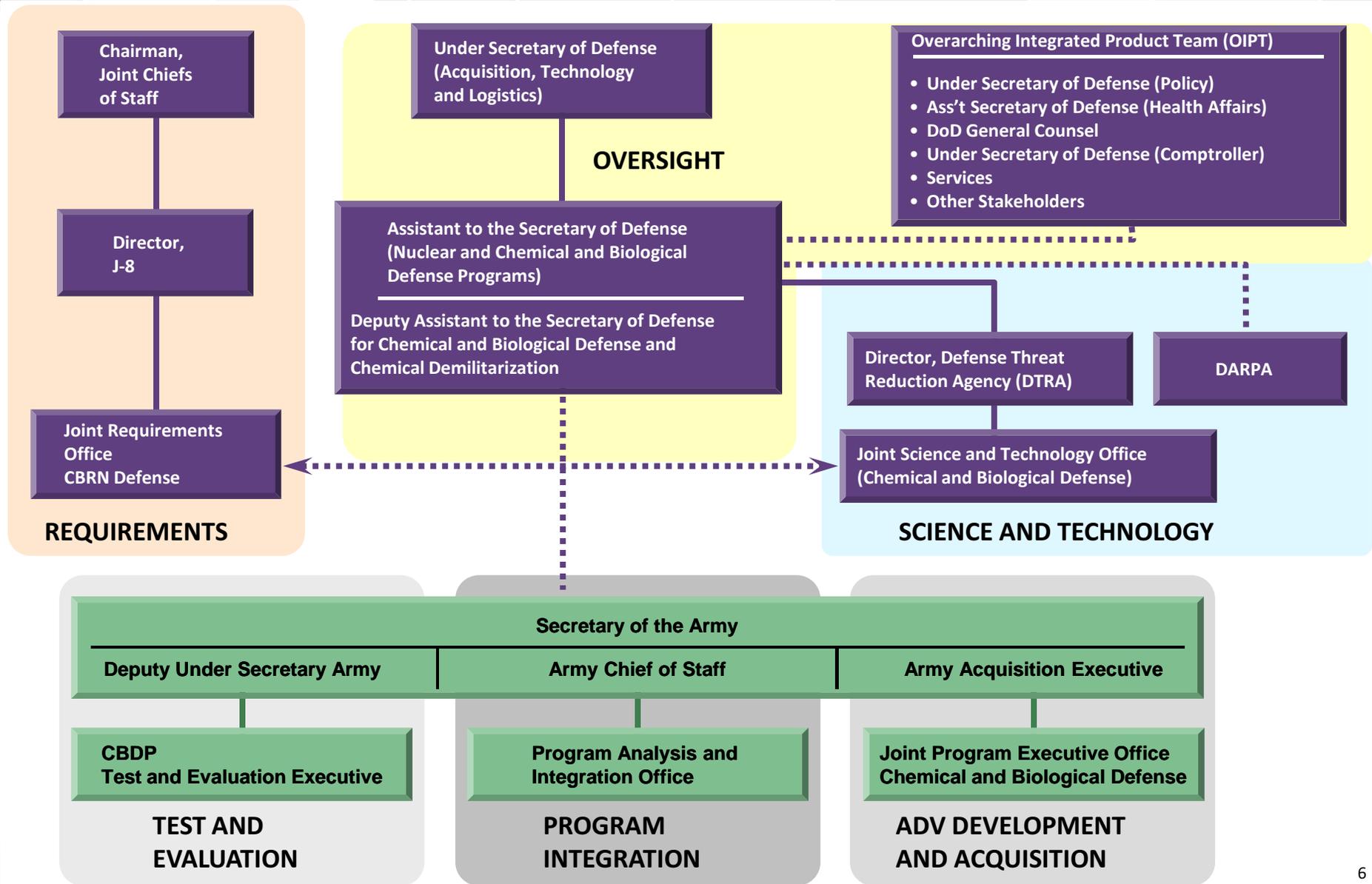
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DoD Chem-Bio Defense Program (CBDP) and PEO-CBD (Program Executive Office-CBD)



CBRN Defense Operational Elements and Capabilities



SENSE



Joint Bio Point Detection System (JBPDs)



Joint Bio Standoff Detection System (JBSDS)



NBCRV

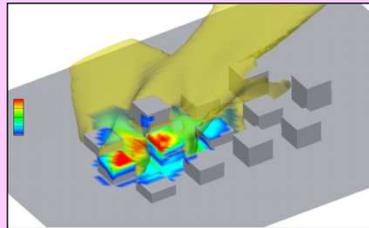


JCAD

SHAPE



Joint Warning and Reporting Network



Joint Effects Model (JEM)



Joint Operations Effects Federation (JOEF)

SHIELD



Joint Vaccine Acquisition Program



JSLIST



JSGPM



CB Protected Shelter

SUSTAIN



Joint Bio Agent Identification & Diagnostic System (JBAIDS)

