CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2 Exhibit)

DATE
June 2001

BUDGET ACTIVITY
RDT&E DEFENSE-WIDE/
BA3 - Advanced Technology Development

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

	COST (In Thousands)	FY 2000 Actual	FY 2001 Estimate	FY 2002 Estimate							
	Total Program Element (PE) Cost	44705	59905	69249							
CB3	CHEMICAL BIOLOGICAL DEFENSE (ADV TECH DEV)	7590	16410	18688							
CP3	COUNTERPROLIFERATION SUPPORT (ADV TECH DEV)	10240	10245	12575							
TB3	MEDICAL BIOLOGICAL DEFENSE (ADV TECH DEV)	17710	22980	26611							
TC3	MEDICAL CHEMICAL DEFENSE (ADV TECH DEV)	9165	10270	11375							

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BUDGET ACTIVITY
RDT&E DEFENSE-WIDE/
BA3 - Advanced Technology Development

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

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. Work conducted under this PE transitions to and provides risk reduction for Demonstration/Validation (PE 0603884BP) and Engineering/Manufacturing Development (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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DATE: June 2001

BUDGET ACTIVITY: **RDT&E DEFENSE-WIDE/ BA3 - Advanced Technology Development**

PE NUMBER AND TITLE: **0603384BP CHEMICAL/BIOLOGICAL DEFENSE (ADVANCED DEVELOPMENT)**

B. Program Change Summary:	FY 2000	FY 2001	FY 2002	
FY 2001 President's Budget	56991	46594	53283	
Appropriated Value	57110	57894	0	
Adjustment to Appropriated Value	0	0	0	
a. Congressional General Reductions	0	-407	0	
b. SBIR/STTR	-825	0	0	
c. Omnibus or Other Above Threshold Reductions	-14815	0	0	
d. Below Threshold Reprogramming	3392	2550	0	
e. Rescissions	-157	-132	0	
Adjustments to Budget Years Since FY 2001 PB	0	0	15966	
FY2002/2003 President's Budget	44705	59905	69249	

Change Summary Explanation:

Funding: FY02 - Increases to the technology base to accelerate the investigation and development of CBD technologies, support response to emerging threat requirements, and protect critical technology base infrastructure. (CB3 $11,167K; CP3 $1.278K; TB3 $3,843K; TC3 $406K). General reduction to fund higher priority efforts (-$1,066K) and increase for inflation assumptions ($338K).

Schedule:

Technical:

CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2A Exhibit)

DATE: June 2001

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA3 - Advanced Technology Development	0603384BP CHEMICAL/BIOLOGICAL DEFENSE (ADVANCED DEVELOPMENT)	CB3

COST (In Thousands)		FY 2000 Actual	FY 2001 Estimate	FY 2002 Estimate							
CB3	CHEMICAL BIOLOGICAL DEFENSE (ADV TECH DEV)	7590	16410	18688							

A. Mission Description and Budget Item Justification:

Project CB3 CHEMICAL BIOLOGICAL DEFENSE (ADV TECH DEV): 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 Demonstration and Validation efforts. This project funds the Joint Service Fixed Site Decontamination (JSFXD) Program, the Joint Service Warning and Identification LIDAR (Light Detection And Ranging) Detector (JSWILD) Program,(JSWILD is transitioning to ARTEMIS in CP4, in FY01 and CA4, in FY02 and beyond.) the Joint Service Sensitive Equipment Decontamination (JSSED) Program, the Joint Chemical/Biological Agent Water Monitor (JCBAWM), the Joint Biological Standoff Detection System (JBSDS), and the Joint Service Wide Area Detector (JSWAD). Additionally, this program funds the Small Unit Biological Detector (SUBD), Consequence Management Interoperability Service (CMIS), and the force medical protection ACTD (formerly known as the Chemical Biological Individual Sampler (CBIS).

CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2A Exhibit)

DATE: June 2001

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA3 - Advanced Technology Development	0603384BP CHEMICAL/BIOLOGICAL DEFENSE (ADVANCED DEVELOPMENT)	CB3

FY 2000 Accomplishments:

▪	5001	JSWILD - Continued fabrication of brass-board system to include high energy laser, custom electronics and software, and advanced algorithms for complete hemispherical detection of chemical materials such as rains, aerosols, and vapors at tens of kilometers range. Initiated AoA for technology and completed planning for demonstration.
▪	1260	JSSED - Conducted a formal AoA validating the three-block approach to solve JSSED requirements. Completed required acquisition documentation and prepared statements of work for acquisition contracts. Initiated an effort to transfer Block I technology approach into a suitable candidate for Block III operational decontamination. Examined the potential use of combined thermal/steam approaches to address JSSED Block II decontamination.
▪	329	Monopack and Residual Life Initiatives - Transitioned a candidate material (monopack) to the Joint Protective Aircrew Ensemble program. Completed the technology survey and identified the four best technical approaches to develop residual life indicators for protective clothing.
▪	1000	JSFXD - Completed MS I documentation for Blocks I, II, and III of the program representing respectively, a family of decontaminants, family of applicators, and decontamination of skin and casualties. Conducted FEA for skin contaminants. Completed draft reports on the phase one evaluation of eight candidate decontamination systems to include: chemical efficacy (reaction kinetics and product studies, residual post decontamination contact hazard and off-gassing hazard); assessment of bio-simulant efficacy; compatibility test with a variety of materials; detector interference evaluation; and a literature review and assessment of the toxicology and environmental soundness of the components contained in the decontaminants.
Total	7590	

