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CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2 Exhibit)	DATE February 2003
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BUDGET ACTIVITY RDT&E DEFENSE-WIDE/ BA3 - Advanced Technology Development (ATD)	PE NUMBER AND TITLE 0603384BP CHEMICAL/BIOLOGICAL DEFENSE (ATD)
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COST (In Thousands)	FY 2002 Actual	FY 2003 Estimate	FY 2004 Estimate	FY 2005 Estimate	FY 2006 Estimate	FY 2007 Estimate	FY 2008 Estimate	FY 2009 Estimate	Cost to Complete	Total Cost
Total Program Element (PE) Cost	80198	107763	103725	98843	85019	89626	89870	86800	Continuing	Continuing
CB3 CHEMICAL BIOLOGICAL DEFENSE (ATD)	18531	47349	33414	33027	25908	30903	31328	31914	Continuing	Continuing
CM3 WMD - CIVIL SUPPORT TEAM (ATD)	4650	2354	2459	2449	2435	2430	0	0	0	16777
CP3 COUNTERPROLIFERATION SUPPORT (ATD)	11791	11075	4714	5257	4575	4122	3196	3255	Continuing	Continuing
TB3 MEDICAL BIOLOGICAL DEFENSE (ATD)	34554	35515	49939	44621	39530	39527	42528	38573	Continuing	Continuing
TC3 MEDICAL CHEMICAL DEFENSE (ATD)	10672	11470	13199	13489	12571	12644	12818	13058	Continuing	Continuing

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BUDGET ACTIVITY
**RDT&E DEFENSE-WIDE/
 BA3 - Advanced Technology Development (ATD)**

PE NUMBER AND TITLE
0603384BP CHEMICAL/BIOLOGICAL DEFENSE (ATD)

A. Mission Description and Budget Item Justification: This program element demonstrates technologies that enhance the ability of U.S. forces to defend against, and survive chemical and biological (CB) warfare. This PE funds advanced technology development for Joint Service and Service-specific requirements in both medical and non-medical CB defense areas. The medical program aims to produce drugs, vaccines, and medical devices as countermeasures for CB threat agents. Specific areas of medical investigation include: prophylaxis, pretreatment, antidotes and therapeutics, personnel and patient decontamination, and medical management of casualties. In the non-medical area, the focus is on demonstrations of CB defense technologies, including biological detection, chemical detection, and decontamination. These demonstrations, conducted in an operational environment with active user and developer participation, integrate diverse technologies to improve DoD Chemical/Biological Warfare (CBW) defense and deterrence. These demonstrations are leveraged by the Counterproliferation Support Program and include remote Biological Detection. Also research efforts are planned to evaluate technologies for Weapons of Mass Destruction Civil Support Teams (WMD-CSTs). Work conducted under this PE transitions to and provides risk reduction for System Integration/Demonstration (PE 0603884BP/PE 0604384BP) activities. The work in this PE is consistent with the Joint Service NBC Defense Research, Development, and Acquisition (RDA) Plan. This PE also provides for the conduct of advanced technology development in the areas of real-time sensing, accelerated BW operational awareness, and the restoration of operations following a BW/CW attack. This program is dedicated to conducting proof-of-principle field demonstrations, and tests of system-specific technologies to meet specific military needs.

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B. <u>Program Change Summary:</u>	<u>FY 2002</u>	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
Previous President's Budget (FY 2003 PB)	75266	249842	106003	100922
Current Biennial Budget Estimates (FY 2004/2005)	80198	107763	103725	98843
Total Adjustments	4932	-142079	-2278	-2079
a. Congressional General Reductions	0	-167379	0	0
b. Congressional Increases	0	25300	0	0
c. Reprogrammings	-655	0	0	0
d. SBIR/STTR Transfer	-1273	0	0	0
e. Other Adjustments	0	0	-2278	-2079

Change Summary Explanation:

Funding: FY02 - Title IX Adjustment (+\$8,200K TB3).

FY03 - Transfer to the Department of Homeland Security Bioterrorism initiatives (-\$162,000K HS3).

FY03 - Adjustment for CBD (+\$22,000K CB3; +\$3,300K TB3) to help fund technology advancements in the areas of chemical and biological agent detection and identification, decontamination, and individual/collective protection.

Schedule:

Technical:

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COST (In Thousands)	FY 2002 Actual	FY 2003 Estimate	FY 2004 Estimate	FY 2005 Estimate	FY 2006 Estimate	FY 2007 Estimate	FY 2008 Estimate	FY 2009 Estimate	Cost to Complete	Total Cost
CB3 CHEMICAL BIOLOGICAL DEFENSE (ATD)	18531	47349	33414	33027	25908	30903	31328	31914	Continuing	Continuing

A. Mission Description and Budget Item Justification:

Project CB3 CHEMICAL BIOLOGICAL DEFENSE (ATD): This project demonstrates technology advancements for Joint Service application in the areas of chemical and biological agent detection and identification, decontamination, and individual/collective protection which will speed maturing of advanced technologies to reduce risk in system-oriented integration/demonstration efforts. This project funds the Joint Service Family of Decontamination Systems (JSFDS) program, the Joint Service Active Standoff CW Detection System (ARTEMIS) program, the Joint Service Sensitive Equipment Decontamination (JSSED) Program, the Joint Biological Standoff Detection System (JBSDS), the Joint Service Wide Area Detector (JSWAD), and Joint Operational Effects Federation (JOEF). Additionally, this program funds the Small Unit Biological Detector (SUBD), Consequence Management Interoperability Service (CMIS), and the Chemical Biological Individual Sampler (CBIS).

B. Accomplishments/Planned Program

	<u>FY 2002</u>	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
Detection	467	2642	9601	17200

FY 2002 Accomplishments:

- 467 Standoff Detection - Completed testing and evaluation of selected hyperspectral systems.

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<p>FY 2002 Accomplishments (Cont): Total 467</p> <p>FY 2003 Planned Program:</p> <ul style="list-style-type: none"> • 1200 Lightweight Integrated CB Detection - Continue evaluation and development of DOE's micro chem lab to meet Joint Modular CB detector requirements. • 1442 Point Detection, Detector Modifications - Complete and demonstrate standard operating procedures for wet chemistry test kits and aerosol collectors/samplers as a "quick fix" for new chemical targets. Complete modification of point detection systems to enhance performance against new chemical targets. Continue assessment of modifications on system impacts to power usage, reliability, and overall system life expectancy. <p>Total 2642</p> <p>FY 2004 Planned Program:</p> <ul style="list-style-type: none"> • 510 Standoff, Sensor Assessment Non Traditional Agent (NTA) - Complete development of spectral database. Construct breadboard surface contamination monitor. • 1475 Biological Sample Preparation System (BSPS) for Biological Identification (DTO-CB20) - Demonstrate feasibility in an multi-agent, multiplexed PCR assay that will be cost-effective. Complete system design and initiate system build to use multi-agent, multiplexed PCR assay based on analysis of alternative study. • 831 Point Detection, Detector Modifications - Complete assessment of modifications on system impacts to power usage, reliability, and overall system life expectancy. 		
Project CB3/Line No: 037	Page 5 of 56 Pages	Exhibit R-2a (PE 0603384BP)

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FY 2004 Planned Program (Cont):

- 2557 Planning, Training and Analysis - Preparation for transition of the fighterbase and casualty modules to Joint Operational Effects Federation (JOEF) program to support Block 1 Demonstration. Complete the first phase of independent verification of software. Baseline RESTOP ACTD results as model validation. Deliver airbase representation module and generic airbase module to DTRA/CB and TD.
- 492 Environment - Transition VLSTRACK Version 4 capabilities to the JEM Block I and JOEF programs. Continue development of advanced predictive capabilities (MESO). Enhance the ability to analyze transport and flows over complex terrain and around structures such as ships (enhancements include addressing biological agent slurry transport, dusty agent behavior, and complex agent sources and sinks).
- 3736 Detection of Agent in Water - Initiate limited utility assessment to demonstrate technology. Develop assessment criteria and initiate a prototype design and build for the assessment.

Total 9601

FY 2005 Planned Program:

- 3000 Biological Sample Preparation System (BSPS) for Biological Identification (DTO-CB20) - Complete build and demonstrate an automated system for multi-agent, multiplexed PCR assay with automated sample preparation.
- 3000 Biological Sample Preparation System (BSPS) for Biological Identification (DTO-CB20) - Complete build and demonstrate an automated system for multi-agent, multiplexed PCR assay with automated sample preparation.
- 5900 Lightweight Integrated CB Detection - Transition downselected technology to Advanced Concept Development (6.3), design brass boards, and initiate brass board builds. Complete Milestone A.

