CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2 Exhibit)

DATE: **February 2002**

BUDGET ACTIVITY: **RDT&E DEFENSE-WIDE/ BA2 - Applied Research**

PE NUMBER AND TITLE: **0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)**

COST (In Thousands)		FY 2001 Actual	FY 2002 Estimate	FY 2003 Estimate	FY 2004 Estimate	FY 2005 Estimate	FY 2006 Estimate	FY 2007 Estimate	Cost to Complete	Total Cost
	Total Program Element (PE) Cost	93172	146431	262177	95242	94494	92528	91171	Continuing	Continuing
CB2	CHEMICAL BIOLOGICAL DEFENSE (APPLIED RESEARCH)	56925	91432	68817	54007	52828	56281	54451	Continuing	Continuing
HS2	HOMELAND SECURITY (APPLIED RESEARCH)	0	0	137000	0	0	0	0	0	137000
TB2	MEDICAL BIOLOGICAL DEFENSE (APPLIED RESEARCH)	22428	36513	38386	24085	25097	17826	18148	Continuing	Continuing
TC2	MEDICAL CHEMICAL DEFENSE (APPLIED RESEARCH)	13819	18486	17974	17150	16569	18421	18572	Continuing	Continuing

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DATE: **February 2002**

BUDGET ACTIVITY: **RDT&E DEFENSE-WIDE/ BA2 - Applied Research**

PE NUMBER AND TITLE: **0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)**

A. Mission Description and Budget Item Justification: The use of chemical and biological weapon systems in future conflicts is an increasing threat to the United States. Funding under this PE sustains a robust program, which reduces the danger of a chemical and/or biological (CB) attack and enables U.S. forces to survive and continue operations in a CB environment. The medical program focuses on development of vaccines, pretreatment and therapeutic drugs, and on casualty diagnosis, patient decontamination, and medical management. In the non-medical area, the emphasis is on continuing improvements in CB defense materiel, including contamination avoidance, decontamination, and protection systems. This program also provides for conduct of applied research in the areas of real-time sensing and immediate biological countermeasures. This PE also provides for investigative efforts to perform a Homeland Security requirements process, concept and technology demonstrations of new system concepts that will shape the development for environmental monitoring, medical surveillance, and data mining/fusion/analysis subsystems. The work in this PE is consistent with the Joint Service NBC Defense Research, Development, and Acquisition (RDA) Plan. Efforts under this PE transition to and provide risk reduction for Advanced Technology Development (PE 0603384BP), Demonstration/Validation (PE 0603884BP), and Engineering and Manufacturing Development (PE 0604384BP). This project includes non-system specific development directed toward specific military needs and therefore is correctly placed in Budget Activity 2.

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DATE: **February 2002**

BUDGET ACTIVITY: **RDT&E DEFENSE-WIDE/ BA2 - Applied Research**

PE NUMBER AND TITLE: **0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)**

B. Program Change Summary:		**FY 2001**	**FY 2002**	**FY 2003**
Previous President's Budget (FY 2002 PB)		81061	125481	105680
Appropriated Value		80000	147281	0
Adjustments to Appropriated Value		0	0	0
a. Congressional General Reductions		-560	-850	0
b. SBIR/STTR		-1373	0	0
c. Omnibus or Other Above Threshold Reductions		13000	0	0
d. Below Threshold Reprogramming		2284	0	0
e. Rescissions		-179	0	0
Adjustments to Budget Years Since FY 2002 PB		0	0	156497
Current Budget Submission (FY 2003 PB)		93172	146431	262177

Change Summary Explanation:

Funding: FY01 - Congressional increase (+$13,000K CB2); SBIR adjustment (-$1,373); Congressional general reduction (-$560K); Recissions (-$179K); Below threshold adjustments (+$2,284K).

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Funding (cont.)

FY02 - Congressional adjustments to support various CBD applied research programs (+$21,800K CB2). Congressional general reductions (-$850K).

FY03 - Increases to the technology base to fund a Homeland Security Support effort identified in the new Project HS2 (+$137,000K). Increases to the technology base for key science and technology efforts in support of the Administration's priorities (Enhanced Chemical and Biological Defense Initiatives) (+$12,750K, CB2; +$5,750K, TB2; +$1,500K, TC2). Inflation adjustments to reflect current assumptions (-$503K).

Schedule:

Technical:

C. **Other Program Funding Summary:** See section B in the R2A's

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D. Execution: (Organizations receiving 10% or more of execution year funding)

Labs/Centers:

TB2 - U.S. Army Medical Research Institute of Infectious Diseases, Ft. Detrick, MD; CB2 - Soldier Biological Chemical Command, APG-EA, MD; CB2 - Naval Research Lab, Washington, DC

Universities:

CB2 - Texas Tech, Lubbock, TX, and University of South Florida, Tampa, FL

FFRDCs: None

Contractors: None

Other: None

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

DATE: **February 2002**

BUDGET ACTIVITY: **RDT&E DEFENSE-WIDE/ BA2 - Applied Research**

PE NUMBER AND TITLE: **0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)**

PROJECT: **CB2**

COST (In Thousands)		FY 2001 Actual	FY 2002 Estimate	FY 2003 Estimate	FY 2004 Estimate	FY 2005 Estimate	FY 2006 Estimate	FY 2007 Estimate	Cost to Complete	Total Cost
CB2	CHEMICAL BIOLOGICAL DEFENSE (APPLIED RESEARCH)	56925	91432	68817	54007	52828	56281	54451	Continuing	Continuing

A. Mission Description and Budget Item Justification:

Project CB2 CHEMICAL BIOLOGICAL DEFENSE (APPLIED RESEARCH): This project addresses the urgent need to provide all services with defensive materiel to protect individuals and groups from threat chemical-biological (CB) agents in the areas of detection, identification and warning, contamination avoidance via reconnaissance, individual and collective protection, and decontamination. The project provides for special investigations into CB defense technology to include CB threat agents, operational sciences, modeling, CB simulants, and nuclear, biological, chemical (NBC) survivability. This project focuses on horizontal integration of CB defensive technologies across the Joint Services. The Defense Technology Objectives (DTOs) provide a means to shape the development of selected technologies within this project.

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

DATE: February 2002

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA2 - Applied Research	0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)	CB2

FY 2001 Accomplishments:

- 1223 Advanced Adsorbents for Protection Applications (DTO-CB08) - Prepared and evaluated single adsorbent materials and bed compositions identifying the optimal adsorbent bed composition for mask filters in the Joint Service General Purpose Mask (JSGPM) against both Toxic Industrial Chemicals (TICs) and CB agents.
- 805 Enzymatic Decontamination (DTO-CB09) - Optimized formulations of V-agent (persistent nerve agent) enzymes and H-agent (blister) reactive materials for application in dispersion systems and identified new V-agent enzymes and increased the activity of enzymes with hydrolytic activity on V-agents. Continued the search for H-agent active enzymes.
- 2050 Chemical Imaging Sensor (DTO-CB19) - Demonstrated a 16-pixel spectrometer in real-time operation at 100 Hz (on-line process of data). This capability represents the first time use of high performance computers for real-time on-line processing for this application. System is capable of being mounted on platforms with objective speeds in excess of 1,000 miles per hour with an imaging capability.
- 2789 Biological Sample Preparation System (BSPS) for Biological Identification (DTO-CB20) - Demonstrated BSPS at Joint Field Trials (JFT). Eight bacterial and viral materials gene probe assays were developed and evaluated for the automated platforms. Identified throughput issues with automated gene probe based platform. Identified technological issues in protein separation and concentration affecting sensitivity and interferent rejection of background materials in electrospray ionization mass spectroscopy.
- 319 Standoff Biological Aerosol Detection (DTO-CB35) - Initiated analysis of existing data and identified top candidates for further evaluation to provide improved biological standoff capability. Identified and developed key performance requirements to develop biological standoff capability.

CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2A Exhibit)	DATE February 2002
BUDGET ACTIVITY **RDT&E DEFENSE-WIDE/** **BA2 - Applied Research**	PE NUMBER AND TITLE **0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)**
	PROJECT **CB2**

FY 2001 Accomplishments (Cont):

- 710 Universal End of Service Life Indicator for NBC Mask Filters (DTO-CB36) - Identified and screened several color-changing passive (non-powered) technologies against representative chemical agent, simulant, and toxic industrial organic vapors and acid gasses. Initiated screening of two alternative candidate general-indicator technologies, metalloporphyrins, and polymerized diacetylenes.
- 1319 Joint Chemical Biological Agent Water Monitor (JCBAWM) (DTO-CB37) - Completed preliminary design of integrated CB water monitor based on the most mature technology currently available, using an open architecture to ensure that new and improved technology can be used to update the overall system with minimal effort. Developed test protocols for testing system. Initiated development of transition criteria for Milestone A decision.
- 4750 Man-portable Detectors - Continued insertion of semi-conductive metal oxide (SMO) technology (and Surface Acoustic Waves (SAWs) when required) into a chemical detector brassboard. Based on user inputs, determined the operational parameters of a man-portable detection system. Joint Service requirements were used to determine the response parameters and operating environment. Demonstrated an integrated prototype detector system for CW agents under laboratory and field conditions.
- 13000 CB Countermeasures - Completed first year research in CB Countermeasures with 25 diverse tasks in CB detector development, CB medical toxicology and vaccine research, fast detection methods for biological contaminants in food, new protective materials development, novel decontamination methods, novel blood assays for biologicals, improved methods for Weapons of Mass destruction first responders, improved hospital response techniques, and modeling of biological contamination spread.
- 1561 Improved CB Detection - Enhanced performance of high sensitivity passive stand-off detector by increasing hardware sensitivity, characterizing and removing background variables, and improving system detection software.

CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2A Exhibit)	DATE February 2002

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA2 - Applied Research	**0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)**	**CB2**

FY 2001 Accomplishments (Cont):

- 2200 Collective Protection - Completed Front-End Analysis (FEA) and Master Plan (MP) model for NBC collective protection systems identifying requirements and prioritizing technologies for system development in terms of maturity, risk, applicability, and cost. Continued Residual Life Indicator (RLI) chemical sensor testing with simulants, TICs, and agents. Produced and tested immobilized filter beds. Completed measurement of breakthrough and equilibrium data of current adsorbents against TICs and assessed adsorptive/chemisorptive properties. Conducted lab scale testing to validate the Pressure Swing Adsorption model. Fabricated and evaluated advanced materials, structural, and hermetic seal technologies for shelter systems.
- 8111 Decontamination - Completed demonstration of sensitive equipment decontamination methodology and finalized transition of technology for Block I of the Joint Service Sensitive Equipment Decontamination (JSSED) program. Selected technologies to be demonstrated for the decontamination of sensitive interiors (JSSED Block II) focusing on thermal approaches. Evaluated approaches for operational decontamination of sensitive equipment and interiors on the move (JSSED Block III). Investigated alternative approaches to improve efficiency of V-agent (persistent nerve agent) enzymes. Broadened the scope of enzymatic decontamination processes evaluating potential systems for non-traditional agents. Validated oxidative processes in aqueous and mixed/aqueous/organic solvent systems as solutions, emulsions or microemulsions. Examined dendritic assembly systems incorporating mono ethanol amine functionality and performed preliminary agent challenges. Continued the evaluation of novel solid matrices. Continued efforts to determine the fate of agent on common environmental surfaces associated with fixed site facilities. Conducted study to evaluate the hazard posed by potential reaerosolization of BW materials. Transferred oversight of this area to Supporting Science and Technology Business Area.

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BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA2 - Applied Research	0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)	CB2

FY 2001 Accomplishments (Cont):

- 1647 Individual Protection, Clothing - Completed material test procedures which allow detailed characterization of all permselective membranes and a predictive mechanistic hypothesis, and demonstrated several excellent barrier membranes produced via relatively simple chemical modification of Nafion¬. Initiated a Dual Use Science and Technology (DUST) effort to manipulate and optimize textile structures using current nanofiber technology and electrostatic treatments to reduce aerosol permeation. Investigated nanofiber membrane bonding/integration methods and conducted aerosol tests on membranes produced. Identified toxic industrial chemicals of interest and developed test methodology for assessing the effectiveness of protective clothing against those chemicals. Conducted investigations to identify polymers and determine guidelines for optimal ions, doses, and other parameters for enhancing the permselectivity of membranes. Initiated a DUST effort to produce membrane based protective garments for civilian and military use.
- 609 Individual Protection, Masks - Constructed a parametric skeleton model of candidate helmet/mask concepts to help identify those with most potential for long-term solutions. Conducted technology feasibility studies for numerous technologies identified during the Individual Protection Front-End Analysis (IP FEA) to determine their applicability for future protective masks.

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BUDGET ACTIVITY **RDT&E DEFENSE-WIDE/** **BA2 - Applied Research**	PE NUMBER AND TITLE **0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)**
	PROJECT **CB2**

FY 2001 Accomplishments (Cont):

- 3712 Modeling and Simulation - Developed models for simulation of CB weapons effects on joint force operations for incorporation into advanced simulations such as Joint Conflict and Tactical Simulation (JCATS), Joint Simulation System (JSIMS), Joint Modeling and Simulation System (JMASS), and Joint Warfare System (JWARS). Initiated coupling of CB environment and high resolution meteorological models for incorporation of CBW hazard prediction/tracking into forward-deployed meteorological forecast/nowcast operations. Continued development of advanced CBW environment models for more accurate, higher-resolution atmospheric transport and fate predictions in complex and urban terrain for battlespace awareness and contamination avoidance. Developed additional models for Joint Service CB defense equipment for application in Simulation Based Acquisition (SBA). Transitioned current version of the Simulation, Training, and Analysis for Fixed Sites (STAFFS) model to the Center for Army Analysis for evaluation. Enhanced development of STAFFS model for simulation of CBW effects on operations at Aerial Port of Debarkation (APOD) and Sea Port of Debarkation (SPOD). Continued validation studies and software documentation materials for Vapor, Liquid, Solid Tracking (VLSTRACK) version 3.
- 1860 Biological Identification and Reagents - Completed analysis of accumulated ambient background data from United Kingdom and Portal Shield Program and identified gaps for further study as indicated by analysis. Completed generation and screening of recombinant antibodies against selected bio agents using biased genetic libraries. Incorporated recombinant antibodies into Enzyme Linked Immuno Sorbent Assay (ELISA) and bio-sensors for test/evaluation, and transitioned best candidates to Critical Reagents Program (CRP).
- 1150 Food and Water - Evaluated alternative technologies; e.g., surface enhanced Raman, molecular imprinted polymers, gas chromatograph-ion mobility spectrophotometer for risk reduction in support of the Joint Chemical Biological Agent Water Monitor (JCBAWM).

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BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA2 - Applied Research	**0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)**	**CB2**

FY 2001 Accomplishments (Cont):

- 1847 Supporting Science and Technology - Completed initial toxicology study using simulant powder and initiated persistent nerve agent aerosol toxicology study in the new nose-only exposure chamber for extremely hazardous aerosols. Measured quantitative performance of candidate aerosol collectors for advanced point biodetection technology. Demonstrated a new aerosol collector using mini-scale manufacturing technology that substantially reduces power consumption compared to fielded collectors while maintaining high collection efficiency over the respirable particle size from 1-10 micrometers diameter. Continued to provide controlled biosimulant aerosol challenges for Joint Service, DARPA, and DOE experimental equipment in preparation for the JFT.
- 2216 Low Level Chemical Agent Operational Toxicology Studies - Published non-persistent nerve agent exposure data analyses (lethality endpoint) on rats. Completed non-persistent nerve agent miosis threshold studies in rats for extended exposure durations. Initiated second generation nerve agent potency ratio studies in rats for toxicological effects to characterize concentration-time Ct relationships for low-level, longer vapor duration exposures. This data is required to validate and verify alarm and warning levels for detector and protection systems.

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BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA2 - Applied Research	**0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)**	**CB2**

FY 2001 Accomplishments (Cont):

- 5047 Leap Ahead Technologies - Conducted technology feasibility studies for numerous technologies identified during the IP FEA to determine their applicability for future protective masks. Investigated advanced respiratory and percutaneous protection technologies identified in IP FEA to reduce thermal load and breathing resistance. Selected new simulant for emerging agents. Published interim assessment of data gaps in threat agent data and needs for improved simulants in CB defense materiel development to define FY02 program priorities. Completed a simulant database for selecting appropriate simulants in materiel development. Initiated assessment of data gaps in threat agent data and needs for improved simulants in CB defense materiel development. Instituted a simulant database for selecting appropriate simulants in materiel development and established a repository for chemical simulants and a standard biological simulant laboratory. Overcame technology barriers in developing simulants for emerging agents. Continued efforts in developing force differentiation assay (FDA). Refined discrimination algorithms and chamber test optical fluorescence/shape analysis and pyrolysis-gas chromatography-ion mobility spectrometry; two promising technologies capable of downsizing and providing classification among biological particles without fluids. Completed initial analysis of RADAR multi-mission sensor and identified other disparate sensors. Initiated exploration of chip-based phylogenetic assay for highly multiplexed biological agent detection.

Total 56925

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RDT&E DEFENSE-WIDE/ BA2 - Applied Research	**0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)**	**CB2**

FY 2002 Planned Program:

- 1100 Advanced Adsorbents for Protection Applications (DTO-CB08) - Evaluate composite adsorbent beds and select optimal compositions for single pass filter applications for Individual Protection (IP) and Collective Protection (CP) against Toxic Industrial Chemicals (TIC) and CB agents.
- 900 Enzymatic Decontamination (DTO-CB09) - Complete development of enzymatic formulations and transition to either the Joint Service Family of Decon Systems as a product improvement or to follow-on efforts under the Superior Decontamination System program. Potential H-agent enzymes have been identified, optimization is in progress.
- 2400 Chemical Imaging Sensor (DTO-CB19) - Demonstrate a 16-pixel spectrometer operating at 360 Hz with off-line processing of data. Initiate planning to include preparing for a Milestone A decision on the technology for transition of brassboard design and build in support of Joint Service Wide Area Detection (JSWAD) program.
- 1600 Biological Sample Preparation System (BSPS) for Biological Identification (DTO-CB20) - Redesign and initiate modification of FY01 bioagent Polymerized Chain Reaction (PCR) breadboard for 20-minute sample processing and multifrequent, multiplexed (MM) capabilities. Develop six MM bioagent PCR assays (three containing two gene targets each for three bioagents and three containing a single gene target for each bioagent in a binary mixture from three bioagents).
- 1800 Standoff Biological Aerosol Detection (DTO-CB35) - Complete establishment of system requirements and conduct down selection based on weighted criteria. Establish technical potential of top ranked technologies. Perform testing, analyze data, and identify strengths and weaknesses on the top five rated technologies for the next generation standoff system.