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DATE: June 2001

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA3 - Advanced Technology Development	0603384BP CHEMICAL/BIOLOGICAL DEFENSE (ADVANCED DEVELOPMENT)	CB3

FY 2001 Planned Program:

▪	2142	JSWILD - Complete build of, and demonstrate, brassboard system, and transition technology to ARTEMIS (Active Standoff CW Detection System).
▪	2386	JSSED - Conduct development of sensitive equipment/items decontamination technologies (Block I) with emphasis on the advanced development of technologies for interior decontamination (Block II/III).
▪	2388	Detection Technologies - Evaluate and support accelerated efforts on technologies with significant potential for demonstration in various Advanced Concept Technology Demonstrations (ACTD) and upcoming mature programs. Effort involves hyperspectral imaging and a test representative radar system to provide cueing and early warning capabilities.
▪	2702	Chemical/Biological Advanced Materials Research - Demonstrate the value of advanced material used in protection concepts for filtration, clothing, and tentage.
▪	742	SUBD - Advance the current component technologies to a final configuration and pay for contract closeout and archiving of data.
▪	3842	CMIS - Start development of a "common operating view" that enables DOD secondary responders to view tactical information in advance of arriving at the scene of a Weapons of Mass Destruction (WMD) incident. Tailor Commercial Off-The-Shelf (COTS) software that is adapted to the "lowest common denominator." Evaluate Geospatial Information System (GIS) data and applications for WMD incidents.
▪	1930	Chemical Biological Individual Sampler (CBIS) - Conduct testing and validation of COTS passive chemical samplers as well as develop the standard analytical method for these samplers. Conduct demonstrations that address critical operations issues.
▪	278	SBIR
Total	16410	

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DATE: June 2001

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA3 - Advanced Technology Development	0603384BP CHEMICAL/BIOLOGICAL DEFENSE (ADVANCED DEVELOPMENT)	CB3

FY 2002 Planned Program:

- 2010 JSSED - Evaluate Block II/III technologies. Perform agent chamber/panel tests to validate performance of candidate technologies on a variety of surfaces. Address material compatibility issues. Initiate documentation of technology findings to support transition to development.
- 503 JSFXD Block III - Conduct down selection screen of candidate skin decontamination identified in the FEA. Compare to baseline M-291 kit. Candidate technologies include the nanoemulsion system developed by the DARPA program and a foam system developed under the Department of Energy Chemical Biological National Security Program. Transition optimal candidate(s) to JSFXD Demonstration/Validation phase for insertion into the FDA approval process.
- 750 Foam Based Decontamination Systems - Conduct evaluation of and modify the DOE foam based decontamination system to meet military challenge levels. Extend the test bed to include Fourth Generation Agents.
- 500 Detection Technologies - Complete assessment of hyperspectral imaging technologies and establish transition points for the highest potential payoff capabilities.
- 2375 JCBAWM - Initiate planning for technology transition to Program Definition and Risk Reduction (PDRR). Initiate design and build of brassboard system for demonstration.
- 2000 Portable Chemical/Biological Detection Technologies - Initiate evaluation of technologies from all sources for feasibility in application to military requirements for potentially man-portable multi-agent chemical and biological detectors with reduced logistics burden. The effort will focus on performance characterization and chamber test with identification of technological shortfalls. Specific initial candidates include DOE micro-CB lab, pyrolysis-GC/IMS, optical particle classifier.

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DATE: June 2001

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA3 - Advanced Technology Development	0603384BP CHEMICAL/BIOLOGICAL DEFENSE (ADVANCED DEVELOPMENT)	CB3

FY 2002 Planned Program (Cont):

- 3550 Biological Detection Technologies - Develop assays and initiate live agent testing of DARPA Micro Array of Gel-Immobilized Compounds (MAGIChip) nucleic acid identification technology for Bacillus species. Initiate automation of DARPA-developed ultraviolet-infrared matrix-assisted laser desorption (MALDI) mass spectrometry (MS). Initiate comparative evaluation for sensitivity and discrimination capability of UV-MALDI and UV-IR MALDI MS candidates from DARPA and electrospray ionization (ESI) MS using aerosol collections in chamber tests. Identify sample processing challenges for improvement.
- 2000 Joint Field Trials - Expand the biological Joint Field Trial concept to a multi-tiered set of evaluation protocols to facilitate the characterization of candidate technology at varying levels of maturity.
- 2000 CB Modeling/Simulation - Accelerate development and demonstration of models describing impacts of CBW on site operations.
- 3000 Technology Transition - Conduct acceptance testing of anthrax antibody mixtures under development for improved affinity. Complete testing of upconverting phosphors. Implement improved sample treatment procedures for MALDI-TOF mass spectrometer and prepare for field evaluation.