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FY 2005 Planned Program (Cont):

- 300 Point Detection, Integrated Non Traditional Agent (NTA) - Complete breadboard for integrated sampling.
- 5000 Detection of Agent in Water - Complete prototype build and assessment methodology.

Total 17200

	<u>FY 2002</u>	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
Protection	0	0	295	1400

FY 2004 Planned Program:

- 295 Individual Protection, Clothing Non Traditional Agent (NTA) - Incorporate and test improved barrier materials in clothing.

Total 295

FY 2005 Planned Program:

- 1400 Self-Detoxifying Materials for Clothing Applications (DTO-CB45) - Demonstrate optimized electrospun self-detoxifying membranes, develop prototypes, and conduct field testing. Optimize reactive nanoparticle-polymer material/process and conduct CWA testing. Field test overgarments treated with N-halamines and other oxidative compounds. Transition technology to industry for scale-up to commercial manufacturing.

Total 1400

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	<u>FY 2002</u>	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
Decontamination	1847	2000	1180	2000

FY 2002 Accomplishments:

- 1847 Sensitive Equipment - Completed Analysis of Alternatives (AOA) for JSSED Blocks II/III. Conducted a thermal decon feasibility study for aircraft and other combat vehicle interiors. Developed a detailed aircraft materials database in support of JSSED Blocks II/III.

Total 1847

FY 2003 Planned Program:

- 2000 Sensitive Equipment - Complete the validation, verification, and accreditation process for the JSSED Block II/III AOA. Complete an advanced development and management plan for items identified by the AOA and complete TRL 4/5 requirements. Develop MS-B transition documentation.

Total 2000

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FY 2004 Planned Program:

- 1180 Oxidative Decontamination Formulation (DTO-CB44) - Demonstrate products with existing applicator systems. Modify or develop alternative applicators. Conduct basic integration of products into a "simulated environment". Conduct robust chamber studies using full-scale conceptual system testing with live agents. Conduct an analysis of alternatives for solution chemistry approaches. Complete the validation, verification, and accreditation process for the AOA and complete an advanced development and management plan for items identified.

Total 1180

FY 2005 Planned Program:

- 2000 Oxidative Decontamination Formulation (DTO-CB44) - Conduct safety, health, and environmental studies. Complete testing IAW the advanced development and management plan developed in FY04. Complete TRL 4/5 requirements.

Total 2000

	<u>FY 2002</u>	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
Supporting Science and Technology	0	0	0	200

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FY 2005 Planned Program:

- 200 Environment - Transition advanced predictive capabilities (MESO) to JEM Block II program. Further enhance the complex terrain and flow around structures modeling capability to address effects of vegetation and surface scavenging.

Total 200

	<u>FY 2002</u>	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
Information Technology Systems	3695	3500	2262	1200

FY 2002 Accomplishments:

- 1036 Chemical and Biological Warfare Effects on Operations (DTO-CB43) - Continued development of a general purpose model of the operations of large fixed-site facilities (air bases, Aerial Ports of Debarkation (APODs) and, Seaports of Debarkation (SPODs)), with the capability to represent chemical and biological warfare (CBW) attacks and their operational impacts. Demonstrated Initial Operational Capability (IOC) for fighter bases.
- 1528 Joint Effects Model (JEM) - Initiated analysis of alternatives and preparation of documentation to support transition to development. Initiated combination of candidate hazard prediction models to single model, and began preparations to demonstrate capability.

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FY 2002 Accomplishments (Cont):

- 1131 Joint Operational Effects Federation (JOEF) - Initiated Analysis of Alternatives (AoA) and market survey. Established Joint System Architecture IPT and Joint T&E IPT. Initiated creation of the Test and Evaluation Master Plan (TEMP). Began preparation to demonstrate the maturity of the JOEF Blk I federate. Initiated Interoperability Assessment and a System Threat Assessment.

Total 3695

FY 2003 Planned Program:

- 3000 Planning, Training and Analysis - Preparation for transition of the fighterbase and casualty modules to Joint Operational Effects Federation (JOEF) program to support Block 1 Demonstration. Complete the first phase of independent verification of software. Baseline RESTOP ACTD results as model validation. Deliver airbase representation module and generic airbase module to DTRA/CB and TD.
- 500 Environment - Transition VLSTRACK Version 4 capabilities to the JEM Block I and JOEF programs. Continue development of advanced predictive capabilities (MESO). Enhance the ability to analyze transport and flows over complex terrain and around structures such as ships (enhancements include addressing biological agent slurry transport, dusty agent behavior, and complex agent sources and sinks).

Total 3500

FY 2004 Planned Program:

- 984 Point Detector Modifications Non Traditional Agent (NTA) - Initiate breadboard for integrated sampling, generic classification in unattended mode.

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FY 2004 Planned Program (Cont):

- 393 Environment - Transition advanced predictive capabilities (MESO) to JEM Block II program. Further enhance the complex terrain and flow around structures modeling capability to address effects of vegetation and surface scavenging.
- 885 Simulation Based Acquisition - Initiate AoA and market survey for Virtual Prototyping System (VPS).

Total 2262

FY 2005 Planned Program:

- 500 Planning, Training and Analysis - Test and finalize toward JOEF transition Block 2. Develop Marine Expeditionary Force HQ, depot, and railhead modules. Perform internal V&V.
- 700 Simulation Based Acquisition - Develop Test and Evaluation Master Plan for VPS. Conduct tech demonstration and downselect among technology candidates.

Total 1200

	<u>FY 2002</u>	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
Advanced Tech Development	12522	38513	20076	11027

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FY 2002 Accomplishments:

- 1690 Miniaturized CB Detectors (MEMS Technology) - Initiated a feasibility study on the use of chemically modified microspheres to detect the presence of select biological agents. Prototypes were configured as a reader and interchangeable assay cartridges that contains the microspheres.
- 115 Future Threat Agent Studies - Completed stirred reactor kinetic studies of fielded and developmental decontaminants on non-traditional threat agents.
- 10717 Technical Transition - Developed improved sample processing methodologies for UV MALDI-TOF mass spectrometer. Initiated production of upconverting phosphors (UCP) and tickets for test and evaluation. Identified and initiated evaluation of candidate antibodies for specificity and sensitivity against anthrax. Initiated development of catalytic oxidation filtration device. Initiated development of infrared MALDI-TOF mass spectrometer for improved pathogen discrimination. Initiated reformulation and evaluation of Sandia foam for applications to military decontamination. Initiated test and evaluation of Sandia gas microchem lab for vapor agent detection and assessment of fluidic microchem lab for biological detection. Initiated development of improved sample handling technology for incorporation into handheld automated nucleic acid analyzer (HANAA). Assessed performance of anthrax MAGIChip (MicroArray of Gel Impregnated Compounds).

Total 12522

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FY 2003 Planned Program:

- 750 Standoff Sensor Assessment, Non Traditional Agents (NTA) - Establish infrastructure to develop spectral signature. Develop spectral signature database. Assess optical techniques to detection NTAs.
- 567 Fielded Decontamination Assessment, Non Traditional Agent (NTA) - Complete assessment of fielded decon system for NTAs.
- 2777 Technical Readiness Evaluation - Conduct Technology Readiness Evaluations (TRE) of point and standoff CB detection systems. Conduct contact hazard evaluations using NATO protocols. Conduct off-gas hazard evaluations using NATO/TTCP protocols.
- 12500 Technical Transition - Develop improved sample processing interface for UV MALDI-TOF mass spectrometer and incorporate into DARPA BioTOF device. Complete evaluation of upconverting phosphors for bio identification. Complete evaluation of anthrax-specific antibodies identified in FY02. Evaluate and refine catalytic oxidation filtration device. Initiate development of pathogen agents database with UV/IR MALDI and construct automated sample processing interface. Complete evaluation of Sandia foam for military decon. Complete development of sample handling interface for HANAA. Extend MAGICChip capability to address additional pathogen agents. Initiate assessment of additional technologies in detection, decontamination, and filtration from other government agencies.
- 2119 Miniature Chemical and Biological Detectors - Develop and validate miniaturized chemical and biological threat agent sensor technologies.
- 7700 Rapid Response Countermeasures to Biological and Chemical Threats - Design, test and evaluate rapid response countermeasures to biological and chemical threats.