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RDT&E DEFENSE-WIDE/ BA2 - Applied Research	**0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)**	**CB2**

FY 2002 Planned Program (Cont):

- 800 Universal End of Service Life Indicator (ESLI) for NBC Mask Filters (DTO-CB36) - Develop baseline data characterizing the performance of the most promising ESLI technologies. Assess performance parameters such as reaction time, range of detection, and effects of temperature and humidity using carbon bed test cells; select best candidate technologies based on baseline data.
- 3100 Joint Chemical Biological Agent Water Monitor (JCBAWM) (DTO-CB37) - Complete construction of initial breadboard. Complete testing to identify shortfalls. Demonstrate technologies and transition technologies to Advanced Technology Development.
- 4000 Environmental Fate of Agents (DTO-CB42) - Identify standard construction and natural environmental materials and initiate study interactions of these materials with VX (nerve) using novel in situ methods. Conduct a field test with VX (nerve), GD (nerve), and HD (blister) agents. Develop refined laboratory methodologies to support these studies. Define previously unaccounted environmental loss mechanisms and provide results for improvement of hazard modeling. Refine relevant physical property data related to chemical hazard evolution.
- 1000 Chemical and Biological Warfare Effects on Operations (DTO-CB43) - Test and finalize fighter base representation. Expand development of Aerial Port of Debarkation (APOD) methodology. Start preliminary data gathering and development of Sea Port of Debarkation (SPOD) model. Continue model infrastructure development and detailed operations effect (work/rest cycle, shift change, Mission Oriented Protective Posture (MOPP), dewarn, etc.).
- 1600 Oxidative Decontamination Formulation (DTO-CB44) - Optimize oxidative formulations using a peroxycarbonate approach and evaluate commercial catalysts to improve oxidation rates for peracid-based decontaminants for use as a replacement for DS-2. Begin kinetics, toxicity, and material compatibility testing.

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RDT&E DEFENSE-WIDE/ BA2 - Applied Research	0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)	CB2

FY 2002 Planned Program (Cont):

- 1200 Self-Detoxifying Materials for Chemical and Biological Protective Clothing (DTO-CB45) - Investigate the use of N-halamine fabric treatment for the detoxification biological and chemical agents. Identify and incorporate color change sensors for agent deactivation into membranes and test for effectiveness. Investigate the use of hyperbranched nanoreactors for agent deactivation. Select reactive nanoparticles and formulate candidate films and fibers for improved barrier protection.
- 2800 Air Purification Systems - Initiate development of test apparatus and methodology for testing anti-microbial filters/treatments for collective and individual protection. Perform modeling and testing of lab- and sub-scale anti-microbial air purification devices, which have potential to enhance biosafety and reduce operating costs associated with air purification.
- 3500 Bioinformatics - Adapt bioinformatic approaches developed for the human genome project to produce meaningful generalizations about the large number of candidates that can be potentially used for biological threat agents and their varied or engineered properties. Begin integrating comprehensive and interactive databases maintained and updated with fundamental properties of biological agents of military interest. Initiate development of data mining tools to analyze microbial information specifically tailored to military assessment and decision making for CB defense. Begin the development of predictive algorithms embedded into databases developed above to understand biological threats, allow generalizations, assess risk of emerging biological threats, and suggest the course of defense response under specific circumstances (e.g., pathogenic genes in unnatural host context, or potential threat of engineered genomes).

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RDT&E DEFENSE-WIDE/ BA2 - Applied Research	0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)	CB2

FY 2002 Planned Program (Cont):

- 9000 Joint Biological and Chemical Terrorism Response Project - Continue development of rapid anthrax test method for blood and environmental samples initiated in CB Countermeasures. Initiate development of rapid test for smallpox and plague. Complete revision of medical training and reference for treatment of chemical and biological exposures for non-military hospitals. Continue development and initial testing of the wide area biological counterterrorism surveillance and detection tool. Develop protocols for safe transport of biologically contaminated clinical samples. Continue development and initial testing of a transportable fiber optic detector for biological threat agents found in the field. Continue research into identification of the factors affecting bioterrorism toxicants and toxins. Continue assessment and recommendations for hospital hygiene practices dealing with bioterrorism. Complete the selection of biological and chemical isolation suits for bioterrorism response.
- 1000 Common Asset for Biological Security - Develop genome based bioinformatics tools, assess performance, and apply to gene chip detection/identification technologies.
- 3500 CB Countermeasures - Continue investigations into mechanisms of cell death after exposure to chemical and biological agents. Continue development of non-woven protective suits for response to chemical and biological threats. Continue investigations into feasibility of employing selenium bound receptors to destroy and eliminate infectious biological agents. Continue development of embedded miniature chemical detectors for employment in critical and sensitive sites.
- 1000 Integrated Detection of Energetic and Hazardous Materials - Build, test, and refine Cylindrical Ion Trap Mass Spectrometer (CITMS). Continue to test Ion Trap Mass Spectrometer (ITMS) methodologies for the point detection of BW agents. Develop theoretical limits of detection via neutron initiated gamma-ray spectroscopy. Investigate application of advanced transforms on various detection methodologies.

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RDT&E DEFENSE-WIDE/ BA2 - Applied Research	0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)	CB2

FY 2002 Planned Program (Cont):

- 6000 Biological Identification - Continue development of Force Discrimination Assay (FDA). Develop and test concepts toward automation of chip-based phylogenetic analysis of biological materials. Initiate feasibility study to determine technological issues associated with microwave spectroscopy of biological materials under ambient conditions. Explore novel concepts in protein separation and concentration technology to increase sensitivity and reduce interference from background materials in electrospray ionization mass spectroscopy. Develop database and validation methodology for multiple gene target reagents for biological agents. Evaluate quantum dot technology for application to enhance antibody ticket technology for improved stability and sensitivity. Identify optimum combinatorial peptides as biological recognition elements and evaluate against traditional reagents.
- 1000 CB Regenerative Air Filtration System - Initiate modeling and testing of lab- and sub-scale temperature swing adsorption (TSA) air filtration devices, which have potential to reduce operating cost, logistics tail, and labor requirements associated with frequent filter changes.
- 1045 Collective Protection, Filtration - Continue chemical sensor Residual Life Indicator (RLI) testing and start physical sensor testing. Continue determination of TIC breakthrough and equilibrium testing for advanced adsorbents. Initiate proof-of-principle testing and evaluation of 50 CFM pressure-temperature swing filter to validate model. Demonstrate single pass filter concepts using nano-materials. Initiate evaluation of electrostatic filter particulate/aerosol capture enhancement. Determine degradation effects of TICs on HEPA filters and ways to mitigate. Start assessing feasibility of open and closed circuit air supply and rebreather technologies. Assess effects of chemical agents and TICs on ceramic ion membranes; assess oxygen generation and carbon dioxide scrubbing technologies.

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FY 2002 Planned Program (Cont):

- 1100 Collective Protection, Shelters - Continue development and evaluation of advanced shelter materials (shell, support, airlocks, liner, seams, and seals). Initiate development and assessment of chemistries for self-decontaminating shelter materials. Assess and mitigate failure mechanisms of shelter materials from conventional weapons effects.
- 1316 Sensitive Equipment, Decontamination - Continue developmental efforts to address JSSED Block II and III approaches focusing on thermal and plasma technology and spot cleaning methodology using non-ozone depleting solvents with reactive solid suspensions.
- 1068 Solution Chemistry, Decontamination - Develop solution approaches for Superior Decontamination Systems combining novel chemical and biochemical technologies into a unified approach.
- 881 Solid Phase Chemistry, Decontamination - Evaluate the physical limitations of novel solid phase technology for decontamination operations. Areas under investigation include nanoscale metal oxides and zeolites. Implement findings from these studies into other areas of the program and determine the best future uses for these materials.
- 3075 Individual Protection, Clothing - Fabricate uniforms from the best candidate aerosol threat mediation materials that will then be characterized for their system aerosol performance. Initiate the testing of fielded and developmental protective garment materials to evaluate their effectiveness against selected TICs and particulate aerosols. Conduct laboratory trials to enhance the permselectivity of membranes by ion implantation, and characterize the material physical properties and CB agent protection capabilities of those trial membranes. Demonstrate through a DUST effort the large scale production of protective membrane-based garments for military and civilian applications through the fabrication of numerous and varied garment items. Identify the most promising permselective membrane candidates and initiate the characterization of those candidates.