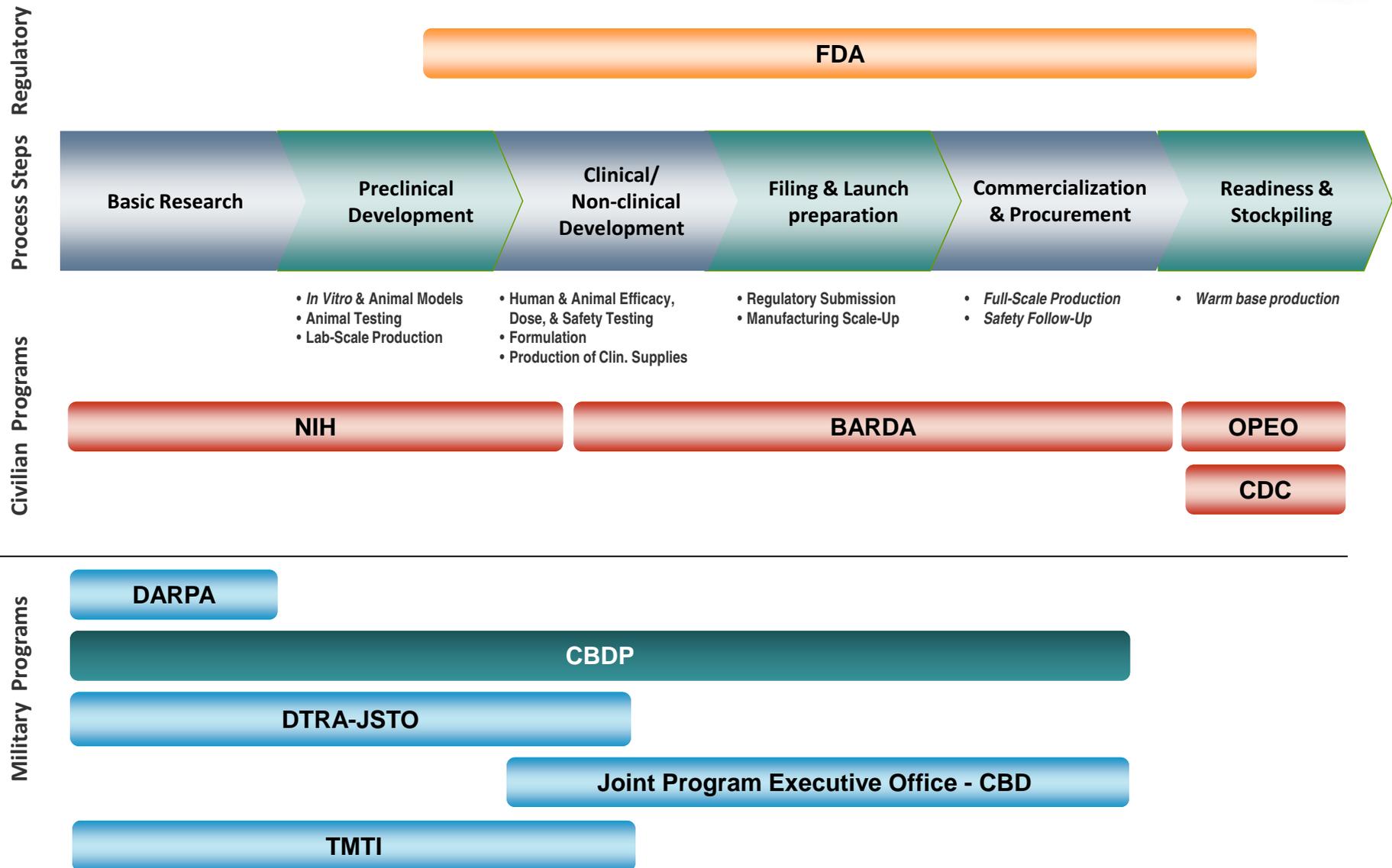


Antidote Treatment, Nerve Agent Autoinjector (ATNAA)



Joint Service Transportable Decon System

No Single Agency has Visibility into the Entire Development Portfolio



“Full Spectrum” CBRN Capabilities

7 FDA Approvals; 14 IND Submissions In The Next 5 Years

DUAL PURPOSE

- Integrated Portfolio to collaboratively develop MCM
- Radiation CM Collaboration:
 - HHS – Hemat Syndrome
 - DoD – GI Syndrome
- 26 signed Agreements to collaborate on product development/procurement
- Critical Reagents Program (> 200 products)
- VaxDesign & Alt Manufact Process

PROPHYLAXIS: “BODY ARMOUR” – Preserves the Fighting Force



TRANSCEND OPERATIONAL LEVELS

- Warfighter / First Responder
- Carried Items:
 - AAS / ATNAA
 - CANA/ INATS
 - SNAPP
 - Bioscavenger
 - Vaccines
 - Biosurveillance at Tactical, Operational

Interagency / International Partnerships

Return on Investment



DIAGNOSTIC: “BIOSURVEILLANCE” – Alerts the Fighting Force

NATIONAL STRATEGIC RESOURCE ALTERNATIVES

- No Unique Training Systems Required for JBAIDS – Influenza Panels H1N1 & H5N1
- Extended Shelf Life – Time Temperature Indicators (TTIs) and Item Unique Identifiers (IUIDs)



THERAPEUTIC: “BODY TREATMENT” – Restores the Fighting Force

BROADENED THREAT

- JBAIDS
- All Developmental Nerve Agent Products Protect Against Traditional & NTA
- Broad Spectrum Vaccines: Botulinum, Filovirus – Common Platform
- Platform Technologies for Vaccines



Medical Chemical Biological Defense

Capabilities and Products



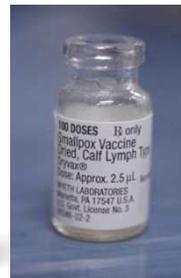
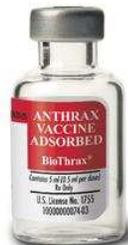
- Provide medical solutions for military requirements to protect and sustain the force in a chemical or biological warfare environment



Integrated Diagnostic Systems



- Preserve total force effectiveness in a chemical or biological warfare environment
 - Prevent casualties
 - Provide **effective treatment** of casualties for rapid return to duty
 - Provide rapid, far-forward **diagnosis** of chemical or biological weapons exposure



Transformational Medical Technologies Initiative (TMTI)