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<p>FY 2003 Planned Program (Cont):</p> <ul style="list-style-type: none"> • 3000 CBRN Threat Test Using Public/Private Assets (Sensor Net) - Design and evaluate a sensor network using existing public and private assets that is capable of enhancing the response to chemical/biological/radiological/nuclear threats. • 2000 Bioterrorism/Agroterrorism Prediction and Risk Assessment - Develop novel strategies and tools to assist in predicting risk from bioterrorism/agroterrorism. • 3600 Advanced Chemical Detector - Explore and validate an advanced chemical threat agent detector. • 1400 High Intensity Pulsed Radiation Facility for Chem-Bio Defense - Develop and evaluate the utility of high intensity pulsed radiation for chemical and biological threat remediation. • 2100 Bioterrorism Defense and Advanced Sensors - Explore and validate the utility of advanced sensor technologies in combating bioterrorism. <p>Total 38513</p> <p>FY 2004 Planned Program:</p> <ul style="list-style-type: none"> • 2458 Technical Readiness Evaluation - Conduct Technology Readiness Evaluations (TRE) of point and standoff CB detection systems. Conduct stirred reactor, contact hazard and off gas testing on emerging decontaminants not tested previously. • 17618 Technical Transition - Complete development of integrated UV MALDI-TOF and IR MALDI-TOF mass spectrometers. Complete catalytic oxidation filtration device. Complete evaluation of MAGIChip. Continue assessment of technologies in detection, decontamination, and filtration from other government agency programs. <p>Total 20076</p>		
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- FY 2005 Planned Program:**
- 1749 Technical Readiness Evaluation - Conduct Technology Readiness Evaluations (TRE) of point and standoff CB detection systems. Conduct stirred reactor, contact hazard and off gas testing on emerging decontaminants not tested previously.
 - 9278 Technical Transition - Conduct competitive assessment of all mature mass spectrometric biodetection approaches. Complete assessment of selected technologies in detection, decontamination, and protection from other government agency programs identified for evaluation in previous FY.

Total 11027

	<u>FY 2002</u>	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
SBIR/STTR	0	694	0	0

FY 2003 Planned Program:

- 694 SBIR

Total 694

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C. <u>Other Program Funding Summary:</u>	<u>FY 2002</u>	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>	<u>FY 2006</u>	<u>FY 2007</u>	<u>FY 2008</u>	<u>FY 2009</u>	<u>To Compl</u>	<u>Total Cost</u>
BJ4 BIOLOGICAL DEFENSE (ACD&P)	1521	3487	0	0	0	0	0	0	0	5008
CA4 CONTAMINATION AVOIDANCE (ACD&P)	15758	19662	35470	7486	2500	2500	12500	2500	Cont	Cont
CO4 COLLECTIVE PROTECTION (ACD&P)	0	4177	5000	0	0	0	0	0	0	9177
CP3 COUNTERPROLIFERATION SUPPORT (ATD)	11791	11075	4714	5257	4575	4122	3196	3255	Cont	Cont
CP4 COUNTERPROLIFERATION SUPPORT (ACD&P)	14720	12763	20623	15075	24381	25516	26075	26597	Cont	Cont
DE4 DECONTAMINATION SYSTEMS (ACD&P)	5986	6634	28243	17886	6816	3880	0	6687	Cont	Cont
IP4 INDIVIDUAL PROTECTION (ACD&P)	13801	0	0	0	0	0	0	0	0	13801

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COST (In Thousands)	FY 2002	FY 2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	Cost to	Total Cost
	Actual	Estimate	Complete							
CM3 WMD - CIVIL SUPPORT TEAM (ATD)	4650	2354	2459	2449	2435	2430	0	0	0	16777

A. Mission Description and Budget Item Justification:

Project CM3 WMD - CIVIL SUPPORT TEAM (ATD): This project funds Pre-Systems Acquisition in support of Consequence Management teams around the Nation. National Guard Weapons of Mass Destruction Civil Support Teams (WMD CST) are being established in every state. These teams were created based upon the Defense Reform Initiative Directive #25 (DRID #25), Integrating National Guard and Reserve Component Support for Response to Attacks Using Weapons of Mass Destruction (WMD). The role of the Civil Support Teams (CSTs) were further codified in the National Security Strategy of October 1998, which builds upon the National Guard's ties to the communities throughout the nation, and its long-standing tradition of responding to national emergencies. The strategy allows the National Guard to provide forces and resources that the emergency manager requires to manage the potentially catastrophic effects of a WMD situation. The National Guard, as the lead organization for military support to local and state authorities, leverages its geographic dispersion across the nation to reduce response times, and allow for the majority of the country to be protected. As a result of Presidential and Secretary of Defense directives, the Department of Defense established the Weapons of Mass Destruction Civil Support Teams (WMD CST) to rapidly respond in support of a local incident commander to assess a suspected WMD incident scene, advise them of appropriate courses of action that will protect local populations from loss of life, injury, and significant property damage, and facilitate the development of their requests for assistance (RFAs) based on CST knowledge of available local, state and federal resources that can assist in the mitigation of a WMD emergency.

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This program funds the purchase and testing of commercial-off-the-shelf (COTS)/government-off-the-shelf (GOTS) components on the existing Table of Distribution and Allowances (TDA) of Weapons of Mass Destruction Civil Support Teams (WMD CST), and evaluates new commercial products being considered for the WMD CST TDA for performance and ability to meet requirements.

B. Accomplishments/Planned Program

	<u>FY 2002</u>	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
Consequence Management	4650	0	0	0

FY 2002 Accomplishments:

- 4650 WMD CST - Consequence Management - Researched detection strategies of bioweapons use in the human population. Gene chip technology was investigated to help determine, in as little as a few hours, if a human was exposed to, and infected by, a biological agent. Tested blood samples to see which specific genes are turned in response to infections by the disease organism.

Total 4650

	<u>FY 2002</u>	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
WMD - CIVIL SUPPORT TEAMS	0	2319	2459	2449

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FY 2003 Planned Program:

- 600 WMD CST- Initiate purchase and evaluate for modification, commercial-off-the-shelf (COTS) components on the Table of Distribution and Allowances (TDA) of the Weapons of Mass Destruction Civil Support Teams (WMD-CSTs).
- 1250 WMD CST - Initiate evaluation of new commercial products being considered for TDA to determine performance and ability to meet WMD CST requirements.
- 469 WMD CST - Initiate planning and support for test program for commercial equipment.

Total 2319

FY 2004 Planned Program:

- 2000 WMD CST - Continue evaluation of new commercial products being considered for TDA to determine performance and ability to meet WMD CST requirements.
- 459 WMD CST - Initiate targeted technology Analysis of Alternatives for Department of Defense (DoD) civil support to WMD Consequence Management response for follow-on technology insertion options.

Total 2459

FY 2005 Planned Program:

- 2000 WMD CST - Continue evaluation of new commercial products being considered for TDA to determine performance and ability to meet WMD-CST requirements.
- 449 WMD CST - Continue targeted technology Analysis of Alternatives for Department of Defense (DoD) civil support to WMD Consequence Management response for follow-on technology insertion options.

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FY 2005 Planned Program (Cont):
Total 2449

	<u>FY 2002</u>	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
SBIR/STTR	0	35	0	0

FY 2003 Planned Program:

- 35 SBIR

Total 35

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C. <u>Other Program Funding Summary:</u>	<u>FY 2002</u>	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>	<u>FY 2006</u>	<u>FY 2007</u>	<u>FY 2008</u>	<u>FY 2009</u>	<u>To Compl</u>	<u>Total Cost</u>
CA4 CONTAMINATION AVOIDANCE (ACD&P)	15758	19662	35470	7486	2500	2500	12500	2500	Cont	Cont
CM5 WMD - CIVIL SUPPORT TEAM (SDD)	0	977	984	14202	390	0	0	0	0	16553
CM6 WMD - CIVIL SUPPORT TEAM (RDT&E MGT SUPPORT)	0	1555	1574	1568	1559	1555	0	0	0	7811
JA0004 WMD - CIVIL SUPPORT TEAM EQUIPMENT	25000	18647	7858	2983	43270	1560	0	0	0	99318

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	COST (In Thousands)	FY 2002	FY 2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	Cost to	Total Cost
		Actual	Estimate	Complete							
CP3	COUNTERPROLIFERATION SUPPORT (ATD)	11791	11075	4714	5257	4575	4122	3196	3255	Continuing	Continuing

A. Mission Description and Budget Item Justification:

Project CP3 COUNTERPROLIFERATION SUPPORT (ATD): The mission of the Counterproliferation Program (CP) is to address shortfalls in the Department of Defense (DoD) capability to defend against and counter the proliferation of Weapons of Mass Destruction (WMD). By focusing on near term results, the CP accelerates delivery of new tools, equipment, and procedures to combat forces. Under the passive defense pillar, CP enhances the efforts of the Chemical and Biological Defense Program. This project funds a variety of programs to defend our forces against WMD, such as the Biological Detection (BIODET) and Counter Proliferation Support (Non-System) (CTP (NS)) efforts, Restoration of Operations (RestOps), Contamination Avoidance at Seaport of Debarkation (CASPOD), and Advanced Concept Technology Demonstrations Planning and Development (ACTD-PD).