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RDT&E DEFENSE-WIDE/ BA2 - Applied Research	0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)	CB2

FY 2002 Planned Program (Cont):

- 1515 Individual Protection, Masks - Conduct helmet/mask long-term model concept feasibility assessment. Initiate the development of concepts for the next generation general purpose mask. Compare existing filtration media with reactive iodine media with respect to biocidal efficacy and in physical properties (such as pressure drop and dust/particulate removal), and initiate development of conceptual combined biocidal/dust filter. Screen sorbent media structures identified during the Individual Protection Front-End Analysis (IP-FEA) and follow-on surveys and select best candidates for further development. Screen advanced lens materials and coating technologies identified in the IP-FEA and follow-on surveys, and identify best candidates for further development. Investigate new technologies and concepts for protective masks to improve protection, flow dynamics, heat and moisture transfer, and fogging.
- 1750 CB Battle Management, Information Systems Technology (IST) - Conduct Battle Management Front End Analysis to identify optimum investment strategy. Complete analysis/report on FY01 tests of non-CB sensors against CB simulant disseminations. Expand database on non-CB sensor performance through measurement against additional dissemination approaches. Conduct studies to assess value added through data fusion of networked multiple same-type disparate sensors and multiple different disparate sensors.
- 3000 CB Environment, IST - Complete methodology documentation and validation of VLSTRACK. Increase computational speed and concentration fluctuation representation in next-generation hazard evolution model MESO (small scale used to measure atmospheric motion) with concurrent validation. Improve high resolution computational fluid dynamics model (CBW-CFX) to address realistic droplet size distributions and biological agent decay. Initiate coupling of numerical weather prediction models with existing CBW dispersion codes. Initiate refinement of hazard evolution codes to better incorporate effects of the environment on chemical agents.

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BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA2 - Applied Research	**0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)**	**CB2**

FY 2002 Planned Program (Cont):

- 1000 CB Planning, Training, Analysis, IST - Initiate simulation hazard modeling for systems and forces via distributed simulations systems. Initiate examination of sensitivity of hazard evolution/prediction models for agent toxicity.
- 1500 Simulation Based Acquisition, IST - Identify and plan for highest priority prototyping demonstrations; initiate coupling of CBD commodity area object models with demonstrated prototyping system. Initiate definition of performance and technical specifications of an eventual virtual prototype system to improve acquisition of CBD materiel.
- 4370 Integrated CB Point Detection - Characterize biomarkers observed in Py-GC-IMS sensors against performance matrix of sensitivity, selectivity, and interference rejection for optimal design trade-off analysis. Initiate exploration of new concepts for small, combined chemical and biological identifiers. Evaluate and develop novel concepts, methodologies, and techniques for biological discrimination, advanced aerosol handling, and triggering capabilities for chemical aerosols.
- 4500 Biological Standoff - Investigate novel approaches to detection and discrimination of biological aerosols in standoff mode. Examine application of improved laser sources and methodologies and develop spectral database and methodologies to support assessment of new approaches such as Brillouin scattering, Mueller matrix Light Detection and Ranging (LIDAR), and millimeter wave spectroscopy. Investigate potential applicability of UV and IR imaging.
- 2800 Integrated CB Standoff Detection - Initiate a program to develop technology to detect the presence of CBW contaminants on surfaces, for use in vehicular and handheld systems. Initial studies will focus on active and passive optical technologies that could be employed on or from a vehicular platform. Conduct assessment of standoff technologies that may be implemented simultaneously against chemical and biological agents.

CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2A Exhibit)	DATE February 2002

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA2 - Applied Research	0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)	CB2

FY 2002 Planned Program (Cont):

- 2600 Aerosol Technology - Continue to measure quantitative performance of candidate aerosol collectors for advanced point biological detection technology. Initiate the design of a new generation of aerosol concentrators using mini-machining technology to reduce size, power consumption, and weight, in order to meet stringent requirements for advanced miniature detection systems. Initiate design of advanced aerosol inlets to meet Joint Service requirements for high collection efficiency over the respirable particle size range at wind speeds up to 60 mph. Continue to provide controlled biological simulant aerosol challenges for Joint Service, DARPA, and DOE experimental equipment in preparation for the Joint Field Trials (JFT).
- 3100 Threat Agents - Continue assessment of gaps in threat agent data, and identify requirements for improved simulants in CB defense materiel development. Initiate a program of synthesis, toxicology screening, and characterization of new threat materials (to include persistence properties of novel agents) identified as urgent needs while continuing assessment of long-term needs. Initiate validation studies on simulant BG spores, improvement of simulant Erwinia herbicola, and selection of new simulants for novel chemical agent aerosols.
- 5000 Low Level Chemical Agent Operational Toxicology Studies - Complete meiosis threshold studies for second generation agents (GF) in rats over extended exposure durations. Complete GF potency ratio studies on rats. Initiate non-rodent animal studies on G agents to support the extrapolation of data to humans. Develop methodology for third generation agents (VX) inhalation studies to characterize Ct relationships for low level longer duration exposures. Develop CWA tissue dose metric to quantify exposure and predict toxicological response.

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

DATE: **February 2002**

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA2 - Applied Research	**0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)**	**CB2**

FY 2002 Planned Program (Cont):

- 2965 Fourth Generation Agents (FGA) - Modify point detection systems to enhance performance against new chemical targets and characterize effect of modifications on performance to existing chemical targets and on interference rejection. Broaden spectral knowledge base in order to predict performance of active and passive IR sensors for detection of surface contamination. Examine novel materials and material treatment solutions to decrease penetration of aerosol particulates through overgarments. Examine novel material treatment solutions to decrease penetration of aerosol particulates through overgarments.
- 1547 SBIR - Small Business Innovative Research efforts.

Total 91432

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

DATE: **February 2002**

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA2 - Applied Research	**0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)**	**CB2**

FY 2003 Planned Program:

- 1214 Advanced Adsorbents for Protection Applications (DTO-CB08) - Test and transition optimum material/bed configurations for regenerative filter, single pass, and catalytic based air-purification applications.
- 2000 Biological Sample Preparation System (BSPS) for Biological Identification (DTO-CB20) - Complete the initial modification and test the breadboard. Demonstrate the FY02 multifrequent, multiplexed (MM) assays on the system. Optimize the FY02 MM bioagent PCR assays.
- 3500 Standoff Biological Aerosol Detection (DTO-CB35) - Construct and characterize breadboards based on the results of the downselect and user input. Initiate field testing and evaluation of final breadboards.
- 4000 Environmental Fate of Agents (DTO-CB42) - Determine VX fate on concrete under lab conditions. Initiate GD fate on sand and grass. Select and characterize thickened agent formulations. Refine model structure to incorporate concrete matrix substrate parameters and initiate prediction analysis for field validation studies for FX. Initiate validation and extend laboratory studies using field protocols.
- 1200 Chemical and Biological Warfare Effects on Operations (DTO-CB43) - Initiate development and testing of Sea Port of Debarkation (SPOD) model.
- 2100 Oxidative Decontamination Formulation (DTO-CB44) - Conduct decontamination efficacy testing against an expanded test bed of agents. Continue material compatibility testing. Optimize formulations using a peracid approach.
- 1500 Self-Detoxifying Materials for CB Protective Clothing (DTO-CB45) - Optimize N-halamine fabric treatment and characterize for detoxifying biological and chemical agents. Initiate electrospinning scale-up and identify membrane processing methodology. Characterize the candidate films and fibers fabricated using reactive nanoparticles.

CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2A Exhibit)	DATE February 2002

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA2 - Applied Research	0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)	CB2

FY 2003 Planned Program (Cont):

- 2000 Collective Protection, Filtration - Fabricate and test candidate nano-material adsorbents for single pass filter concepts.
- 1500 Collective Protection, Shelters - Continue development and testing of technologies leading to self-decontaminating soft wall shelters. Continue conventional weapons effects (CWE) study of shelter components and develop predictive model. Develop CWE mitigation improvements and field test to validate predictive model and new designs.
- 1500 Sensitive Equipment, Decontamination - Demonstrate decontamination technology solutions for JSSED Block II and III using thermal and plasma technology and spot cleaning methodology using reactive solid suspensions.
- 3500 Solution Chemistry, Decontamination - Optimize formulations for chemical and biological decontamination systems. Initiate material compatibility testing and efficacy testing on an expanded agent test bed for promising approaches.
- 900 Solid Phase Chemistry, Decontamination - Develop and demonstrate novel solid and sorbent decontamination technology using nanoscale metal oxides and zeolites.
- 2150 Individual Protection, Clothing - Complete evaluation of fielded and developmental protective garment materials to determine their effectiveness against selected TICs and particulate aerosols. Develop and produce a first generation membrane that has optimized permselectivity through ion implantation. Modify the best permselective membrane candidate materials to optimize their moisture vapor transport properties and evaluate those materials.
- 2000 CB Battle Management, Information Systems Technology (IST) - Expand studies to address data fusion approaches for multiple sensors. Assess value added at system-level (multiple networked CB sensors and non-CB sensors) through modeling and demonstration. Initiate examination of methods to improve real-time, network-aided decision making, and visualization of network responses.