Mission: Protect the Warfighter from emerging and genetically engineered biological threats by providing a novel response capability from identification of pathogens through the development of Medical Countermeasures (MCM)

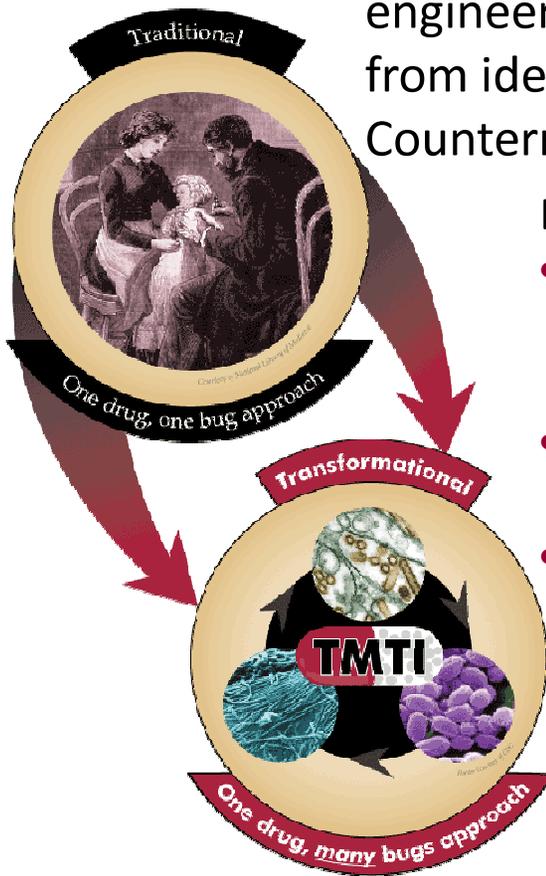
Designed to spur innovative research to develop:

- **Technologies** to characterize unknown pathogens and rapidly develop medical countermeasures to newly identified threats

- **Broad spectrum MCM** that are FDA approved

• **TMTI is:**

- Pursuing countermeasures targeting common disease pathways or enhance the host's immune system
- Integrating best efforts within government, academia, DoD, biotech industry, and small and large pharmaceutical corporations
- Providing seamless “end-to-end” product development
- Eliminating capability gaps by adding promising candidate technologies to the pipeline



Medical Chemical Biological Defense

Training and Education



Publications

- Medical Management of Biological Casualties Handbook
- Medical Management of Chemical Casualties Handbook
- Field Management of Chemical Casualties Handbook
- Textbook of Military Medicine: Medical Aspects of Chemical & Biological Warfare

Training Courses

- Medical Management of Chemical and Biological Casualties
- Field Management of Chemical and Biological Casualties
- Hospital Management of Chemical, Biological, Radiological, Nuclear & Explosive Incidents Course (HM-CBRNE)
- Resident and Satellite Courses
- DMRTI – Basic online courses and others



Equip medical personnel to manage chemical and biological agent casualties

Armed Forces Radiobiology Research Institute

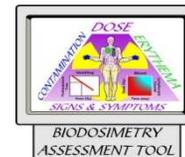
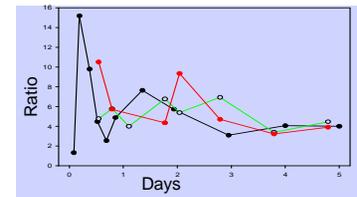


- **Mission:** conduct research in the field of radiobiology and related matters essential to the operational and medical support of the Department of Defense and the Military Services.



- **Aids to MTF Commanders:**

- Countermeasure development
- Biodosimetry technique development
- Biodosimetry Assessment Tool
- Medical Effects of Ionizing Radiation Course



ASD/HA/FHP&R/MCM

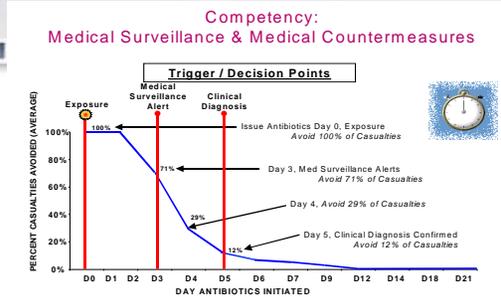


- DoD Health Affairs responsible for promulgating DoD medical policy for use of CBRN medical countermeasures
- Work in close collaboration with Joint Requirements Office/Joint Staff, CBDDP/AT&L, PEO-CBD, and DoD Laboratories
- DoD promulgates medical policy – the military services carry out that medical policy – Army, Navy, and Air Force