Total 18688

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DATE: June 2001

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA3 - Advanced Technology Development	0603384BP CHEMICAL/BIOLOGICAL DEFENSE (ADVANCED DEVELOPMENT)	CP3

COST (In Thousands)		FY 2000 Actual	FY 2001 Estimate	FY 2002 Estimate							
CP3	COUNTERPROLIFERATION SUPPORT (ADV TECH DEV)	10240	10245	12575							

A. Mission Description and Budget Item Justification:

Project CP3 COUNTERPROLIFERATION SUPPORT (ADV TECH DEV): The mission of the Counterproliferation Program (CP) is to address shortfalls in the Department of Defense (DoD) deployed 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), Biological Non-Systems (BIO Non Sys) efforts, Critical Reagents Program (CRP), Restoration of Operations (RESTOPS) and a Planning and Development for Advanced Concept Technology Demonstrations (ACTD-PD).

CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2A Exhibit)

DATE: June 2001

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA3 - Advanced Technology Development	0603384BP CHEMICAL/BIOLOGICAL DEFENSE (ADVANCED DEVELOPMENT)	CP3

FY 2000 Accomplishments:

▪	2818	BIODET - Initiated development of biological identification system using nucleic acids to allow for a less expensive and broader biological detection capability. Transitioned upconverting phosphor technology development and explored effectiveness in assays. Tested first generation of Biological Time of Flight Mass Spectrometer in Joint Field Trial Testing. System deemed not ready for transition to prototype development.
▪	382	CRP - Developed recombinant reagents to increase specificity/sensitivity and lower production costs.
▪	3280	BIO Non Sys - Initiated development of automated sample preparation technology for Polymerase Chain Reaction (PCR) devices. Initiated development and evaluation of a generic detector, Time of Flight Mass Spec/Mass Spec (TOF MS/MS), multiplexed assays and associated reagents, and investigated Red Team recommendations. Supported the development of a small, portable, single assay, PCR detector for testing in Joint Field Trials.
▪	3760	RESTOPS - Initiated development of next generation chemical/biological transport models (to include complex terrain and urban environment) and simulations for Commander in Chief (CINC) Logistics/Warfighting Planning Tools for use in the RestOps ACTD. Initiated development of novel universal chemical/biological decontaminants for use in the RestOps ACTD and fixed site decontamination programs.
Total	10240	

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DATE: June 2001

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA3 - Advanced Technology Development	0603384BP CHEMICAL/BIOLOGICAL DEFENSE (ADVANCED DEVELOPMENT)	CP3

FY 2001 Planned Program:

▪	974	ACTD-PD - Perform technology maturity evaluations for selection of technologies for Integrated Chemical Biological ACTD.
▪	1779	BIODET - Produce nucleic acid primer libraries for testing and continue development of a biological detection capability using nucleic acids. Transition to CB3 for test, evaluation, and further assay development against live agents under tech transfer funds.
▪	378	CRP - Continue to develop reagents (antibodies and antigens) that are critical to the development, testing, and support of CP biological detection systems.
▪	5917	BIO Non Sys - Continue development and evaluation of generic detectors (TOF MS/MS, Ultra Violet) and associated algorithms to provide increased warning time for tactical battlefield applications. Continue development, testing, and evaluation of automated sample preparation technology and protocols for Polymerase Chain Reaction (PCR) devices to improve identification specificity and sensitivity in future biological systems.
▪	1024	RESTOPS - Continue development of universal novel chemical/biological decontaminants for use in the RestOps ACTD and fixed site decontamination programs. Initiate synthetic environment tool for technology selection for RestOps scenarios. Initiate testing of warfare agents on RestOps scenario surfaces for use in modeling and simulation. Initiate development of maturing technologies for RestOps demonstrations.
▪	173	SBIR
Total	10245	

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DATE: June 2001

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA3 - Advanced Technology Development	0603384BP CHEMICAL/BIOLOGICAL DEFENSE (ADVANCED DEVELOPMENT)	CP3

FY 2002 Planned Program:

▪	1928	ACTD-PD - Perform technology maturity evaluations, perform analysis of alternative technologies, and prepare acquisition strategy for Contamination Avoidance for Seaports of Debarkation (CASPOD) Advanced Concept Technology Demonstration.
▪	2487	BIO Non Sys - Initiate development and testing of improved UV detectors, UV micro-lasers, and algorithms. Initiate prototype development and testing of an optical based detector using high affinity nucleic acid aptamer chips. Initiate challenges to detector systems in development using Red Teams. Initiate development and testing of a new improved collector/concentrator and pre-separator devices for filtering and cleaning environment air samples.
▪	3684	BIO Non Sys - Continue development and evaluation of generic detectors (TOF MS/MS, UV) and associated algorithms to provide increased warning time for tactical battlefield applications. Continue development, testing, and evaluation of automated sample preparation technology and protocols for Polymerase Chain Reaction (PCR) devices to improve identification specificity and sensitivity in future biological systems.
▪	3000	BIO Non Sys - Develop decontaminants, equipment, procedures, techniques, and tactics for decontamination of wide body and other aircraft.
▪	1476	RESTOPS - Continue synthetic environment tool for technology selection for RestOps scenarios. Continue testing of warfare agents on RestOps scenario surfaces for use in modeling and simulation. Continue development of maturing technologies for RestOps demonstrations.
Total	12575	

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BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA3 - Advanced Technology Development	0603384BP CHEMICAL/BIOLOGICAL DEFENSE (ADVANCED DEVELOPMENT)	TB3

COST (In Thousands)		FY 2000 Actual	FY 2001 Estimate	FY 2002 Estimate							
TB3	MEDICAL BIOLOGICAL DEFENSE (ADV TECH DEV)	17710	22980	26611							

A. Mission Description and Budget Item Justification:

Project TB3 MEDICAL BIOLOGICAL DEFENSE (ADV TECH DEV): 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); current Science and Technology Plans (STEPs) in medical biological defense (diagnostic technology, bacterial therapeutics, toxin therapeutics, viral therapeutics, bacterial vaccines, toxin vaccines, and viral vaccines), directed research efforts (Bioadhesion Research and Medical Chemical/Biological Counterterrorism Support); and efforts to transition promising medical biological defense technologies from the Defense Advanced Research Projects Agency (DARPA).

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DATE: June 2001

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA3 - Advanced Technology Development	0603384BP CHEMICAL/BIOLOGICAL DEFENSE (ADVANCED DEVELOPMENT)	TB3

FY 2000 Accomplishments:

- 1000 Common Diagnostic Systems (DTO) - Demonstrated alternative technical options that are compatible with the field medical laboratory for portable nucleic analysis of a broad range of biological threat agents in laboratory-based studies.
- 600 Medical Countermeasures for Encephalitis Viruses (DTO) - Developed vaccine candidates for Venezuelan equine encephalitis (VEE) virus type 1E and western equine encephalitis virus and tested for safety in animals.
- 1900 Medical Countermeasures for Staphylococcal Enterotoxins (SE) (DTO) - Recommended SE vaccine candidate for transition to advanced development. Defined manufacturing process and produced clinical grade SEB. Determined that neutralizing antibody response is a relevant surrogate endpoint of clinical efficacy. Completed dose and schedule studies needed for human clinical trial recommendations. Completed a pre-read package for submission to the FDA for preliminary regulatory evaluation of the SE vaccine candidate.
- 900 Multiagent Vaccines for Biological Threat Agents (DTO) - Compared and assessed the immunogenicity of individual and combined vaccine components in vaccine delivery platforms that could serve as multiagent vaccines.
- 1097 Diagnostic Technologies - Compared the performance characteristics of new medical diagnostic approaches, reagents, and devices for the rapid recognition of infections caused by Bacillus anthracis (B. anthracis), Yersinia pestis (Y. pestis), Francisella tularensis (F. tularensis), Brucella sp., alphaviruses, and filoviruses in laboratory-based studies. Compared technical options such as enzyme-linked immunosorbent, electrochemiluminescence, and time resolved fluorescence assays for more sensitive immunodetection of bacterial antigens and toxins in laboratory-based studies.
- 193 Therapeutics, Bacterial - Correlated in vitro antibiotic sensitivity results on Burkholderia mallei (B. mallei) (glanders) with a case study, and recommended a treatment regime for human glanders based on these data.
- 1939 Therapeutics, Toxin - Evaluated efficacy of licensed drugs (e.g., pentoxifylline) that inhibit SE-induced pro-inflammatory cytokines and are protective after a lethal SEB exposure.

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RDT&E DEFENSE-WIDE/ BA3 - Advanced Technology Development	0603384BP CHEMICAL/BIOLOGICAL DEFENSE (ADVANCED DEVELOPMENT)	TB3

FY 2000 Accomplishments (Cont):