B. Accomplishments/Planned Program

	<u>FY 2002</u>	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
ACTD PLANNING AND DEVELOPMENT	1809	1760	4714	5257

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<p>FY 2002 Accomplishments:</p> <ul style="list-style-type: none"> • 1809 ACTD-PD - Performed technology selections, performed analysis of alternative technologies, and prepared acquisition strategy for Contamination Avoidance for Seaports of Debarkation (CASPOD) Advanced Concept Technology Demonstration. <p>Total 1809</p> <p>FY 2003 Planned Program:</p> <ul style="list-style-type: none"> • 1760 ACTD-PD - Perform CONOPS evaluation of FY04/05 Modeling and Simulation candidate ACTD. Perform technology demonstration of coupled technologies for FY04/05 candidate ACTD. <p>Total 1760</p> <p>FY 2004 Planned Program:</p> <ul style="list-style-type: none"> • 1503 ACTD-PD - Perform CONOPS evaluation of FY05 candidate ACTD, prepare planning documents for FY05 candidate ACTD. • 2020 ACTD-PD - Perform technology demonstrations on CB environment simulation technologies for future CB environment simulation for Combatant Commander and Service exercises. • 1191 ACTD-PD - Conduct technology maturity evaluation tests of FY05 ACTD candidate technologies. <p>Total 4714</p>		
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FY 2005 Planned Program:

- 3757 ACTD-PD - Initiate technology maturity evaluations for selection of technologies for future ACTD candidate.
- 1500 ACTD-PD - Initiate planning for ACTD candidate, explore potential CONOPS with ACTD candidate technologies.

Total 5257

	<u>FY 2002</u>	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
BIODETECTION PROGRAM	0	2208	0	0

FY 2003 Planned Program:

- 2208 RestOps - Conduct RestOps ACTD lessons learned study and complete report on RestOps ACTD. Initiate transition planning for technology acquisition from the RestOps ACTD.

Total 2208

	<u>FY 2002</u>	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
COUNTERPROLIFERATION SUPPORT (NON-SYSTEM)	8194	3408	0	0

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FY 2002 Accomplishments:

- 1811 CASPOD - Developed exercise scenarios for CASPOD ACTD. Performed a Table Top Exercise for CB defense of a Seaport for the CASPOD operational sponsor,. Initiated CONOPS development by the operational sponsor of CASPOD ACTD. Performed management support functions for the CASPOD ACTD.
- 2150 RestOps - Demonstrated decontamination procedures for a wide body aircraft at Eglin AFB and demonstrated decontamination applicators using current Aircraft System Program Office (SPO) approved decontaminants and two proposed decontaminants.
- 3686 RestOps - Performed agent transfer and wind tunnel tests for agent studies applicable to procedures used in the RestOps ACTD demonstration. Developed computer-based interactive training tools for the RestOps ACTD. Supported RestOps technology vignette efforts at Osan Air Base and Dugway Proving Ground.
- 547 Joint Service Installation Pilot Project (JSIPP) - Performed assessments on nine installations for the JSIPP project. Modeled locations for biological detection equipment.

Total 8194

FY 2003 Planned Program:

- 2016 CASPOD - Perform technical testing of technologies for the CASPOD ACTD.
- 867 CASPOD - Develop and test techniques, tactics, and procedures for the use of the CASPOD ACTD technologies. Acquire test equipment, provide test participants and evaluators, develop environmental compliance documentation for tests and preliminary demonstration.

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FY 2003 Planned Program (Cont):

- 525 RESTOPS - Perform Large Frame Aircraft Decontamination Demonstration (LFADD) project.

Total 3408

	<u>FY 2002</u>	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
RESTOPS ACTD	1788	3534	0	0

FY 2002 Accomplishments:

- 550 RestOps - Continued development of a synthetic environment tool for technology selection in RestOps scenarios.
- 1238 RestOps - Performed evaluation of models to be used in the demonstration of the RestOps ACTD. Developed assessment tools to be used in simulating Biological Warfare for RestOps demonstration.

Total 1788

FY 2003 Planned Program:

- 3534 RestOps - Complete evaluation of technologies in final demonstration. Transition continues in FY04 to CP4 for residual support projects.

Total 3534

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	<u>FY 2002</u>	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
SBIR/STTR	0	165	0	0

FY 2003 Planned Program:

- 165 SBIR

Total 165

C. <u>Other Program Funding Summary:</u>	<u>FY 2002</u>	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>	<u>FY 2006</u>	<u>FY 2007</u>	<u>FY 2008</u>	<u>FY 2009</u>	<u>To Compl</u>	<u>Total Cost</u>
CP4 COUNTERPROLIFERATION SUPPORT (ACD&P)	14720	12763	20623	15075	24381	25516	26075	26597	Cont	Cont

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COST (In Thousands)	FY 2002 Actual	FY 2003 Estimate	FY 2004 Estimate	FY 2005 Estimate	FY 2006 Estimate	FY 2007 Estimate	FY 2008 Estimate	FY 2009 Estimate	Cost to Complete	Total Cost
TB3 MEDICAL BIOLOGICAL DEFENSE (ATD)	34554	35515	49939	44621	39530	39527	42528	38573	Continuing	Continuing

A. Mission Description and Budget Item Justification:

Project TB3 MEDICAL BIOLOGICAL DEFENSE (ATD): This project funds preclinical development of safe and effective prophylaxes and therapies (vaccines and drugs) for pre- and post-exposures to biological threat agents. This project also supports the advanced technology development of diagnostic devices to rapidly diagnose exposure to biological agents in clinical samples. A broad range of technologies involved in the targeting and delivery of prophylactic and therapeutic medical countermeasures and diagnostic systems is evaluated so that the most effective countermeasures are identified for transition to Advanced Development. Transitioning candidate vaccines, therapeutics, and diagnostic technologies to Advanced Development requires the development of scientific/regulatory technical data packages to support the Food and Drug Administration (FDA) Investigational New Drug (IND) process and DoD acquisition regulations. Categories for this project include Defense Technology Objectives (DTOs); science and technology program areas in medical biological defense (diagnostic technologies, bacterial therapeutics, toxin therapeutics, viral therapeutics, bacterial vaccines, toxin vaccines, and viral vaccines), directed research efforts (Bioadhesion Research, Medical Countermeasures, Advanced Diagnostics, Vaccines, and Vaccine Stabilization); and efforts to transition promising medical biological defense technologies from the Defense Advanced Research Projects Agency (DARPA).