Army CBRNE Medical Defense

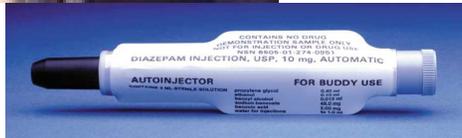
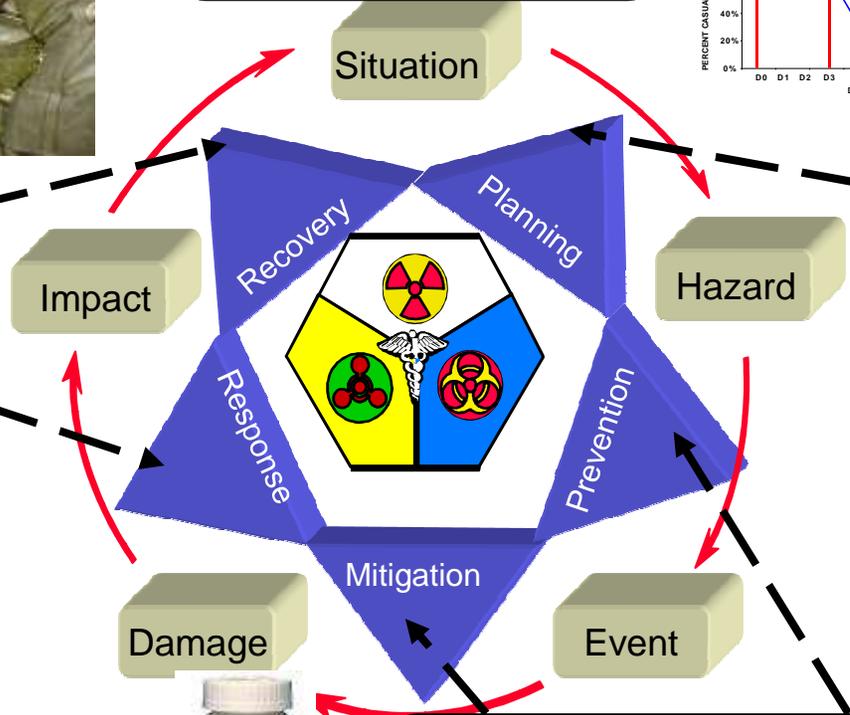


SENSE:
Syndromic surveillance;
CBRN exposure quantification



SUSTAIN:
Patient decontamination;
Patient movement;
Treatment;
Psychological support
and care

SHAPE:
Disease modeling;
Hazard prediction;
Casualty estimation;
Medical asset visibility



SHIELD:
Medical CBRN Defense
Material (MCDM);
Vaccines and prophylaxis;
Individual and collective
protection

NAVY MEDICINE CBRN (INSTALLATION PROTECTION PROGRAM)



- IPP – Installations level tailored, integrated, and effective Chemical, Biological, Radiological, Nuclear (CBRN) protection capability.
- Command Naval Installations Command (CNIC) –
 - Designated executive agent
 - Standardized Navy compliance and allocation
 - Sustainment
- Navy Medicine
 - Office of Primary Responsibility
 - CNIC input endorsement
 - CBRN pharmaceutical countermeasures
 - First receivers

Air Force MC-CBRN Capabilities



HSMR



■ Home Station Medical Response Program

- Patient Decontamination
- In-patient Medical Response
- Pharmaceuticals
- Lab Response
- Threat Agent Detection
- Field treatment Team
- Triage
- Clinical
- Medical Unit Security
- Public Health



EMEDS



■ Rapid response force consists of EMEDS plus:

- Biological Augmentation Team
- Bioenvironmental NBC Team
- AF Radiological Assessment Team
- Infectious Disease Team
- Medical Patient Decontamination
- Mental Health Team
- Preventive Aerospace Medicine Teams
- Theater Epidemiological Team



CP -EMEDS



Back-up Slides

<http://www.acq.osd.mil/cp/>

CBDP Vision and Mission

(Proposed)



VISION

Ensure DOD capabilities in support of Homeland Defense and Overseas Contingencies are unconstrained by existing and emerging chemical, biological, radiological, and nuclear (CBRN) threats

MISSION

Provide global chemical, biological, radiological, and nuclear defense capabilities in support of the National Military Strategies

No Single Agency has Visibility into the Entire Development Portfolio



Process Steps/Regulatory

FDA



- *In Vitro* & Animal Models
- Animal Testing
- Lab-Scale Production

- Human & Animal Efficacy, Dose, & Safety Testing
- Formulation
- Production of Clin. Supplies