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

DATE: **February 2002**

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA2 - Applied Research	**0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)**	**CB2**

FY 2003 Planned Program (Cont):

- 3000 CB Environment, IST - Improve next-generation model (MESO) to include wet bio modifications, improved accuracy over rough terrain, and further improvements to boundary layer physics. Evaluate performance of computational fluid dynamics model (CBW-CFX) on ships and fixed land structures and identify areas for improvement. Demonstrate performance of coupled weather CBW dispersion model. Evaluate performance of hazard evolution codes updated by agent environmental effects data.
- 1403 CB Planning, Training, Analysis, IST - Demonstrate HLA or DIS application of hazard models. Conduct statistical analysis of results of agent toxicity load variation in several hazard prediction models for fixed site application.
- 1000 Simulation Based Acquisition, IST - Initiate testing of prototyping models against highest priority CBD objects. Develop and demonstrate a breadboard virtual prototype system.
- 3700 Biological Identification - Complete development of Force Discrimination Assay (FDA). Continue development and testing automation of chip-based phylogenetic analysis of biological materials. Complete feasibility study to determine technological issues associated with microwave spectroscopy of biological materials under ambient conditions. Integrate concepts in protein separation and concentration technology to increase sensitivity and reduce interference from background materials into electrospray ionization mass spectroscopy. Continue development of database and validation methodology for multiple gene target reagents for biological agents. Laboratory demonstrate quantum dot technology for application to enhance antibody ticket technology for improved stability and sensitivity. Downselect and laboratory demonstrate combinatorial peptides as biological recognition elements as candidate replacements against traditional reagents. Continue the standardization of biological simulant materials for test and evaluation efforts.

CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2A Exhibit)	DATE February 2002

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA2 - Applied Research	0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)	CB2

FY 2003 Planned Program (Cont):

- 4800 Integrated CB Point Detection - Continue exploration of new concepts for small, combined chemical and biological identifiers. Expand feasibility studies of "low consumable or reagentless" concepts. Develop and test the improved Py-GC-IMS concept for chemical and biological discrimination. Downselect techniques and initiate breadboard design for chemical and biological aerosol sample processing.
- 4000 Biological Standoff - Downselect among candidate bio standoff technologies identified in FY02. Pursue investigation of most promising approaches.
- 2200 Chemical Standoff - Improve the sensitivity of the Chemical Imaging Sensor with integration of high sensitivity passive infrared technology. Provide the next generation of passive detection system with 10-100 fold improvement in sensitivity in comparison to current developmental systems.
- 3000 Aerosol Technology - Continue to measure quantitative performance of candidate aerosol collectors for advanced point biological and chemical detection technology, and operating at the Joint Service low temperature requirements (-28 degrees F). Fabricate and test the first brassboards of a new generation of aerosol concentrations and collectors using mini-machining technology to reduce the size, power consumption, and weight of aerosol components in order to meet the stringent requirements for advanced detection systems. Fabricate and test the first brassboards of advanced aerosol inlets to meet Joint Service requirements for high collections efficiency over the respirable particle size range and for wind speeds up to 60 mph. Continue to provide controlled biosimulant aerosol challenges and begin providing chemical agent simulant aerosol challenges for Joint Service, DARPA, and DOE experimental equipment in preparation for the JFT.

CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2A Exhibit)	DATE February 2002

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA2 - Applied Research	**0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)**	**CB2**

FY 2003 Planned Program (Cont):

- 4000 Threat Agents - Complete the assessment of long-term needs in threat agent data and needs for improved simulants in CB defense materiel development, and participate in a collaborative inter-agency laboratory program to fill the data gaps and improve simulants. Continue to synthesize, toxicologically screen, and characterize identified new threat materials and to fill identified data gaps for established threats, including persistence properties of novel agents. Continue selection and validation of improved simulants for threat CB materials.
- 5000 Low Level Chemical Agent Operational Toxicology Studies - Complete non-rodent GB inhalation studies to characterize Ct relationships for low level, longer duration exposures. Complete methodology development for third generation agent (VX) inhalation exposures and initiate VX studies in rats. Continue dose-metric methodology efforts to understand internal dosage following exposures. Develop methods for physiological modeling to understand the impact of route of exposure on toxicological effects from low level concentration and extended duration exposures to nerve agents.
- 3750 Fourth Generation Agents (FGA) - Optimize materials and material treatment solutions for overgarments evaluated in FY02 to improve protection against aerosol particulates. Complete investigation of impact of modifications on initial set of point detectors. Complete collection of IR spectral data and model performance of IR sensors against FGAs.
- 3000 Detection of Contaminants on Surfaces - Downselect the most mature technology. Design and build a breadboard system to demonstrate the technology to detect the presence of CBW contaminants (including FGAs) on surfaces.
- 900 End-of-Service-Life-Indicators (ESLI) for Filters (DTO CB.36) - Incorporate best candidate technologies into viable mask filter prototypes. ESLI prototypes will be evaluated with modified military or commercial mask filters using a variety of representative containment challenges to enhance design and determine optimum location of ESLI.

Total 68817

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

DATE: **February 2002**

BUDGET ACTIVITY: **RDT&E DEFENSE-WIDE/ BA2 - Applied Research**

PE NUMBER AND TITLE: **0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)**

PROJECT: **CB2**

B. Other Program Funding Summary:

	FY 2001	FY 2002	FY 2003	FY 2004	FY 2005	FY 2006	FY 2007	To Compl	Total Cost
CB3 CHEMICAL BIOLOGICAL DEFENSE (ADV TECH DEV)	15935	21553	27248	33964	33721	26599	31800	Cont	Cont
CP3 COUNTERPROLIFERATION SUPPORT (ADV TECH DEV)	9944	12492	11738	5327	5368	4697	4242	Cont	Cont

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

DATE: **February 2002**

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA2 - Applied Research	**0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)**	**HS2**

COST (In Thousands)		FY 2001 Actual	FY 2002 Estimate	FY 2003 Estimate	FY 2004 Estimate	FY 2005 Estimate	FY 2006 Estimate	FY 2007 Estimate	Cost to Complete	Total Cost
HS2	HOMELAND SECURITY (APPLIED RESEARCH)	0	0	137000	0	0	0	0	0	137000

A. Mission Description and Budget Item Justification:

Project HS2 HOMELAND SECURITY (APPLIED RESEARCH): The intent of the Biological Defense Homeland Security Support program, as envisioned by the Office of Homeland Security, is to provide an integrated Homeland Security capability to detect, mitigate, and respond to biological-related incidents. This capability will be achieved primarily through the integration of enhanced biological detection capabilities and the fusion of medical surveillance systems, wide-area environmental sensors, access control point monitors, and information management systems that will reduce the vulnerability of U.S. assets or will impact national interests. The prototype-fielded systems will be integrated and demonstrated in DOD installations and urban areas and will include medical surveillance and access point integration technologies, biological and meteorological sensors, mobile biological analytical instruments, and enhanced integrated biological information network integrated into upgraded command control communications network. This project provides for investigative efforts to perform a Homeland Security requirements process and shape the development of selected technologies for environmental monitoring, medical surveillance, and data mining/fusion/analysis. Funding for this project also supports applied microbial threat assessment research and establishment of a panel of nationally recognized experts to assist in development of the research program, strategic plan, investment strategy, and policy for the Biological Counterterrorism Research Program.

FY 2001 Accomplishments: None

FY 2002 Planned Program: No planned program

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

DATE: **February 2002**

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA2 - Applied Research	**0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)**	**HS2**

FY 2003 Planned Program:

- 55000 Applied Microbial Threat Assessment Research - Staff program office with appropriate programmatic and technical personnel, utilizing contractors, IPAs, and military/civilian government employees as appropriate. Develop program policy, strategic program plan, and short, mid and long-term investment strategy. The program office, with support of the senior advisory panel and interagency coordination group, will identify a first tier of research topics, solicit extramural research to support the program, and award research contracts and grants to support the identified program goals.
- 5400 Signature Analysis - Investigate and demonstrate signature data base concept incorporating threat genomic profiles, environmental test bed (surrounding community) analysis profiles, and normality recognition/characterization base.
- 4000 Signature Analysis - Conduct baseline studies to characterize background at two DoD bases for the initial test beds and urban areas.
- 4900 Signature Analysis - Conduct initial baseline studies and analysis and data gathering for regional, state, and national demonstration.
- 7900 Medical Surveillance - Conduct applied research on technologies to provide point-of-care diagnostic capabilities in DoD installations and civilian hospitals and clinics. The focus of the investigative efforts will be DNA micro array diagnostics, advance multiplex polymerase chain reaction (PCR) based detection concepts, protein chips, and host response genetic fingerprinting.
- 7000 Medical Surveillance - Conduct applied research on medical surveillance technologies needed to adapt systems for the specific environments of the test beds.

CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2A Exhibit)	DATE February 2002

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA2 - Applied Research	**0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)**	**HS2**

FY 2003 Planned Program (Cont):

- 3700 Medical Surveillance - Conduct applied research on patient syndromic reporting technologies to identify and track the proliferation of diseases through military and civilian populations.
- 3200 Medical Surveillance - Conduct applied research on technologies to integrate data from military and civilian hospital and pharmaceutical databases in a data reporting and recording environment.
- 6400 Environmental Monitoring - Conduct studies on adapting advanced networked point-detection technologies and algorithms for use in layered applications to protect wide areas and structures.
- 6200 Environmental Monitoring - Conduct applied research on advanced laser induced fluorescence technologies and algorithms to enable stand-off detection of bioagents over wide urban areas.
- 4200 Environmental Monitoring - Conduct studies on mobile/transportable detection systems for surveillance and monitoring of incident sites while preserving evidence for later forensic analysis.
- 7300 Access Control Point Monitoring - Conduct applied research to adapt stand-off technologies and algorithms to specific access control point applications for test beds.
- 1600 Access Control Point Monitoring - Conduct studies to adapt advanced video surveillance applications to complement biodetectors for the test bed systems.
- 4000 Access Control Point Monitoring - Conduct applied research on advanced non-destructive detection technologies for application in confined areas (e.g., ports-of-entry, special events) to increase their specificity and sensitivity to identified biological pathogens.
- 3600 Data Mining, Fusion, and Analysis - Modeling and Analysis - Investigate existing plume dispersion models for biodefense in military and urban applications.

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BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA2 - Applied Research	**0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)**	**HS2**

FY 2003 Planned Program (Cont):

- 3600 Data Mining, Fusion, and Analysis - System Development - Conduct studies of advanced data collection, storage, analysis, and decision support technologies for test bed applications.
- 2000 Data Mining, Fusion, and Analysis - Related Databases - Conduct studies to identify relevant databases and data elements (pharmaceutical databases, veterinary databases) and establish data mining algorithms to extract information to support biodefense objectives.
- 1000 Requirements Analysis, System Integration and Program Support - Baseline Self Assessment (BSA) - Conduct research expanding existing BSA capabilities for vulnerability identification and analysis for urban areas.
- 3000 Requirements Analysis, System Integration and Program Support - Mission Area Assessments - Conduct a mission area assessment to support biological defense for homeland security.
- 3000 Requirements Analysis, System Integration and Program Support - Requirements Analysis and Process Development - Conduct a study to identify system-level and subsystem-level requirements for biological defense test beds based on tasks identified in mission area assessments.

Total 137000

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

DATE: **February 2002**

BUDGET ACTIVITY: **RDT&E DEFENSE-WIDE/ BA2 - Applied Research**

PE NUMBER AND TITLE: **0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)**

PROJECT: **HS2**

B. Other Program Funding Summary:

	FY 2001	FY 2002	FY 2003	FY 2004	FY 2005	FY 2006	FY 2007	To Compl	Total Cost
HS3 HOMELAND SECURITY (ADV TECH DEV)	0	0	162000	0	0	0	0	0	162000
HS4 HOMELAND SECURITY (DEMVAL)	0	0	55000	0	0	0	0	0	55000
HS6 HOMELAND SECURITY (MANAGEMENT SUPPORT)	0	0	6000	0	0	0	0	0	6000
HS9000 HOMELAND SECURITY PRODUCTION	0	0	30000	0	0	0	0	0	30000

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DATE: **February 2002**

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA2 - Applied Research	**0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)**	**TB2**

COST (In Thousands)		FY 2001 Actual	FY 2002 Estimate	FY 2003 Estimate	FY 2004 Estimate	FY 2005 Estimate	FY 2006 Estimate	FY 2007 Estimate	Cost to Complete	Total Cost
TB2	MEDICAL BIOLOGICAL DEFENSE (APPLIED RESEARCH)	22428	36513	38386	24085	25097	17826	18148	Continuing	Continuing

A. Mission Description and Budget Item Justification:

Project TB2 MEDICAL BIOLOGICAL DEFENSE (APPLIED RESEARCH): This project funds applied research on the development of vaccines, therapeutic drugs, and diagnostic capabilities to provide an effective medical defense against validated biological threat agents including bacteria, toxins, and viruses. Innovative biotechnological approaches and advances will be incorporated to obtain medical systems designed to rapidly identify, diagnose, prevent, and treat disease due to exposure to biological threat agents. Categories for this project include Defense Technology Objectives (DTO); science and technology programs in medical biological defense (diagnostic technology, bacterial therapeutics, toxin therapeutics, viral therapeutics, bacterial vaccines, toxin vaccines, and viral vaccines); and directed research efforts (medical countermeasures, genetically engineered threat countermeasures, and vaccines).

FY 2001 Accomplishments:

- 600 Common Diagnostic Systems (DTO) - Established preclinical models to evaluate rapid nucleic acid analysis options that enhance the recognition of infections caused by a broad range of biological threat agents. Prepared and optimized new molecular diagnostic reagents, controls, and protocols compatible with emerging portable nucleic acid analysis systems for identifying biological threat agents prior to conducting comprehensive evaluation trials.

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BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA2 - Applied Research	0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)	TB2

FY 2001 Accomplishments (Cont):

- 400 Medical Countermeasures for Brucella (DTO) - Continued to develop and qualify in vitro systems in mice and higher animal species to reliably quantitate the intensity of potentially protective immune responses and determine the immune system components that eliminate infection with candidate live vaccines. Determined the stability of live, attenuated vaccine strain over time, using the mouse model. Developed additional live vaccine candidates with multiple attenuating mutations.
- 700 Medical Countermeasures for Encephalitis Viruses (DTO) - Developed higher animal species models of Venezuelan equine encephalitis (VEE) virus type 1E and initiated development of a higher animal species model for VEE virus type 3A. Completed the development of vaccine candidates for VEE virus type 3A.
- 500 Multiagent Vaccines for Biological Threat Agents (DTO) - Improved vaccine delivery platforms (naked DNA and VEE replicon systems) to optimize their efficiency for use as multiagent vaccines.
- 573 Needle-less Delivery Methods for Recombinant Protein Vaccines (DTO) - Identified appropriate assays for toxin-specific recombinant protein antibodies/other indicators of immunity. Identified lead commercial or proprietary devices and formulations for vaccine delivery. Identified intradermal and respiratory routes having the most potential for success for needle-less vaccine delivery.
- 160 Recombinant Plague Vaccine Candidate (DTO) - Developed assays and reagents for determining correlates for immunity for the recombinant plague vaccine candidate. Performed additional experiments supporting use of the anti-F1 competitive ELISA as an in vitro correlate to protection. Demonstrated proof-of-concept for mouse passive transfer as a surrogate marker of protection and for microphage cytotoxicity inhibition assay as a potential new in vitro correlate to protection.

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BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA2 - Applied Research	0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)	TB2

FY 2001 Accomplishments (Cont):

- 500 Recombinant Protective Antigen (rPA) Anthrax Vaccine Candidate (DTO) - Optimized purification methodology to minimize the number of isoforms in purified preparations of rPA, separated the isoforms and determined their biological activities. Initiated a study to evaluate isoform immunogenicity and ability to protect against anthrax infection in the rabbit model. Initiated a study in the rabbit model to determine the requirement for formaldehyde to stabilize formulated rPA vaccine preparations. Initiated studies to develop a mouse potency assay and determine in vitro correlate of immunity for the rPA vaccine candidate. Developed antibodies in the rabbit against rPA to support continuing passive immunity studies.
- 2696 Diagnostic Technologies - Prepared new diagnostic reagents and devices compatible with emerging immunological platforms and rapid nucleic acid analysis systems for enhanced recognition of infections with validated biological threats. Evaluated 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) of military interest. Identified field sites for the comprehensive validation of rapid diagnostic methods that will provide performance data prior to transitioning to advanced development.
- 557 Therapeutics, Bacterial - Optimized animal models for therapeutic indices. Evaluated in vivo activity of selected antimicrobials in established in vitro biochemical assays. Evaluated next generation antibiotics for therapeutic efficacy against bacterial threat agents. Designed an animal model for in vivo evaluation of selected compounds to protect against parenteral and aerosol infection by glanders and anthrax bacteria. Performed in vivo studies to evaluate therapeutic compounds against glanders.

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BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA2 - Applied Research	0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)	TB2

FY 2001 Accomplishments (Cont):

- 5066 Therapeutics, Toxin - Standardized assays for high-throughput screening of small molecule inhibitors of botulinum and staphylococcal enterotoxin B (SEB) toxin ligand-receptor interaction. Developed a cell-free enzymatic assay for ricin toxicity and screening inhibitors and developed a quantitative ricin neutralization assay to evaluate immune response in humans following vaccination. Solved three dimensional structure of the bound and unbound serotype B botulinum neurotoxin (BoNT) by x-ray crystallography to better characterize the active site for inhibitor development. Established a transgenic mouse colony and showed that lymphocytes from the mice react similarly to human lymphocytes to various biological warfare agents. Generated panels of monoclonal antibodies that neutralize BoNT serotype A and SE serotypes A, B, C1, and D.
- 3729 Therapeutics, Viral - Developed a rabbitpox-rabbit animal model for analysis and characterization of candidate antiviral compounds for therapeutic activity. Investigated mechanisms of Ebola and Marburg virus (MBGV) pathogenesis in higher animal species models to define likely targets in agent pathogenesis and identify potential mediators of shock.
- 5047 Vaccines, Bacterial - Evaluated previously identified virulence factors as vaccine candidates for Y. pestis. Optimized the animal model for aerosol exposure to B. mallei (glanders) for use in assessing vaccine candidates. Continued research on existing surrogate markers of protection against plague, identified additional markers, and demonstrated surrogate efficacy in the mouse model against aerosol plague infection by passive transfer of F1 capsular and V antigen antibody. Identified surrogate markers for anthrax and demonstrated surrogate efficacy in the rabbit model against parenteral anthrax infection by passive transfer of rPA antibody. Obtained plasmids to carry foreign genes for constructing vaccine strains in avirulent rough mutants of Brucella in order to evaluate Brucella as a possible multiagent vaccine platform.