B. Accomplishments/Planned Program

	<u>FY 2002</u>	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
Therapeutics	12628	6835	14694	17427

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FY 2002 Accomplishments:

- 757 Therapeutics, Bacterial - Evaluated, in animal models, selected immunomodulators in combination with efficacious antibiotics for protection against bacterial threat agents.
- 2711 Therapeutics, Toxin - Evaluated lead candidate licensed therapeutic drugs that also inhibit staphylococcal enterotoxin B (SEB)-induced intoxication.
- 1514 Therapeutics, Viral - Continued evaluating formulations or prodrugs to overcome problems with metabolism, bioavailability, or pharmacokinetics of compounds with otherwise acceptable antiviral profiles for orthopox viruses.
- 1146 Therapeutics, Medical Countermeasures - Enhanced advanced technology development of broad-spectrum therapeutic countermeasures for exposure to various biological threats.
- 6500 Therapeutics, Title IX - Expanded collection of blood from anthrax-vaccine-immunized donors and for purification of anthrax-immune globulin (IgG) from collected blood at the Centers for Disease Control and Prevention (CDC) for use in evaluating anthrax-immune IgG as a post-exposure treatment for anthrax. Expanded extramural research to create and characterize human monoclonal antibodies (MAbs) to botulinum neurotoxins (BoNT) as potential therapeutic countermeasures and expanded extramural resources for process development and purification of MAbs identified as lead candidates. Expanded in-house confocal microscopy resources for real-time observation of toxin trafficking in viable cells. Expanded in-house Nuclear Magnetic Resonance capabilities for measurement of the structure of peptide-based therapeutic candidates against BoNT. Resourced an agreement with CDC for higher animal species and related supplies required for pre-clinical studies of cidofovir as a therapeutic for exposure to orthopox viruses.

Total 12628

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FY 2003 Planned Program:

- 923 Therapeutics, Bacterial - Conduct comparative assessment for safety and efficacy of immunomodulators and other types of broad-spectrum compounds against multiple bacterial threat agents.
- 3945 Therapeutics, Toxin - Prepare sufficient amounts of lead inhibitors of botulinum toxin and SEB intoxication for testing ex vivo or in vivo. Evaluate feasibility of drugs approved by FDA for septic shock as adjunct SE therapeutics using in vitro assays.
- 1767 Therapeutics, Viral - Evaluate the combined approach of antiviral drug therapy and immunotherapy in treatment of disease from filoviruses. Continue evaluating formulations or prodrugs to overcome problems with metabolism, bioavailability, or pharmacokinetics of compounds with otherwise acceptable antiviral profiles for orthopox viruses.
- 200 Therapeutics, Therapy for Smallpox and Other Pathogenic Orthopoxviruses (DTO) - Begin assessment and development of a clinical study site where sufficient monkeypox exists naturally in order to characterize the clinical course and pathogenesis of monkeypox.

Total 6835

FY 2004 Planned Program:

- 2470 Therapeutics, Bacterial - Continue the assessment of selected compounds for safety and efficacy against multiple bacterial threat agents in small animal models.
- 8723 Therapeutics, Toxin - Standardize in vivo concept model systems for assessment of therapeutic efficacy and surrogate endpoints of human clinical efficacy for botulinum and SE intoxication. Test FDA-approved drugs for septic shock as adjunct SE therapeutics in vivo.

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FY 2004 Planned Program (Cont):

- 3101 Therapeutics, Viral - Complete the evaluation of one antiviral drug formulation for orthopox viruses. Continue evaluating second drug formulation or prodrugs for orthopox viruses.
- 400 Therapeutics, Therapy for Smallpox and Other Pathogenic Orthopoxviruses (DTO) - Complete the assessment of the clinical study site to determine feasibility for use in a field trial of cidofovir to treat human monkeypox.

Total 14694

FY 2005 Planned Program:

- 2890 Therapeutics, Bacterial - Advance the assessment of selected compounds for safety and efficacy against multiple bacterial threat agents in higher animal species.
- 10208 Therapeutics, Toxin - Test lead monoclonal antibody therapeutic systems in animal models for effectiveness as passive immunotherapeutics against botulinum neurotoxins. Conduct proof-of-concept studies in animal models with lead compounds shown to have potential as inhibitors of botulinum neurotoxins or SEs.
- 4029 Therapeutics, Viral - Continue evaluating new drug formulations or prodrugs for orthopox viruses.
- 300 Therapeutics, Therapy for Smallpox and Other Pathogenic Orthopoxviruses (DTO) - Complete technical data package supporting the drug (cidofovir) license holder's request to FDA to approve a labeled indication for pre- and post-exposure treatment for smallpox.

Total 17427

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	<u>FY 2002</u>	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
Diagnostics	3532	4070	5323	6149

FY 2002 Accomplishments:

- 1000 Diagnostics, Common Diagnostic Systems (DTO) - Completed an analysis of alternatives of portable nucleic analysis systems for detecting and identifying nucleic acids from a broad range of biological threat agents in clinical specimens. Prepared technical data package to support transitioning the common diagnostic systems candidate out of technology base and preparation of a medical device application to the FDA.
- 1611 Diagnostic Technologies - Compared new diagnostic reagents, devices, and protocols in preclinical studies before transitioning to the regulatory compliant medical laboratory. Evaluated candidate diagnostic technologies in field-based studies and in a regulated medical center clinical laboratory prior to transitioning out of technology base. Developed and evaluated new diagnostic assays for biological warfare threat agents and successfully transitioned selected assays out of the technology base. Enhanced advanced medical diagnostic capabilities for presymptomatic detection of biological warfare agent (BWA) infection.
- 921 Diagnostics, Advanced Diagnostics - Enhanced advanced technology development efforts toward the development of advanced medical diagnostic capabilities for early presymptomatic detection of BWA infection.

Total 3532

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FY 2003 Planned Program:

- 2470 Diagnostic Technologies - Continue comparing alternative diagnostic technologies in laboratory-based and field-based studies prior to transition to the field medical laboratory. Compare overlapping diagnostic technologies that can be integrated into a single comprehensive platform capable of identifying a broad range of biological threat agents in clinical specimens in laboratory-based and field-based studies. Continue to develop, evaluate, and transition diagnostic assays out of the technology base in support of the Joint Biological Agent Identification and Diagnostic System (JBAIDS) acquisition program.

- 1600 Diagnostics, Improved Immunodiagnostic Platform (DTO) - Identify immunodiagnostic technology options offering performance and design characteristics capable of addressing operational requirements of the JBAIDS acquisition program. Demonstrate technical capability for detection of at least three biological agents (including toxins) within two hours with the immunodiagnostic technology options. Conduct comparative laboratory evaluation trial of the immunodiagnostic technology options and identify top performing immunodiagnostic platforms based on results of the laboratory evaluation trial.

Total 4070

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FY 2004 Planned Program:

- 3323 Diagnostic Technologies - Continue to compare alternative diagnostic technologies in laboratory-based and field-based studies prior to transition to the field medical laboratory. Continue to compare overlapping diagnostic technologies that can be integrated into a single comprehensive platform capable of detecting and identifying a broad range of biological threat agents in clinical specimens in laboratory-based and field-based studies. Continue to develop, evaluate, and transition diagnostic assays out of the technology base in support of the JBAIDS acquisition program.
- 2000 Diagnostics, Improved Immunodiagnostics Platform (DTO) - Complete interlaboratory evaluation of top performing immunodiagnostic technology options. Perform a multi-center evaluation trial of the top performing immunodiagnostic platforms and prepare a technical data package detailing results of the multi-center trial. Recommend immunodiagnostic technologies for incorporation into JBAIDS acquisition program.

Total 5323

FY 2005 Planned Program:

- 6149 Diagnostic Technologies - Continue to compare alternative diagnostic technologies in laboratory-based and field-based studies prior to transition to the field medical laboratory. Initiate a detailed analysis of alternatives for an advanced integrated diagnostic system capable of detecting and identifying a broad range of biological threat agents in clinical specimens in laboratory-based and field-based studies using a combination of appropriate technologies. Continue to develop, evaluate, and transition diagnostic assays out of the technology base in support of the JBAIDS acquisition program.

Total 6149

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	<u>FY 2002</u>	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
Vaccines	12394	10280	9922	11045

FY 2002 Accomplishments:

- 1600 Vaccines, Medical Countermeasures for Brucella (DTO) - Prepared pilot lot of lead live attenuated vaccine candidates using processes consistent with the intent of current Good Manufacturing Practices (cGMP) and used the pilot vaccine lot to perform pre-investigational new drug (IND) animal studies. Determined relative efficacy of lead candidates against Brucella melitensis in higher animal species challenge model.
- 800 Vaccines, Medical Countermeasures for Encephalitis Viruses (DTO) - Elicited sufficient cross protective immunity in higher laboratory animals to satisfy Operational Requirements Document (ORD) requirement for immunity against VEE virus types IE. Provided product development support for producing vaccine substrate for anticipated Phase 1 trial. Redirected eastern equine encephalitis (EEE) and western equine encephalitis (WEE) virus vaccine development back to discovery and focused the DTO on a multivalent VEE vaccine candidate.
- 1700 Vaccines, Multiagent Vaccines for Biological Threat Agents (DTO) - Completed testing for safety and efficacy in animal models of candidate products (individually and combined) intended for use in a multiagent vaccine.
- 1205 Vaccines, Alternative Delivery Methods for Recombinant Protein Vaccines (DTO) - Assessed the quantitative relationships between toxin-specific antibodies or other indicators of immunity in mucosal surfaces and blood. Continued standardization of animal models for evaluating novel adjuvants and vaccine delivery systems.