- Regulatory Submission
- Manufacturing Scale-Up

- Full-Scale Production
- Safety Follow-Up

- Warm base production

Civilian Programs

NIH

BARDA

OPEO

CDC

Military Programs

DARPA

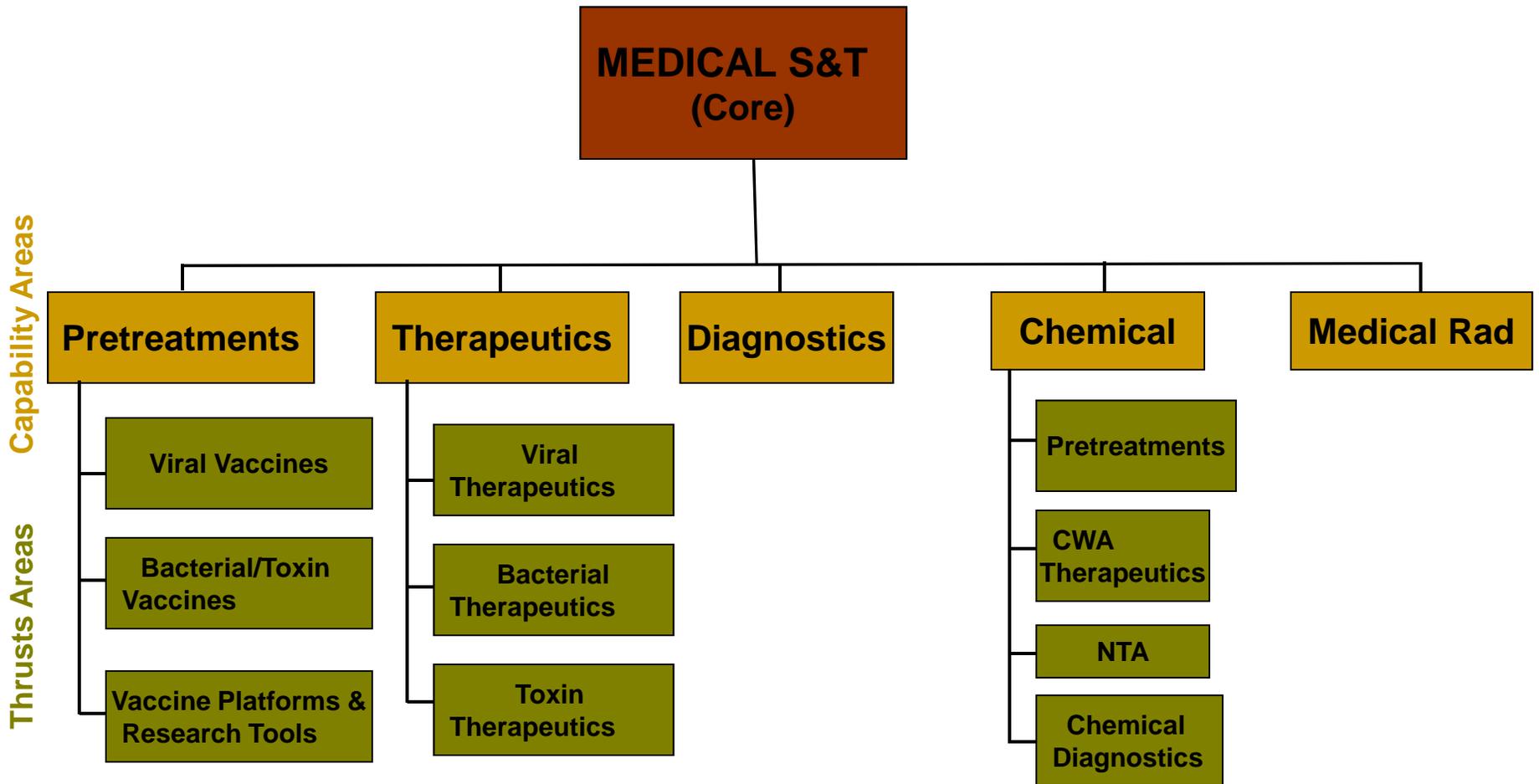
CBDP

DTRA-JSTO

Joint Program Executive Office - CBD

TMTI

JSTO-CBD Medical Science & Technology Division



Biological Pretreatments/Therapeutics

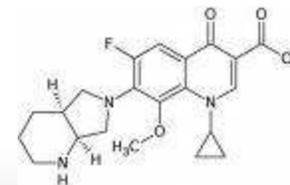
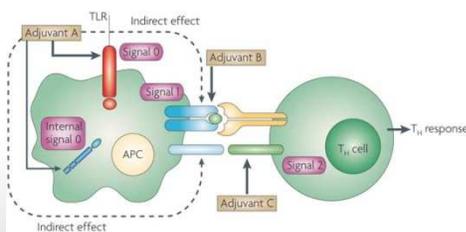


PreTx Mission: Generate vaccines that protect the war fighter from aerosolized viral, bacterial, and toxin threat agents

Thera Mission: Develop FDA-licensable drugs to treat exposure to biological warfare agents. Exploit new technologies to develop novel small molecule therapeutics for bacterial, viral and toxin threat agents

- Evaluate novel single- and multi-agent/-valent vaccine platforms against BW agents
- Test vaccine candidates for immunogenicity and efficacy in animal models
- Exploit cutting-edge technologies to characterize the human immune response
- Identify correlates of immune protection
- Minimize immune interference between vaccines
- Consider needle-free delivery methods
- Evaluate novel adjuvants
- Incorporate thermo-stabilization technologies to allow use of our vaccines in diverse theaters
- Develop animal models to support FDA licensure

- Conduct high-throughput screens of small molecule libraries to identify novel drug candidates
- Determine structure activity relationships of candidate small molecule therapeutics and optimize their activity through medicinal chemistry
- Develop enzymatic and cell based assays amenable to high throughput screening
- Test and evaluate candidate compounds in relevant animal models of threat agent exposure
- Determine efficacy of FDA approved drugs against Biodefense agents



Chemical Pretreatments/Therapeutics



Pre Tx Mission: *Develop medical pretreatments and prophylactics to protect the warfighter against CWA, both traditional and non traditional*

Thera Mission: *Develop FDA-licensable drugs to treat exposure to chemical warfare agents*

- Identify and characterize enzymes with hydrolytic activity toward organophosphorus agents and/or pesticides for pretreatments
- Develop catalytic bioscavengers with broad binding specificity and high catalytic efficiency for the destruction of nerve agents
- Use mutagenesis and directed evolution to improve binding and catalytic efficiency
- Develop therapeutics for exposure to Vesicant agents, to focus on skin, eye, lung, and systemic
 - Focus on broad-based therapeutics against multiple agents and routes of exposures
 - Explore long term effects, wound healing, and cell-based therapeutic technologies
- Develop broad spectrum Reactivators with CNS availability and an enhanced therapeutic window
 - Provide an FDA approved pharmaceutical that will reverse the inhibition of AChE
- Identify compounds that will ameliorate damage from nerve agent intoxication
 - Develop anticholinergis with reduced side effects
 - Develop novel neuroprotectants and anti-seizuregenics
 - Focus on FDA approved neuroprotective drugs



Biological/Chemical Diagnostics



Biological Diagnostics Goal:
Increase sensitivity/specificity while decreasing time to results

Common Analytic Laboratory

Pre-analytic S&T

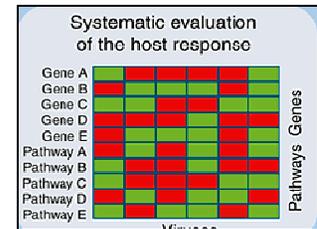
- Sample preparation
- Diagnostic Window
- Characterization