- 1934 Therapeutics, Viral - Compared efficacy in cell culture of candidate antiviral drugs against more than 40 different isolates of variola at the Centers for Disease Control and Prevention. Showed protection of candidate drugs in the lethal aerosol cowpox-mouse model.
- 1143 Vaccines, Bacterial - Compared the currently licensed anthrax vaccine with an investigational next generation (recombinant) anthrax vaccine in the rabbit model; completed transitional studies to facilitate movement of the plague vaccine candidate into advanced development. Evaluated double deletion mutants of B. melitensis in animals and in cultured macrophages for assessment as candidate live, attenuated vaccine strains.
- 2203 Vaccines, Toxin - Finalized preparation of scientific, technical, and regulatory documentation in accordance with FDA and DoD acquisition requirements (transition documentation) supporting the Milestone (MS) I transition of the recombinant multivalent vaccine candidate for botulinum neurotoxins (serotypes A,B,C, and F) and continued process development of serotype E. Made transition recommendation for the chemically deglycosylated ricin A-chain vaccine candidate. Produced genetically engineered antigen candidates using computational design. Developed model systems to evaluate subunit inactivation.
- 1987 Vaccines, Viral - Determined that protection from one Musoke isolate of Marburg virus (MBGV) could protect from Ravn isolate in nonhuman primates.
- 1398 Bioadhesion Research - Initiated in-house and extramural review of a proposal to scientifically and technically evaluate mechanisms that block the adhesion of specific molecules thereby preventing initiation of the disease/toxic process. The proposed research is aimed toward the development of medical countermeasures to two biological warfare threats (B. anthracis and Brucellae spp.) and an infectious disease agent (Norwalk virus).

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BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA3 - Advanced Technology Development	0603384BP CHEMICAL/BIOLOGICAL DEFENSE (ADVANCED DEVELOPMENT)	TB3

FY 2000 Accomplishments (Cont):

- 1416 Medical Chemical/Biological Counterterrorism Support - Requested a proposal for research on the development of technologies to identify chemical and biological warfare agents (CBWA); laboratory procedures specific for the medical diagnosis or identification of CBWA exposure; information relevant to the collection of biological samples (blood, urine, or skin biopsy); and basic training in assay use and transition. The goal is to develop assays for use by the newly constituted National Guard Mobile Analytical Laboratory System.

Total 17710

FY 2001 Planned Program:

- 1000 Common Diagnostic Systems (DTO) - Conduct laboratory-based and field-based evaluation of portable nucleic acid analysis systems that enhance the diagnostic capabilities of field medical laboratories. Evaluate competing technical options for their operational compatibility with the field medical laboratory and a highly regulated medical center clinical laboratory.
- 1400 Medical Countermeasures for Brucella (DTO) - Determine the minimum immunogenic oral dose of the most promising live, attenuated vaccine candidate in nonhuman primates. Establish fermentation conditions for growth of live, attenuated vaccine strain and prepare research master seed and research production seed stocks using processes defined to a level consistent with the intent of current Good Manufacturing Practices (cGMP).
- 600 Medical Countermeasures for Encephalitis Viruses (DTO) - Test vaccine candidates for VEE virus type 1E and western equine encephalitis virus for efficacy in rodent animal models. Test the VEE virus type 1E candidates for safety and efficacy in the nonhuman primate model and define surrogate markers of protection for validation as acceptable markers of vaccine efficacy.

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BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA3 - Advanced Technology Development	0603384BP CHEMICAL/BIOLOGICAL DEFENSE (ADVANCED DEVELOPMENT)	TB3

FY 2001 Planned Program (Cont):

- 1500 Multiagent Vaccines for Biological Threat Agents (DTO) - Test safety and efficacy in animals, of products (individually and combined) intended for use in multiagent vaccines. Develop efficient production protocols compliant with FDA regulations for scale-up production of VEE replicon platform system.
- 914 Needleless Delivery Methods for Recombinant Protein Vaccines (DTO) - Optimize needleless vaccine system components. Establish protocols for studies in animal models. Standardize assays to quantitate toxin-specific antibodies and other indicators of immunity. Standardize animal models.
- 650 Recombinant Plague Vaccine Candidate (DTO) - Prepare a technical data package to support transition to advanced development.
- 750 Recombinant Protective Antigen (rPA) Anthrax Vaccine Candidate (DTO) - Perform comparative efficacy studies in animal models with rPA with AVA. Conduct rPA- and AVA-immune passive transfer studies with homologous sera in mice and rabbits and complete technical data package supporting transition to advanced development.
- 1643 Diagnostic Technologies - Compare alternative medical diagnostic technologies and specimen-processing methods compatible with a comprehensive integrated medical diagnostic system for the rapid recognition of infections by validated biological threats (bacteria, viruses, and toxins) in laboratory-based and field-based studies.
- 818 Therapeutics, Bacterial - Test selected immunomodulators in appropriate animal models for protection against plague and glanders.
- 566 Therapeutics, Toxin - Begin stability testing of the recombinant ricin A-chain that is being used for enzymatic activity studies.
- 1257 Therapeutics, Viral - Determine dose and schedule for lead antiviral drug candidate for intravenous treatment of smallpox. Develop formulations or prodrugs to overcome problems with metabolism, bioavailability, or pharmacokinetics of compounds with otherwise acceptable antiviral profiles for orthopox and filoviruses.