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FY 2002 Accomplishments (Cont):

- 940 Vaccines, Recombinant Plague Vaccine Candidate (DTO) - Performed vaccine efficacy studies in two higher animal species models against aerosol and parental challenges to resolve which is the most appropriate model for demonstrating the protective capability of the vaccine candidate. Continued expanded studies in higher animal species for immunogenicity and passive protection; continued studies to establish a correlate of immunity; and continued to optimize vaccine production and formulation. Incorporated a technical summary of the vaccine candidate into an information package prepared to support entry of the vaccine candidate into component advanced development.
- 1500 Vaccines, Recombinant Protective Antigen (rPA) Anthrax Vaccine Candidate (DTO) - Investigated enhancement of the rPA vaccine candidate with immunostimulatory compounds. Evaluated rPA-induced protective immunity against diverse geographical isolates of B. anthracis. Conducted experiments to develop a mouse potency assay for the rPA vaccine candidate. Initiated long-term rPA efficacy studies in animal models. Incorporated technical summaries of completed rPA vaccine candidate preclinical studies into information package supporting transition of the candidate out of the technology base.
- 262 Vaccines, Bacterial - Continued to identify and validate correlates of protective immunity against anthrax, plague, glanders, and brucella, in support of selected vaccine candidates.

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FY 2002 Accomplishments (Cont):

- 688 Vaccines, Toxin - Continued scaled up production of recombinant botulinum neurotoxin (BoNT) vaccine candidates. Performed formulation studies on a recombinant staphylococcal enterotoxin B (SEB) vaccine candidate. Completed the development of reagents and assays to support process development of recombinant botulinum, ricin, and SEB vaccine candidates. Initiated process development for BoNT vaccine candidates. Supported process development for a SE serotype A (SEA) vaccine candidate and completed efficacy studies. Updated technical data package to support transition of SEA and SEB vaccine candidates out of technology base. Developed mutant recombinant ricin toxin A-chain (rRTA) antigens for potential use as vaccine candidates and initiated animal efficacy studies.
- 1066 Vaccines, Viral - Determined that the Marburg vaccine candidate was unable to protect against divergent strains of Marburg virus. Initiated investigation of other vaccine strategies for the Marburg group of viruses.
- 933 Vaccines - Enhanced advanced technology development and delivery of next-generation and generation-after-next vaccines and strategies, which enhanced the immune response to various classes of biological threats.
- 1700 Vaccines, Title IX - Initiated research to develop a novel three-dimensional cell culture system (Cytomatrix Assay System) that reproduces cellular components required for T-cell mediated immunity and which is intended to provide high-throughput screening capability for evaluating vaccine efficacy prior to initiating animal studies. Purified approximately 200 milligrams each of recombinant protective antigen and recombinant anthrax toxin lethal factor for use as reference standards in anthrax vaccine research. Executed an agreement with the Institute of Medicine and the National Academy of Science to produce a report entitled "Accelerating the Research and Development and Acquisition of Medical Countermeasures against Biological Warfare".

Total 12394

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FY 2003 Planned Program:

- 1700 Vaccines, Medical Countermeasures for Brucella (DTO) - Demonstrate effectiveness of candidate vaccine in higher animal species challenge model for protective efficacy against a single pathogenic brucella species. Prepare a technical data package supporting transition of the optimum brucella vaccine candidate out of technology base.
- 800 Vaccines, Medical Countermeasures for Encephalitis Viruses (DTO) - Identify final formulation of a trivalent VEE vaccine. Perform formulation and vaccine interference studies for VEE multivalent vaccine (for protection against VEE IA/B, VEE IE, VEE 3A). Perform potency and stability studies on VEE vaccine components. Support development of technical data package that addresses FDA requirements for an Investigational New Drug application and that supports transitioning the multivalent VEE vaccine candidate out of technology base.
- 1102 Vaccines, Alternative Delivery Methods for Recombinant Protein Vaccines (DTO) - Perform initial efficacy studies for single recombinant protein delivered by alternate route(s). Propose monovalent vaccine formulations for intranasal, inhalational, and/or transdermal delivery systems. Propose in vitro correlate of immunity for surrogate endpoint of clinical efficacy.
- 1000 Vaccines, Recombinant Plague Vaccine Candidate (DTO) - Continue expanded studies in higher animal species for immunogenicity and efficacy and downselect the best higher animal species model. Continue studies to optimize vaccine production and formulation to support entry of the vaccine candidate into component advanced development. Complete a revised technical data package based on completed studies, to facilitate transition of the vaccine candidate out of technology base.

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FY 2003 Planned Program (Cont):

- 1774 Vaccines, Bacterial - Initiate a comparison of the safe and most efficacious vaccine candidates against select agent exposures. Analyze study data to determine best glanders vaccine candidate(s). Incorporate data for brucella and plague vaccine candidates into technical data packages for these vaccine candidates. Continue assay support and studies on adjuvants and formulations in support of rPA vaccine candidate entry into component advanced development; continue to evaluate the efficacy of rPA immunity against B. anthracis strains of diverse geographic origins; and continue long-term rPA efficacy studies in rabbits and higher animal species.
- 563 Vaccines, Toxin - Complete process development for botulinum toxin serotypes D and G vaccine candidates in the Pichia yeast system. Support advanced development of recombinant SEB vaccine candidate by transitioning laboratory assays and data out of the technology base.
- 1841 Vaccines, Viral - Test promising vaccine strategies in higher animal species for the ability to protect against filoviruses (Marburg and Ebola viruses). Complete research studies for the development of vaccine candidates for WEE virus.
- 1500 Vaccines, Vaccine Stabilization - Develop procedures/technologies to make vaccines more available.

Total 10280

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FY 2004 Planned Program:

- 1700 Vaccines, Alternative Delivery Methods for Recombinant Protein Vaccines (DTO) - Propose formulation/device/route for delivery of combination of multiple recombinant proteins. Perform definitive efficacy studies on monovalent vaccine in second animal model. Evaluate in vitro correlate of immunity.
- 2305 Vaccines, Bacterial - Continue to perform animal studies which support transition of potential vaccine candidates to advanced development. Perform studies to address the mechanism of protective cellular immunity induced by selected vaccine candidates. Continue animal studies supporting phase 2 clinical trials and complete developmental work on the mouse potency assay in support of rPA vaccine candidate development.
- 439 Vaccines, Toxin - Produce and characterize inactivated BoNT light chain vaccine candidates and large-scale truncations of BoNT holotoxins. Clone and express existing BoNT vaccine candidates using selected plant-based expression systems. Initiate studies exploring multivalent vaccine technologies for protection against multiple botulinum neurotoxin serotypes.
- 3478 Vaccines, Viral - Select the best vaccine candidate based on ability to protect against filoviruses. Continue research for the development of vaccine candidates for EEE virus infection. Test promising vaccine candidates for WEE in animal systems.
- 2000 Vaccines, Ricin Vaccine by Protein Engineering (DTO) - Conduct toxicity assays, activity assays, and efficacy studies for lead recombinant ricin toxin A-chain (rRTA) vaccine candidates. Continue laboratory stability studies of the lead rRTA candidate; initiate higher animal species protocol and model development for evaluating the rRTA candidate.

Total 9922

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FY 2005 Planned Program:

- 1700 Vaccines, Alternative Delivery Methods for Recombinant Protein Vaccines (DTO) - Demonstrate proof-of-concept for lead alternate vaccine delivery system(s). Complete preclinical research studies and prepare recommendations to support transition of commercial technology for alternate vaccine delivery out of the technology base.
- 2458 Vaccines, Bacterial - Continue to perform animal studies which support phase 1 clinical trials of selected vaccine candidates against bacterial threat agents. Continue technology base studies in support of the development and eventual FDA licensure of the rPA vaccine candidate.
- 1317 Vaccines, Toxin - Initiate evaluation of inactivated BoNT light chain vaccine candidates as well as large-scale truncations of BoNT holotoxins in animal models. Continue studies on multivalent vaccine candidates to protect against multiple BoNT serotypes, including cloning and expression of genes for novel multivalent vaccine candidates.
- 4070 Vaccines, Viral - Test promising vaccine strategies in higher animal species for ability to protect against filoviruses. Continue research for the development of EEE virus vaccine candidates. Test promising WEE vaccine candidates in higher animal species against WEE virus challenge.
- 1500 Vaccines, Ricin Vaccine by Protein Engineering (DTO) - Complete a comprehensive review potency, efficacy, adjuvant studies, toxicity, and pathology results in rodents and downselect to a single lead recombinant ricin toxin A-chain (rRTA) vaccine candidate for assessment in higher animal species. Conduct efficacy studies in higher animal species with the lead vaccine candidate.