Analytic S&T

- Specific agent targets
- Broad-range pathogen
- Presymptomatic Diag

Post-analytic S&T

- Verify performance
- Improve predictive value
- Referee methods



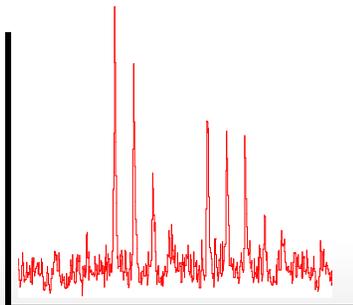
Chemical Diagnostics Mission: Discover, identify, and monitor biomarkers of exposure by developing field products to rapidly detect exposure and complimentary hand-held analytic devices to accurately identify chemical agents

Mass Spec

Spectro WB ChE assay

Solid Phase Micro extraction

Assay Techniques



2010 MHS Conference





Medical Radiological

Mission: *Develop safe and efficacious, broad-spectrum medical radioprotectants (prophylactic) and post-irradiation therapeutic candidates against Acute Radiation Syndrome (ARS) and the Delayed Effects of the Acute Radiation Exposure (DEARE)*

Strategy:

- Accelerate transition of mature Med Rad candidates to advanced product development
- Leverage efforts with promising candidates that are currently in preclinical development for radiation-oncology

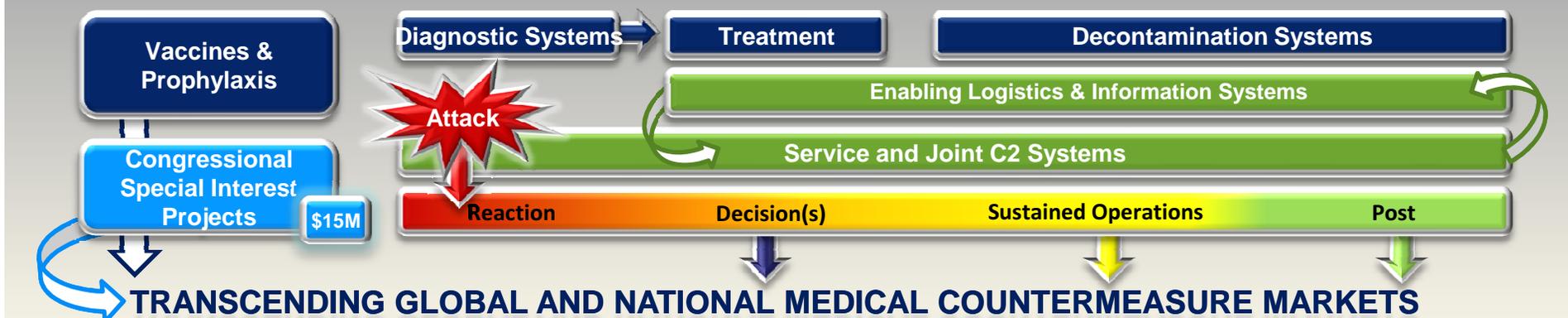
Goals:

- Develop safe and efficacious GI and pulmonary tract radioprotectants
 - prophylactics and post-IR therapeutics for ARS/DEARE
- Develop diagnostic biodosimetry biomarkers



National Defense in Depth

Chemical Biological Medical Systems (CBMS)



Soman Nerve Agent Pretreatment Pyridostigmine (SNAPP)	Critical Reagents Program (CRP) +, NIAID, DHS, NMRC, AFIP, Dugway, ECBC, US Capitol Police, International Monetary Fund,	Convulsant Antidote for Nerve Agents (CANA)
Anthrax Vaccine+ CDC, HHS, DHS	JBAIDS+ – Anthrax, Plague, Tularemia HHS, CDC	Antidote Treatment Nerve Agent Autoinjector (ATNAA)
Smallpox Vaccine+ / Vaccinia Immune Globulin (VIG) IV+ CDC, HHS, DHS	JBAIDS+ – Avian Flu, Swine Flu, Q-Fever, Typhus, Smallpox HHS, CDC	Advanced Anticonvulsant System (AAS)+ NINDS, NIH
Botulinum A/B Vaccine+ HHS	<i>CRP serves as the principal resource of high quality, validated, and nationally standardized biological detection assays & reagents that meet the requirements of the Warfighter.</i>	Improved Nerve Agent Treatment System (INATS)+ HHS
Plague Vaccine+ HHS		Medical Radiation+ HHS
Filovirus Vaccine+ HHS		Technology Readiness Levels (TRLs) + / Manufacturing Readiness Levels (MRLs) + -
Bioscavenger+ HHS		

Supporting Technologies / Tools:

- Item Unique Identifiers (IUIDs)
- Time Temperature Indicators (TTIs)
- Multi-Dose Formulation
- Increased Product Stability
- Alternative Drug Delivery
- Alternative Manufacturing Process (A)
- Artificial Immune System (VaxDesign)

LEGEND:

Products in Development

Fielded Products

* Non-traditional Agents

+ Interagency Collaboration

FMS Foreign Military Sales

Australia	Japan	New Zealand
Canada	Kenya	Singapore
Finland	Kuwait	Switzerland
Germany	Lithuania	United Kingdom

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 approach

Transformational Medical Technologies Initiative (TMTI)