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RDT&E DEFENSE-WIDE/ BA3 - Advanced Technology Development	0603384BP CHEMICAL/BIOLOGICAL DEFENSE (ADVANCED DEVELOPMENT)	TB3

FY 2001 Planned Program (Cont):

- 402 Vaccines, Bacterial - Explore laboratory formulations of candidate glanders and plague vaccines using various adjuvants to enhance immunogenicity.
- 250 Vaccines, Bacterial - Explore laboratory formulations of candidate next generation anthrax vaccine using various adjuvants to enhance immunogenicity.
- 4209 Vaccines, Toxin - Complete the process development (60 L scale-up) for vaccine botulinum toxin serotypes C1 and E in the Pichia yeast system and complete efficacy studies in animal models. Initiate formulation studies on a combinatorial recombinant pentavalent botulinum toxin vaccine. Develop reagents and assays to determine the quality and quantity of botulinum toxin, SE, and ricin vaccines during process development. Prepare technical data package to support IND submission to the FDA for SE vaccine candidate.
- 1443 Vaccines, Viral - Test prime-boost vaccine candidates for Ebola virus in nonhuman primate models. Test VEE replicon-based vaccines packaged in different glycoproteins for immunogenicity and protection against Ebola virus.
- 2000 DARPA Program Transition - Evaluate promising medical biological defense technologies transitioning from DARPA such as plant-based expression of antibodies, novel antiviral agents, and novel vaccine approaches.
- 1500 Bioadhesion Research - Continue research to evaluate mechanisms that block the adhesion of specific molecules thereby preventing initiation of the disease/toxic process. The research is aimed toward the development of medical countermeasures for two biological warfare threats (B. anthracis and Brucellae spp.) and an infectious disease agent (Norwalk virus).

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DATE: June 2001

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA3 - Advanced Technology Development	0603384BP CHEMICAL/BIOLOGICAL DEFENSE (ADVANCED DEVELOPMENT)	TB3

FY 2001 Planned Program (Cont):

▪	1689	Medical Chemical/Biological Counterterrorism Support - Continue research on the development of technologies to identify chemical and biological warfare agents (CBWA); laboratory procedures specific for the medical diagnosis or identification of CBWA exposure; information relevant to the collection of biological samples (blood, urine, or skin biopsy); and basic training in assay use and transition. The goal is to develop assays for use by the newly constituted National Guard Mobile Analytical Laboratory System.
▪	389	SBIR
Total	22980	

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DATE: June 2001

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA3 - Advanced Technology Development	0603384BP CHEMICAL/BIOLOGICAL DEFENSE (ADVANCED DEVELOPMENT)	TB3

FY 2002 Planned Program:

- 1000 Common Diagnostic Systems (DTO) - Complete 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. Prepare technical data package to support submission of a medical device application to the FDA prior to transitioning the candidate to Demonstration and Validation.
- 1600 Medical Countermeasures for Brucella (DTO) - Prepare pilot lot of most promising live, attenuated vaccine candidate using processes consistent with the intent of cGMP and use the pilot vaccine lot to perform pre-IND animal studies. If more than one vaccine candidate is available, determine relative efficacy against B. melitensis in nonhuman primate aerosol challenge model.
- 800 Medical Countermeasures for Encephalitis Viruses (DTO) - Test vaccine candidates for VEE virus type 3 and eastern equine encephalitis (EEE) virus for efficacy in rodent animal models. Test the western equine encephalitis and EEE candidates for safety and efficacy in the nonhuman primate model and define surrogate markers of protection for validation as acceptable markers of vaccine efficacy.
- 1700 Multiagent Vaccines for Biological Threat Agents (DTO) - Complete testing for safety and efficacy in animal models of products (individually and combined) intended for use in a multiagent vaccines.
- 1205 Needleless Delivery Methods for Recombinant Protein Vaccines (DTO) - Define the quantitative relationships between toxin-specific antibodies or other indicators of immunity in mucosal surfaces and blood.
- 940 Recombinant Plague Vaccine Candidate (DTO) - Continue expanded animal studies for immunogenicity and efficacy including the evaluation of long term immunity in nonhuman primates. Continue to optimize formulation of the recombinant plague vaccine candidate.
- 1500 Recombinant Protective Antigen (rPA) Anthrax Vaccine Candidate (DTO) - Evaluate efficacy of rPA in non-human primates and perform passive transfer studies with human AVA-immunized sera in mice and rabbits.

CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2A Exhibit)

DATE: June 2001

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA3 - Advanced Technology Development	0603384BP CHEMICAL/BIOLOGICAL DEFENSE (ADVANCED DEVELOPMENT)	TB3

FY 2002 Planned Program (Cont):