Total 11045

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	<u>FY 2002</u>	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
DARPA Transition	4000	12000	20000	10000

FY 2002 Accomplishments:

- 4000 Defense Advanced Research Projects Agency (DARPA) Program Transition - Continued expansion and definition of medical biological defense technologies transitioned from DARPA. Initiated studies of a small molecule antibiotic effective against anthrax. Initiated research on a B-cell based diagnostic sensor technology for viral and bacterial pathogens. Initiated studies of a superantigen toxin antagonist and developed a screening assay to identify additional compounds.

Total 4000

FY 2003 Planned Program:

- 12000 Defense Advanced Research Projects Agency (DARPA) Program Transition - Continue expansion and definition of medical biological defense technologies transitioned from the DARPA. Complete lead optimization of a small molecule antibiotic, complete in vitro and in vivo safety and efficacy studies, and continue Investigational New Drug (IND) enabling studies. Develop two additional B-cell lines and extend the B-cell based diagnostic sensor technology to include toxin agents. Evaluate superantigen toxin antagonists in vitro assays. Use plant expression vectors to create transgenic whole-plant systems expressing plague vaccine antigens. Produce monoclonal antibodies directed against Ebola virus in transgenic plants (plantibodies). Optimize two classes of bacterial RNA-binding compounds with broad-spectrum antimicrobial activity. Apply DNA shuffling technology to identify novel antigens that show protection in mice against at least two encephalitic alphaviruses.

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<p>FY 2003 Planned Program (Cont): Total 12000</p> <p>FY 2004 Planned Program:</p> <ul style="list-style-type: none"> • 20000 Defense Advanced Research Projects Agency (DARPA) Program Transition - Continue expansion and definition of medical biological defense technologies transitioned from the DARPA. Complete chemical manufacturing and control studies and file the IND for a small-molecule antibiotic effective against anthrax. Develop four additional B-cell lines and evaluate the B-cell based diagnostic sensor technology on clinical samples. Develop a blood assay for the superantigen toxin antagonists. Optimize the plant lines and obtain milligram-quantities of plague vaccine antigens from multiple plant species for in vivo evaluation. Obtain milligram-quantities of Ebola plantibodies for in vitro and in vivo evaluation. Complete lead optimization of bacterial RNA-binding compounds and conduct in vitro and in vivo evaluation of the most effective compounds. Evaluate DNA vaccines developed from the most cross-reactive antigens, obtained through DNA shuffling, in higher animal species for protection against three encephalitic alphaviruses. <p>Total 20000</p> <p>FY 2005 Planned Program:</p> <ul style="list-style-type: none"> • 10000 Defense Advanced Research Projects Agency (DARPA) Program Transition - Conclude characterization and process development of candidate vaccines, therapeutics, and diagnostic technologies mature enough for transition into advanced development. Develop five additional B-cell lines and complete development and performance testing of a 16-channel B-cell based diagnostic sensor. Establish formulation for an orally bioavailable superantigen toxin antagonist. <p>Total 10000</p>		
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	<u>FY 2002</u>	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
Bioadhesion Program	2000	1800	0	0

FY 2002 Accomplishments:

- 2000 Bioadhesion Research Program - Continued to evaluate mechanisms that block the adhesion of pathogens to host cells thereby preventing infection or intoxication. Defined protective epitopes and novel delivery systems for use in vaccine formulations focusing on bioadhesion. Used phage display peptide libraries to identify peptide mimetics and constructed vaccine candidates consisting of covalent conjugates and nanoparticles displaying those peptide mimetics. Characterized immune responses in humans exposed to inhalation and cutaneous anthrax to identify the most immunogenic epitopes. Used microarray technology to characterize the genetic response profiles of vaccinated and/or BWA challenged animals leading to effective immunity.

Total 2000

FY 2003 Planned Program:

- 1800 Bioadhesion Research to Combat Biological Warfare - Generate recombinant anthrax antigens, native protective antigen, lethal factor, and capsular antigens and develop conjugate vaccine formulations. Construct covalent conjugates and nanoparticles displaying various combinations of anthrax antigens and determine immunogenicity in animals. Conjugate various combinations of anthrax toxins and capsular materials and determine the optimal conjugate for generating protective immune responses.

Total 1800

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	<u>FY 2002</u>	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
SBIR/STTR	0	530	0	0

FY 2003 Planned Program:

- 530 SBIR

Total 530

C. <u>Other Program Funding Summary:</u>	<u>FY 2002</u>	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>	<u>FY 2006</u>	<u>FY 2007</u>	<u>FY 2008</u>	<u>FY 2009</u>	<u>To</u>	<u>Total</u>
									<u>Compl</u>	<u>Cost</u>
MB4 MEDICAL BIOLOGICAL DEFENSE (ACD&P)	68596	40536	68008	28968	45255	38601	18800	9540	Cont	Cont
MB5 MEDICAL BIOLOGICAL DEFENSE (SDD)	45032	43621	5880	3087	3653	14961	58971	71758	Cont	Cont

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COST (In Thousands)	FY 2002 Actual	FY 2003 Estimate	FY 2004 Estimate	FY 2005 Estimate	FY 2006 Estimate	FY 2007 Estimate	FY 2008 Estimate	FY 2009 Estimate	Cost to Complete	Total Cost
TC3 MEDICAL CHEMICAL DEFENSE (ATD)	10672	11470	13199	13489	12571	12644	12818	13058	Continuing	Continuing

A. Mission Description and Budget Item Justification:

Project TC3 MEDICAL CHEMICAL DEFENSE (ATD): This project supports the investigation of new medical countermeasures to include antidotes, pretreatment drugs, and topical skin protectants to protect U.S. forces against known and emerging CW threat agents. Capabilities are maintained for reformulation, formulation, and scale-up of candidate compounds using current good laboratory practices. Analytical stability studies, safety and efficacy screening, and preclinical toxicology studies are performed prior to full-scale development of promising pretreatment or treatment compounds. Categories for this project include Defense Technology Objectives (DTOs), science and technology program areas (Pretreatments, Therapeutics, and Diagnostics), and directed research efforts (Low Level Chemical Warfare Agent Exposure and Non-Traditional Agents).

B. Accomplishments/Planned Program

	<u>FY 2002</u>	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
Low Level Chemical Warfare Agent Exposure	0	0	500	1500

FY 2004 Planned Program:

- 500 Low Level Chemical Warfare Agent Exposure - Correlate available data relating to low dose chemical warfare agent (CWA) exposure into a functional database suitable for predicting human toxicity.

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FY 2004 Planned Program (Cont):

Total 500

FY 2005 Planned Program:

- 1500 Low Level Chemical Warfare Agent Exposure - Complete evaluation and recommend potential treatments for low level chemical exposure. Demonstrate surrogate marker(s) to confirm low level chemical exposure. Complete database for predicting human toxicity resulting from low level CWA exposure.

Total 1500

	<u>FY 2002</u>	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
Non-Traditional Agents	1500	2000	5000	5500

FY 2002 Accomplishments:

- 1500 Non-Traditional Agents (NTAs) - Initiated downselection process of best available countermeasure(s) against NTAs. Initiated formulation and bulk production feasibility studies for countermeasures. Planned expedited effort to identify and characterize effective new cholinesterase reactivator compounds effective against NTAs. Initiated synthesis of new cholinesterase reactivator compounds for testing. Planned higher animal species study to establish effectiveness of new oxime.