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BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA2 - Applied Research	**0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)**	**TB2**

FY 2001 Accomplishments (Cont):

- 1166 Vaccines, Toxin - Utilized fermentation process development and scale-up support services and the Pichia yeast expression system to obtain recombinant vaccine candidates for botulinum toxin serotypes D and G and initiated efficacy studies in animals.
- 734 Vaccines, Viral - Explored the addition of cytokine gene co-delivery with Ebola viral genes to achieve protective immunity. Determined additional components required in a vaccine that will protect against the most divergent isolates of MBGV.

Total 22428

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BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA2 - Applied Research	**0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)**	**TB2**

FY 2002 Planned Program:

- 600 Common Diagnostic Systems (DTO) - Complete system integration and verification of approaches, reagents, and protocols for portable devices capable of detecting and identifying nucleic acids from a broad range of biological threat agents in clinical specimens.
- 350 Medical Countermeasures for Brucella (DTO) - Test most efficacious vaccine candidate against Brucella abortus (B. abortus) and B. suis in the mouse lung infection model. Test efficacy against B. melitensis of additional live vaccine candidates in the mouse lung infection model. Continue to develop and validate in vitro systems in mice and higher animal species to reliably quantify the intensity of potentially protective immune responses and determine the immune system components that eliminate infection with candidate vaccines.
- 200 Medical Countermeasures for Encephalitis Viruses (DTO) - Complete development of higher animal species models for Venezuelan equine encephalitis (VEE) virus type 3A. Redirect eastern equine encephalitis (EEE) and western equine encephalitis (WEE) virus vaccine development back to discovery and focus DTO on a multivalent VEE vaccine candidate.
- 300 Multiagent Vaccines for Biological Threat Agents (DTO) - Complete final improvements to the vaccine delivery platforms for their use as multiagent vaccines.
- 593 Needle-less Delivery Methods for Recombinant Protein Vaccines (DTO) - Evaluate formulations for intranasal, inhalation and transdermal application of recombinant proteins intended for use as vaccines. Evaluate available devices for delivery of vaccine using animal models. Develop and standardize assays to quantitate immune status.
- 230 Recombinant Plague Vaccine Candidate (DTO) - Complete determination of the range of protection of the recombinant plague vaccine candidate against other virulent strains of Y. pestis in animals.

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DATE: February 2002

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA2 - Applied Research	0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)	TB2

FY 2002 Planned Program (Cont):

- 500 Recombinant Protective Antigen (rPA) Anthrax Vaccine Candidate (DTO) - Complete evaluation of isoform immunogenicity and ability to protect against anthrax infection in the rabbit model. Complete the determination of formaldehyde requirement for stable rPA vaccine preparations. Complete the development of the mouse potency assay and the determination of the in vitro correlate of immunity for the rPA vaccine candidate. Investigate enhancement of the rPA vaccine candidate with immunostimulatory compounds. Develop antibodies to rPA in higher animal species to support continuing passive immunity studies.
- 5085 Diagnostic Technologies - Continue preparation of diagnostic reagents that will enhance the depth and diversity of current approaches for the rapid recognition of infection by potential biological threat agents. Evaluate preclinical models and standards for evaluating medical diagnostic systems prior to transition to the regulatory compliant medical laboratory.
- 1798 Therapeutics, Bacterial - Optimize and correlate in vitro assays with animal models for selected antibiotic and other therapeutics for bacterial threat agents and examine effects of selected therapies on multiple agent exposures in an animal model. Study the effect of immunomodulators on the host response to B. mallei and Y. pestis candidate vaccines and identify modulators that are effective in enhancing candidate vaccines.
- 7757 Therapeutics, Toxin - Initiate structural stabilization and formulation studies on lead inhibitors of botulinum and SEB toxin activity. Refine in vivo and standardize in vitro screening models for botulinum toxin and SEB intoxication.
- 3595 Therapeutics, Viral - Assess the potential for immunotherapy against Ebola virus in higher animal species models. Complete investigation of mechanisms of Ebola and Marburg virus (MBGV) pathogenesis in higher animal species models to characterize promising surrogate markers of efficacy for therapies.

CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2A Exhibit)	DATE February 2002

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA2 - Applied Research	**0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)**	**TB2**

FY 2002 Planned Program (Cont):

- 4395 Vaccines, Bacterial - Optimize in vitro correlate assays for candidate vaccines against various bacterial threat agents and evaluate the efficacy of additional novel component vaccine candidates (i.e., fusion proteins and antigen cocktails). Optimize formulation and dosage regime of selected vaccine candidates in animals. Determine whether plasmids expressing foreign genes in avirulent Brucella leads to suitable attenuation and immunogenicity in mice.
- 1963 Vaccines, Toxin - Determine whether the recombinant fragment C vaccine candidates can elicit protective immunity in mice against neurotoxins produced by various strains of Clostridium botulinum.
- 2530 Vaccines, Viral - Define the correlates of immunity (i.e., neutralizing antibody, cytotoxic T cells) that protect against disease from MBGV. Develop assays to measure surrogate markers to validate the efficacy of vaccine candidates in established model systems for MBGV. Develop higher animal species models for western equine encephalitis virus.
- 1500 Medical Countermeasures - Enhance applied research efforts toward the development of broad-spectrum therapeutic countermeasures for exposure to broad classes of biological threats.
- 3000 Genetically Engineered Threat Medical Countermeasures - Expand genetic and protein databases to identify and catalogue the various virulence factors, toxic motifs, and host regulatory proteins responsible for the pathologic effects of biological threat agents. Continue curating the genetic information database, evaluating mechanisms of pathophysiology associated with toxin threats, and developing critical proteomics capability.
- 1500 Vaccines - Enhance applied research 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.
- 617 SBIR - Small Business Innovative Research Efforts.

Total 36513

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BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA2 - Applied Research	**0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)**	**TB2**

FY 2003 Planned Program:

- 350 Medical Countermeasures for Brucella (DTO) - Determine whether over-expression of vaccine antigens in candidate live vaccines increases protective efficacy. Continue to develop and validate in vitro systems in mice and higher animal species to reliably quantitate the intensity of potentially protective immune responses and determine the immune system components that eliminate infection complications following use of live attenuated candidate vaccines.
- 200 Medical Countermeasures for Encephalitis Viruses (DTO) - Complete studies on VEE vaccine virus production, genetic stability, and transmission potential of candidate vaccines in competent vector mosquitoes.
- 628 Needle-less Delivery Methods for Recombinant Protein Vaccines (DTO) - Downselect formulations for intranasal, inhalation and/or transdermal delivery of recombinant protein vaccine. Propose commercial or proprietary device for delivery of vaccines.
- 7414 Diagnostic Technologies - Evaluate 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. Design and evaluate new medical diagnostic technologies and specimen-processing methods for the enhanced recognition of infections by potential biological threat agents by field medical laboratories. Continue to evaluate diagnostic technologies by using animal models. Develop field sites for evaluating new diagnostic technologies.
- 1793 Therapeutics, Bacterial - Evaluate novel antibiotics and other therapeutics in established in vitro assays and animal models. Establish a database of therapeutic profiles for various strains of bacterial threat agents.

CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2A Exhibit)	DATE February 2002

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA2 - Applied Research	**0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)**	**TB2**

FY 2003 Planned Program (Cont):

- 8757 Therapeutics, Toxin - Evaluate the outcome of structural stabilization studies on lead inhibitors of botulinum and SE. Standardize in vivo concept model systems for assessment of therapeutic efficacy and surrogate endpoints of human clinical efficacy.
- 3758 Therapeutics, Viral - Continue assessing the potential for immunotherapy against Ebola virus in higher animal species models. Identify pharmacological compounds provided by industry that disrupt filovirus polymerases. Assess therapeutic action of compounds in mouse and higher animal models of filovirus infection.
- 5069 Vaccines, Bacterial - Develop mutants in various agents for in vivo expressed genes to examine role in virulence. Characterize the mechanism(s) of vaccine resistance in selected strains of various agents. Determine mechanisms and correlates of protection with efficacious Burkholderia mallei vaccines.
- 1082 Vaccines, Toxin - Standardize in vivo and in vitro concept model systems for assessment of vaccine efficacy and surrogate endpoints of human clinical efficacy.
- 3585 Vaccines, Viral - Define the correlates of immunity that protect against disease from Ebola virus. Develop assays to measure surrogate markers to validate the efficacy of vaccine candidates in established model systems for Ebola virus. Develop higher animal species models for eastern equine encephalitis virus.
- 1438 Medical Countermeasures - Accelerate research to define criteria for successful therapeutics against toxins and viruses to obtain diverse compounds such as inhibitors, channel-blockers, natural product extracts, and peptides that show promise as potential therapeutics against botulinum neurotoxins, staphylococcal enterotoxin, ricin toxin, and viruses. Continue characterizing and refining the variola non-human primate model for human smallpox for use in determining the effectiveness of post-exposure therapies.