- 2033 Diagnostic Technologies - Compare new diagnostic reagents, devices, and protocols in preclinical studies before transition to the regulatory-compliant medical laboratory. Evaluate candidate diagnostic technologies in field-based studies and in a highly regulated medical center clinical laboratory prior to transitioning to Demonstration and Validation.
- 955 Therapeutics, Bacterial - Evaluate in animal models selected immunomodulators in combination with efficacious antibiotics for protection against bacterial threat agents.
- 4121 Therapeutics, Toxin - Optimize formulation and pharmacodynamics of lead candidate licensed drugs that also inhibit SE-induced intoxication.
- 1910 Therapeutics, Viral - Continue evaluating formulations or prodrugs to overcome problems with metabolism, bioavailability, or pharmacokinetics of compounds with otherwise acceptable antiviral profiles for orthopox and filoviruses.
- 331 Vaccines, Bacterial - Validate correlates of immunity for protection against B. anthracis; evaluate vaccine candidates and correlates of immunity for B. mallei.
- 171 Vaccines, Toxin - Complete formulation studies on a combinatorial recombinant pentavalent botulinum toxin vaccine. Initiate formulation studies on a combinatorial SE vaccine. Complete development of reagents and assays to determine the quality and quantity of recombinant botulinum and SE vaccines during process development. Initiate the process development (60 L scale-up) for botulinum toxin serotypes D and G in the Pichia yeast system and complete efficacy studies. Initiate the process development for SE serotype A and complete efficacy studies. Initiate in vivo concept model systems for assessment of vaccine efficacy and surrogate endpoints of human clinical efficacy for botulinum toxin and SE intoxication.
- 1345 Vaccines, Viral - Determine optimal dose and schedule for vaccination against MBGV. Demonstrate in pivotal animal studies that the vaccine candidate is efficacious against aerosol infection with MBGV.

CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2A Exhibit)

DATE: June 2001

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA3 - Advanced Technology Development	0603384BP CHEMICAL/BIOLOGICAL DEFENSE (ADVANCED DEVELOPMENT)	TB3

FY 2002 Planned Program (Cont):

- 4000 DARPA Program Transition - Expand DARPA transition efforts to include novel molecular method for selecting vaccine antigens, additional antiviral agents, and evaluation of plant-based antibodies as therapeutic agents.
- 1250 Vaccines - Enhance advanced technology development efforts toward innovative approaches for the development and delivery of next generation and generation-after-next vaccines and strategies to enhance the immune response to broad classes of biological threats.
- 1250 Medical Countermeasures - Enhance advanced technology development efforts toward the development of broad-spectrum therapeutic countermeasures for exposure to broad classes of biological threats.
- 500 Advanced Diagnostics - Enhance advanced technology development efforts toward the development of advanced medical diagnostic capabilities.

Total 26611

CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2A Exhibit)

DATE: **June 2001**

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA3 - Advanced Technology Development	**0603384BP CHEMICAL/BIOLOGICAL DEFENSE (ADVANCED DEVELOPMENT)**	**TC3**

COST (In Thousands)		FY 2000 Actual	FY 2001 Estimate	FY 2002 Estimate							
TC3	MEDICAL CHEMICAL DEFENSE (ADV TECH DEV)	9165	10270	11375							

A. Mission Description and Budget Item Justification:

Project TC3 MEDICAL CHEMICAL DEFENSE (ADV TECH DEV): 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 and safety and efficacy screening, in addition to 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 plans (Pretreatments, Therapeutics, and Diagnostics), and directed research on Low Level Chemical Agent Exposure and Fourth Generation Agents.

CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2A Exhibit)

DATE: June 2001

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA3 - Advanced Technology Development	0603384BP CHEMICAL/BIOLOGICAL DEFENSE (ADVANCED DEVELOPMENT)	TC3

FY 2000 Accomplishments:

1300	Active Topical Skin Protectant (DTO) - Advanced the active topical skin protectant (aTSP) research program to MS A. Initiated studies for efficacy and safety of best candidate reactive moieties for aTSP.
600	Chemical Agent Prophylaxis II (DTO) - Initiated studies for efficacy and safety of lead candidate bioscavengers. Estimated the protection achievable by lead candidate scavengers in animal models.
4999	Medical Countermeasures against Vesicants (DTO) - Acquired drugs/compounds in forms acceptable for advanced antivesicant testing. Selected lead candidate countermeasures from in vivo and in vitro screens. Transitioned selected vesicant therapy candidates to MS A. Continued studies of off-the-shelf compound(s) safety and efficacy as therapies for vesicant-induced injury.
97	Diagnostics - Developed an analytical procedure that can measure blister agent sulfur mustard (HD)/DNA adducts for diagnosis of HD exposure in the warfighter for up to seven days after exposure. Developed a gas chromatography/mass spectrometry procedure that measures HD/albumin adducts in plasma with a limit of detection at 1 nM HD exposure, potentially detecting HD levels up to 30 days after exposure.
699	Pretreatments - Expanded physiologically based/pharmacokinetic models to include scavengers in the presence and absence of CW agents.
195	Therapeutics - Determined the efficacy of midazolam against nerve agent seizures in guinea pigs and rhesus monkeys. Transitioned midazolam to Advanced Development.
1275	Low Level Chemical Warfare Agent Exposure - Investigated the effects of sarin, pyridostigmine, botulinum toxins, and pesticides in non-human primates. Studied long-term effects to humans of exposure to nerve agent using data from research done between 1955-1975.
Total 9165	