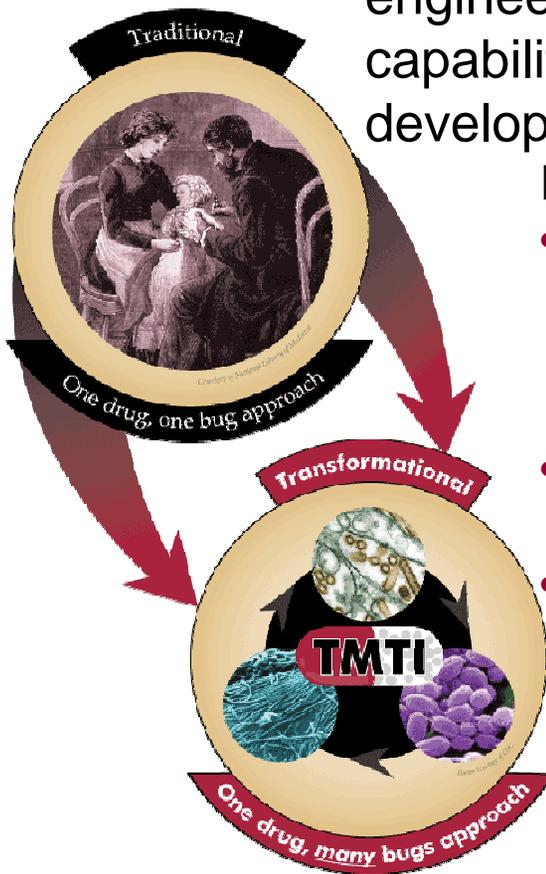
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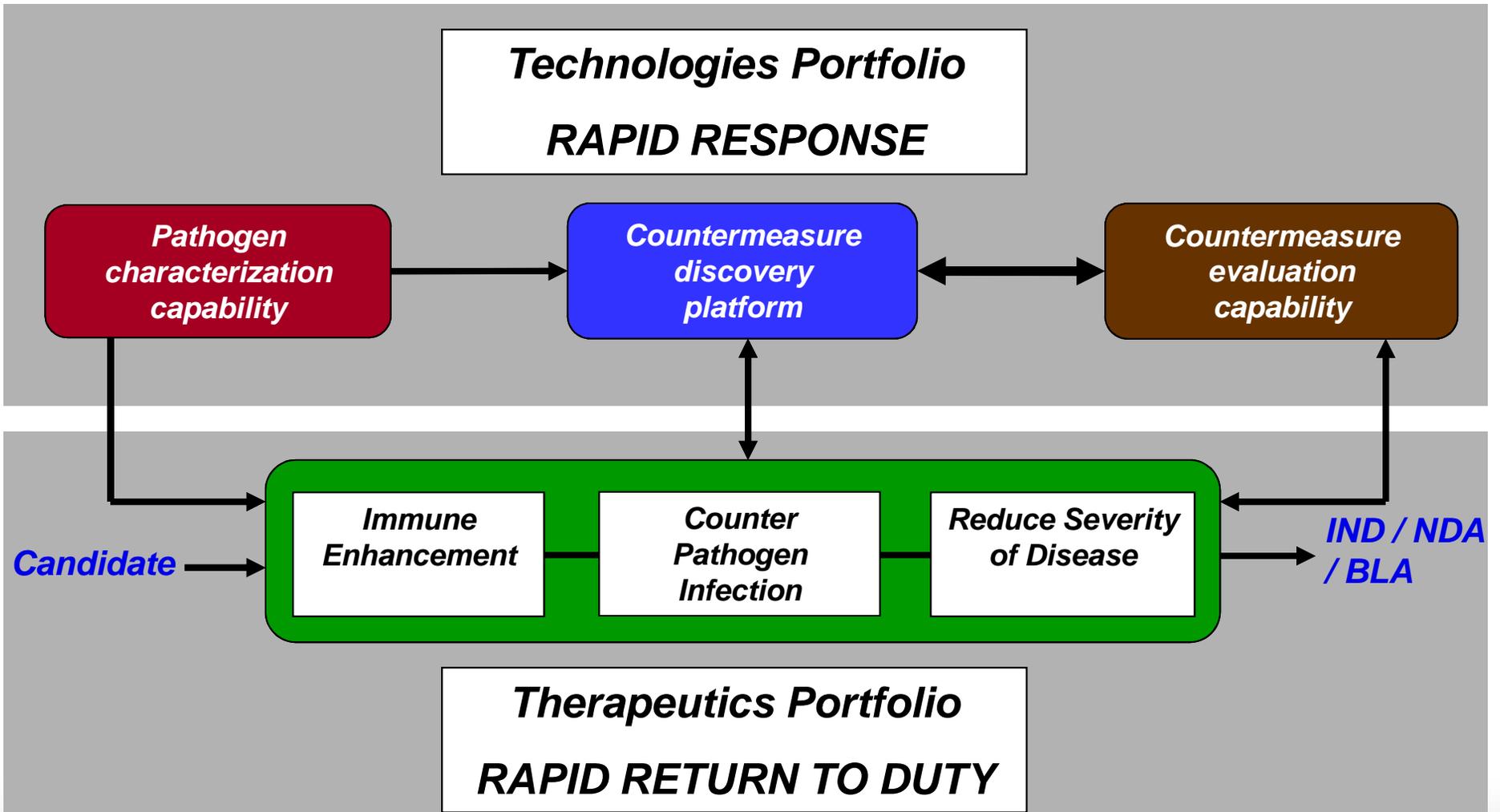
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- Integrating best efforts within government, academia, DoD, biotech industry, and small and large pharmaceutical corporations
- Providing seamless “end-to-end” product development
- Eliminating capability gaps by adding promising candidate technologies to the pipeline



TMTI Portfolio Integration



TMTI Capability Test



As proof of process, one of TMTI's platform capabilities is being tested against the current outbreak of Swine Origin Influenza A H1N1