Total 1500

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<p>FY 2003 Planned Program:</p> <ul style="list-style-type: none"> • 800 Non-Traditional Agents - Compare all nerve agents for induction of neurochemical changes. Evaluate efficacy of anticonvulsants against NTAs. • 1200 Non-Traditional Agents, Improved Oxime (DTO) - Conduct efficacy studies of candidate oxime(s) against traditional nerve agents and NTAs in guinea pigs. Initiate down selection process. Synthesize appropriate quantities of each oxime for required studies. <p>Total 2000</p> <p>FY 2004 Planned Program:</p> <ul style="list-style-type: none"> • 1000 Non-Traditional Agents - Evaluate candidate anticonvulsants for effective dose, time to terminate seizures, and neurochemical changes following NTA exposure. • 4000 Non-Traditional Agents, Improved Oxime (DTO) - Initiate efficacy and pharmacokinetic (PK) studies of candidate oxime(s) for use against traditional nerve agents and NTAs in higher animal species and safety/toxicity studies in two species. Continue the down selection process. <p>Total 5000</p> <p>FY 2005 Planned Program:</p> <ul style="list-style-type: none"> • 500 Non-Traditional Agents - Continue to evaluate candidate medical countermeasures to treat NTA exposure. 		
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FY 2005 Planned Program (Cont):

- 5000 Non-Traditional Agents, Improved Oxime (DTO) - Complete efficacy, safety/toxicity and PK studies of candidate oxime(s) for use against traditional nerve agents and NTAs. Down select the leading candidate oxime(s). Prepare a technical data package that supports requirements for an Investigational New Drug (IND) application and for transition of the best improved, broad-spectrum candidate oxime(s) out of the technology base.

Total 5500

	<u>FY 2002</u>	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
Pretreatments	3838	2128	3352	3107

FY 2002 Accomplishments:

- 1300 Pretreatments, Active Topical Skin Protectant (aTSP) (DTO) - Completed aTSP formulation studies and demonstrated efficacy against estimated exposure levels of chemical warfare agents (CWAs). Selected candidate(s) for transition out of technology base. Developed an M8 chemical agent paper test to evaluate effectiveness of topical skin protectant after challenge with CWAs. Developed and utilized a spectrophotometric method for proof of decontamination of the aTSP. Evaluated the efficacy of candidate aTSPs against cutaneous vapor and liquid sulfur mustard (HD).

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FY 2002 Accomplishments (Cont):

- 1000 Pretreatments, Chemical Agent Prophylaxis II (DTO) - Established higher animal species models to evaluate lead scavengers for safety and efficacy. Pursued development of behavioral safety testing procedures in higher animal species for chemical defense prophylactics. Evaluated and characterized enzyme identified as candidate for transition out of the technology base. Studied the effects of pretreatment with human butyrylcholinesterase scavengers on the toxicokinetics and binding of chemical warfare nerve agents in guinea pigs and higher animal species. Completed program studies and initiated preparation of a technical data package to address Food and Drug Administration (FDA) requirements for an Investigational New Drug (IND) application that supports transition out of the technology base.
- 1538 Pretreatments - Completed development/validation of a process capable of producing sufficient amounts of enzyme scavenger material for clinical trials. Studied safety and efficacy of catalytic scavenger candidates. Conducted pharmacology and toxicology studies on candidate compounds. Continued physiological pharmacokinetic studies of the catalytic scavengers identified (carboxylesterase and paraoxonase-1).

Total 3838

FY 2003 Planned Program:

- 2128 Pretreatments - Complete physiological pharmacokinetic model studies of expected human efficacy with various catalytic scavengers. Verify adequacy of transgenic animal model to produce recombinant catalytic enzyme scavenger.

Total 2128

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FY 2004 Planned Program:

- 3352 Pretreatments - Initiate evaluation of human protein catalytic scavenger. Utilize transgenic animal model to produce adequate amounts of recombinant catalytic enzyme scavenger for pre-clinical testing.

Total 3352

FY 2005 Planned Program:

- 3107 Pretreatments - Complete evaluation of human protein catalytic scavenger as a nerve agent countermeasure. Initiate preparation of technical data package for transition out of the technology base.

Total 3107

	<u>FY 2002</u>	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
Therapeutics	5003	6826	3626	2712

FY 2002 Accomplishments:

- 2000 Therapeutics, Medical Countermeasures for Vesicant Agents II (DTO) - Studied combination therapy approaches to provide protection in animal models. Conducted pharmacokinetic and formulation studies of vesicant countermeasure candidates. Initiated collection of pre-clinical data that will allow a preliminary safety assessment of toxicokinetics (TK) and absorption, distribution, metabolism, and excretion (ADME) of proposed treatments.

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<p>FY 2002 Accomplishments (Cont):</p> <ul style="list-style-type: none"> • 3003 Therapeutics - Determined optimal midazolam anticonvulsant and anticholinergic drug combination and order of administration to obtain maximal anticonvulsant effect against seizures in a higher animal species model. Conducted studies designed to address FDA requirements to license ocular rinse that optimally treats HD-induced injuries. Selected combination therapy approaches that provide highest level of ocular protection and conducted safety and efficacy advanced screening in animal models. Studied efficacy and safety of vesicant countermeasure candidates. Defined pharmacokinetics of anticonvulsant compound for organophosphate-acetylcholinesterase inhibitors. Initiated design of equipment for evaluation of therapeutic agents for pulmonary edema formation in mice following CWA exposure. <p>Total 5003</p> <p>FY 2003 Planned Program:</p> <ul style="list-style-type: none"> • 4000 Therapeutics, Medical Countermeasures for Vesicant Agents II (DTO) - Complete preclinical safety and efficacy studies of selected vesicant therapy candidate compounds. Complete pharmacokinetic studies of vesicant countermeasure candidates. Perform additional studies necessary to completely characterize candidate therapy. Transition vesicant therapeutic candidates out of the technology base. • 2826 Therapeutics - Select optimal anticholinergic drug for inclusion with midazolam anticonvulsant and establish optimal treatment protocol in higher animal species. Complete pre-clinical studies of selected vesicant therapy candidate compounds. Evaluate commercially licensed wound healing medical therapeutics for HD-induced injuries. Evaluate therapeutic agents for pulmonary edema produced by whole-body exposure to CWAs in animal models. <p>Total 6826</p>		
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FY 2004 Planned Program:

- 3626 Therapeutics - Determine efficacy of midazolam anticonvulsant and anticholinergic drug combinations against seizures and lethality produced by all current threat agents in the guinea pig model. Identify improved clinical strategies, such as skin grafting for HD wounds, for optimal treatment of CWA exposure and CWA contaminated conventional wounds.

Total 3626

FY 2005 Planned Program:

- 2712 Therapeutics - Assess application of emerging therapy for organophosphate insecticide poisoning to nerve agent exposure. Continue testing of midazolam and anticholinergic drug combinations against seizures and lethality produced by all current threat agents. Initiate pharmacokinetic evaluations of selected neuroprotectants, anticonvulsants, and antivesicants.

Total 2712

	<u>FY 2002</u>	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
Diagnostics	331	344	721	670

FY 2002 Accomplishments:

- 331 Diagnostics - Continued development of clinical laboratory and hand-held cholinesterase test devices. Evaluated commercially available off-the-shelf wound healing products for HD-induced injuries.

Total 331

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FY 2003 Planned Program:

- 344 Diagnostics - Evaluate hand-held cholinesterase monitor for clinical use. Validate immobilized cholinesterases and nerve agent hydrolyzing enzymes as diagnostics for nerve agent exposure.

Total 344

FY 2004 Planned Program:

- 721 Diagnostics - Develop and test a non-invasive prototype instrument that measures methemoglobin via finger, ear, or toe.

Total 721

FY 2005 Planned Program:

- 670 Diagnostics - Continue testing of acetylcholinesterase and methemoglobin monitor devices that allow instantaneous monitoring of the warfighter.

Total 670

	<u>FY 2002</u>	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
SBIR/STTR	0	172	0	0

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FY 2003 Planned Program:

- 172 SBIR

Total 172

C. <u>Other Program Funding Summary:</u>	<u>FY 2002</u>	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>	<u>FY 2006</u>	<u>FY 2007</u>	<u>FY 2008</u>	<u>FY 2009</u>	<u>To Compl</u>	<u>Total Cost</u>
MC4 MEDICAL CHEMICAL DEFENSE (ACD&P)	1828	1680	4798	9780	4511	4548	4566	4608	Cont	Cont
MC5 MEDICAL CHEMICAL DEFENSE (SDD)	1426	1926	1462	1419	7183	7214	7559	6261	Cont	Cont

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