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DATE: June 2001

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA3 - Advanced Technology Development	0603384BP CHEMICAL/BIOLOGICAL DEFENSE (ADVANCED DEVELOPMENT)	TC3

FY 2001 Planned Program:

- 1300 Active Topical Skin Protectant (DTO) - Demonstrate the efficacy of aTSP candidate formulations in two animal species. Evaluate effectiveness of combinations of selected reactive moieties.
- 700 Chemical Agent Prophylaxis II (DTO) - Examine scavengers derived from human proteins for immune response. Select best nerve agent bioscavenger candidate(s) based on comparison of performance in decision tree network and other differentiating studies.
- 1000 Medical Countermeasures for Vesicant Agents II (DTO) - Evaluate efficacy of lead vesicant countermeasure compounds identified in earlier screening efforts using a decision tree network. Begin vesicant therapy candidate safety and efficacy studies in two animal models.
- 56 Diagnostics - Evaluate modified advanced development equipment or technologies for far-forward screening and confirmation of exposure to blister and nerve agents. Conduct surveys of existing commercial technologies and test suitability of these items.
- 1797 Pretreatments - Test promising new catalytic scavengers for efficacy and safety in two animal models. Determine 3D x-ray crystallographic structure of human carboxylesterase and paraoxon-1.
- 4243 Therapeutics - Evaluate the efficacy of lead vesicant countermeasure compounds identified in earlier screening efforts using a drug decision approach (decision tree network). Begin vesicant candidate safety and efficacy studies in two animal models. Evaluate the optimal treatment strategy for mustard-induced ocular injury using steroid/antibiotic combinations. Evaluate commercially available off-the-shelf wound healing products to treat HD-induced injuries. Determine best anticholinergic(s) for use with midazolam as therapy for nerve agent exposure.
- 1000 Fourth Generation Agents - Select best countermeasures to Fourth Generation Agents based on comparison of protection against lethality, pathology, physiological dysfunction, and behavioral incapacitation.
- 174 SBIR

CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2A Exhibit)

DATE: June 2001

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA3 - Advanced Technology Development	0603384BP CHEMICAL/BIOLOGICAL DEFENSE (ADVANCED DEVELOPMENT)	TC3

FY 2001 Planned Program (Cont):
Total 10270

FY 2002 Planned Program:

- 1300 Active Topical Skin Protectant (DTO) - Complete aTSP formulation studies and demonstrate efficacy against estimated battlefield levels of chemical warfare agents. Select the best candidate(s) for transition to Demonstration and Validation.
- 1000 Chemical Agent Prophylaxis II (DTO) - Establish nonhuman primate animal models to evaluate lead scavengers for safety and efficacy. Convene Milestone I IPR to approve transition of candidate(s) scavengers to advanced development. Transition a chemical warfare agent prophylactic that will protect the warfighter for a period greater than eight hours against exposure to five times the Median Lethal Dosage (LD50) of nerve agent.
- 2000 Medical Countermeasures for Vesicant Agents II (DTO) - Select combination therapy approaches that provide highest level of protection in animal models for safety and efficacy advanced screening. Conduct pharmacokinetic and formulation studies of vesicant countermeasure candidates. Initiate collection of preclinical data that will allow a preliminary assessment of safety. Begin discussion with developer to design GLP studies.
- 829 Diagnostics - Test a prototype noninvasive monitor that measures oxyhemoglobin, deoxyhemoglobin, methemoglobin, and carboxyhemoglobin via finger, ear, or toe.
- 1310 Pretreatments - Complete development/validation of a transgenic animal model capable of producing sufficient amounts of recombinant enzyme scavenger material for clinical trials. Produce nerve agent scavengers in transgenic models and test for safety and efficacy in two animal species. Complete physiologically based pharmacokinetic model studies of expected human efficacy with various scavengers to assist in an IPR downselect process.

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DATE: June 2001

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA3 - Advanced Technology Development	0603384BP CHEMICAL/BIOLOGICAL DEFENSE (ADVANCED DEVELOPMENT)	TC3

FY 2002 Planned Program (Cont):

▪	3436	Therapeutics - Determine optimal combination of midazolam and anticholinergic drug and order of administration tc obtain maximal anticonvulsant effect against seizures in a nonhuman primate model. Conduct studies directed at obtaining Food and Drug Administration (FDA) approval for an ocular rinse that optimally treats mustard-induced injuries. Select combination therapy approaches that provide highest level of protection in animal models for safety and efficacy advanced screening. Conduct pharmacokinetics and formulation studies of vesicant countermeasure candidates. Study efficacy and safety of vesicant countermeasure candidates. Determine window of opportunity for administration of therapy(s) for blister agent HD exposure.
▪	1500	Fourth Generation Agents - Begin downselect process of best available countermeasure(s) against Fourth Generation Agents. Initiate formulation and bulk production feasibility efforts.
Total	11375	