- This exercise has tested capability of one of TMTI's platforms against a real-world emerging threat (SOIV)
- Intent: Demonstrate capability to rapidly respond to an emerging infectious disease
- Laboratory-grade medical countermeasures (MCMs) were generated within 15 days for further testing
- Preliminary test results in animals indicate candidate therapeutic is efficacious
- Follow on laboratory studies are under consideration at this time by the TMTI Program Office
- At present there are no plans to take this through full FDA licensure



TMTI accomplishments have advanced the Nation's ability to successfully counter an emerging biothreat

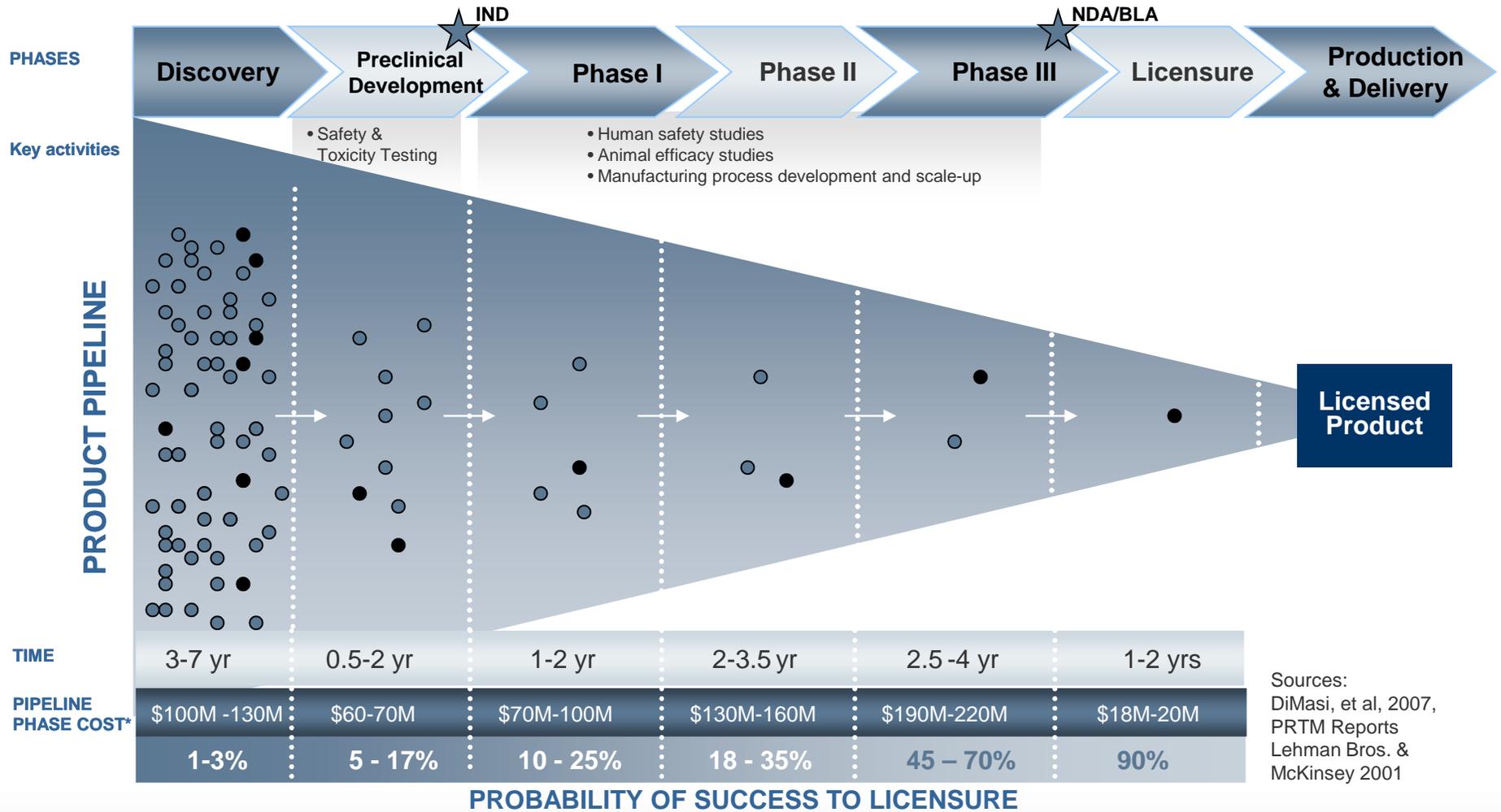
Integrated National Biodefense Medical Countermeasures (MCM) Portfolio:



- End-to-end integration of the national portfolio for biodefense MCM products is necessary to leverage investments and maximize preparedness
- HHS and DoD both develop and procure medical countermeasures for CBRN threats
- An integrated, end-to-end national biodefense portfolio for medical countermeasure products is needed to leverage investments and achieve success
- Supports the MCM planning and alignment called for in HSPD-18 and the vertical and horizontal coordination echoed in HSPD-21
- *Major Objectives:*
 - *Collect and report on overall state of Integrated National Biodefense MCM Portfolio*
 - *Evaluate portfolio probability of success and articulate required investment*
 - *Identify portfolio gaps and overlaps*
 - *Develop recommendations for portfolio (“Implementation Planning”)*
 - *Implement Joint Portfolio Oversight*
 - *Enhance intra-Departmental and inter-Departmental collaboration*
 - *Build portfolio plan into budget planning*

The Portfolio Evaluation Process has been designed to accomplish these objectives

National Biodefense R&D Portfolio Must Be Informed By Industry Benchmarks for MCM Development



Sources:
DiMasi, et al, 2007,
PRTM Reports
Lehman Bros. &
McKinsey 2001

* Out of pocket costs from Discovery through Licensure to develop a single successful product (includes attrition)