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

DATE: **February 2002**

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA2 - Applied Research	**0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)**	**TB2**

FY 2003 Planned Program (Cont):

- 2875 Genetically Engineered Threat Medical Countermeasures - Accelerate research efforts directed toward compiling and prioritizing function-related structural elements that constitute known toxins and virulence factors of biological threat agents. Continue developing integrated databases of protein domains or three-dimensional structural elements identified as virulence factors in biological threat organisms.
- 1437 Vaccines - Evaluate additional vaccine candidates for delivery using the multiagent delivery platform. Develop virus constructs and obtain commercially produced humanized mouse monoclonal antibodies to evaluate protective immune responses. Investigate the potential of live vaccine candidates for bacterial threat agents.

Total 38386

B. Other Program Funding Summary:

	FY 2001	FY 2002	FY 2003	FY 2004	FY 2005	FY 2006	FY 2007	To Compl	Total Cost
TB3 MEDICAL BIOLOGICAL DEFENSE (ADV TECH DEV)	22394	29919	34200	50789	45560	40585	40675	Cont	Cont

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

DATE: **February 2002**

BUDGET ACTIVITY: **RDT&E DEFENSE-WIDE/ BA2 - Applied Research**

PE NUMBER AND TITLE: **0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)**

PROJECT: **TC2**

COST (In Thousands)		FY 2001 Actual	FY 2002 Estimate	FY 2003 Estimate	FY 2004 Estimate	FY 2005 Estimate	FY 2006 Estimate	FY 2007 Estimate	Cost to Complete	Total Cost
TC2	MEDICAL CHEMICAL DEFENSE (APPLIED RESEARCH)	13819	18486	17974	17150	16569	18421	18572	Continuing	Continuing

A. Mission Description and Budget Item Justification:

Project TC2 MEDICAL CHEMICAL DEFENSE (APPLIED RESEARCH): This project funds medical chemical defense applied research and emphasizes the prevention of chemical casualties through application of pharmaceuticals for prevention and treatment of the toxic effects of nerve, blister, respiratory, and blood agents. This project supports applied research of prophylaxes, pretreatments, antidotes, skin decontaminants, and therapeutic compounds that will counteract the lethal, physical, and behavioral toxicities of chemical agents. It also supports development of medical chemical defense materiel that ensures adequate patient care, field resuscitation, and patient management procedures. 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 Fourth Generation Agents).

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

DATE: February 2002

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA2 - Applied Research	0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)	TC2

FY 2001 Accomplishments:

- 1200 Chemical Agent Prophylaxis II (DTO) - Tested best candidates of butyrylcholinesterase scavengers using appropriate model systems. Expanded physiologically based pharmacokinetic (PK) models for use in PK studies of candidate scavengers with/without agent present in a variety of species to include efficacy estimates in humans. Explored approaches for evaluating the human safety of human protein scavengers.
- 4000 Medical Countermeasures for Vesicant Agents II (DTO) - Defined in vitro/in vivo models that can be extrapolated to humans for safety and efficacy studies. Investigated routes of administration for candidate vesicant exposure therapies. Began physicochemical data acquisition for vesicant therapy candidates. Determined in vivo efficacy of candidate vesicant therapies for prevention of mustard-induced pathology.
- 576 Diagnostics - Evaluated commercial off-the-shelf products for potential use as diagnostics for nerve, vesicant, blood, or respiratory agent exposure.
- 2657 Pretreatments - Extended molecular modeling and site-directed mutagenesis research to development of next generation nerve agent bioscavengers. Investigated oxime reactivation of inhibited acetylcholinesterase enzymes at specific protein sites. Identified source of human butyrylcholinesterase (HBuChE) from outdated human blood products and initiated purification process.
- 3386 Therapeutics - Optimized formulations of scavenger enzymes in sponges, towelettes, and surgical pads for use in wound decontamination. Began efforts to acquire human butyrylcholinesterase enzyme in bulk. Screened midazolam plus candidate anticholinergic compounds for improvement in reducing/eliminating nerve agent-induced seizures.

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DATE: **February 2002**

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA2 - Applied Research	**0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)**	**TC2**

FY 2001 Accomplishments (Cont):

- 1000 Low Level Chemical Warfare Agent (CWA) Exposure - Initiated studies of pharmacological, physiological, and toxicological effects of exposure to low level CWAs. Investigated new sensitive biochemical and histological assay technologies for use in low level CWA exposures. Investigated potential biological markers that would indicate past exposure to low dose CWAs.
- 1000 Fourth Generation Agents (FGAs) - Assessed the efficacy of currently fielded classical nerve agent countermeasures or nerve agent countermeasures in advanced or exploratory development against FGAs.

Total 13819

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DATE: February 2002

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA2 - Applied Research	0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)	TC2

FY 2002 Planned Program:

- 1000 Chemical Agent Prophylaxis II (DTO) - Determine, through discussions with the FDA, the type(s) of data required for submission with an investigational new drug application for a human recombinant catalytic protein. Identify sources of human butyrylcholinesterase (HBuChE) for purification. Prepare sufficient amounts of purified HBuChE to test efficacy in two animal models. Transition HBuChE out of technology base. Vector/gene testing for bioscavenger delivery is continued in the technology base program.
- 3000 Medical Countermeasures for Vesicant Agents II (DTO) - Evaluate improved animal models for screening candidate combination therapies for mustard exposure. Define side effects, establish adversity levels, and collate available industrial documentation. In addition, evaluate potential treatments for mustard-induced pulmonary injury under controlled conditions.
- 1381 Diagnostics - Modify cholinesterase testing assay technology to generate diagnostic information on large sample sizes.
- 4740 Pretreatments - Continue development of potential transgenic/bioengineered for production of next generation nerve agent catalytic scavenger. Identify/develop animal models for tests of new scavenger candidate(s). Begin preliminary efficacy studies with catalytic scavengers of nerve agents. Characterize new scavengers. Renew identification of a cyanide pretreatment/treatment compound.
- 2552 Therapeutics - Initiate studies based on external program review to include assessing candidate agents for efficacy in saving vulnerable neurons and improving neurobehavioral outcome in suitable animal models of soman-induced status epilepticus. Develop criteria for evaluating neuronal salvage after status epilepticus. Evaluate improved animal models for screening combinations of anticonvulsant candidate therapies. Determine the potentiative effect(s) of combinations of anticonvulsants. Identify and validate animal models. Determine the essential ingredients for a rinse solution to optimally treat mustard-induced ocular injury.

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DATE: **February 2002**

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA2 - Applied Research	**0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)**	**TC2**

FY 2002 Planned Program (Cont):

- 1000 Low Level Chemical Warfare Agent (CWA) Exposure - Continue to study biological markers of low dose exposures and investigate selectivity of the markers for CWAs. Evaluate potential genetic and central nervous system perturbations following low level CWA exposures.
- 4500 Fourth Generation Agents (FGAs) - Assess the efficacy and prioritize potential approaches for improving the effectiveness of newly proposed nerve agent countermeasures. Evaluate oxime effectiveness against FGAs. Evaluate newly identified anticonvulsants for improved survival after exposure to FGAs. Assess the effects of in vivo persistence of FGAs on current countermeasure efficacy. Confirm cardiac pathology seen after exposure to FGAs.
- 313 SBIR - Small Business Innovative Research Efforts.

Total 18486

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

DATE: **February 2002**

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA2 - Applied Research	**0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)**	**TC2**

FY 2003 Planned Program:

- 1000 Medical Countermeasures for Vesicant Agents II (DTO) - Identify therapeutic window for administering compounds to mitigate the effects of mustard exposure. Evaluate combination therapies for sulfur mustard exposure in animal models.
- 2711 Diagnostics - Continue development of analytical methods to measure biological matrices (e.g., blood, urine, tissue) following CWA exposure. Develop confirmatory forensic diagnostic capabilities and rapid screening technology for field applications.
- 5982 Pretreatments - Expand physiologically based pharmacokinetic models to include scavengers as a component in the presence and absence of chemical warfare agents. Utilize animal model(s) from which cyanide pretreatment/treatment data can be extrapolated to humans. Initiate studies to evaluate potential pretreatments for mustard exposure using animal models. Investigate effectiveness of butyrylcholinesterase to prevent toxicity from exposure to low levels of CWA.
- 2781 Therapeutics - Evaluate new FDA-approved drugs for treatment of mustard-induced ocular injury. Optimize formulation for an ocular rinse that treats mustard-induced ocular injury.
- 2000 Low Level Chemical Warfare Agent (CWA) Exposure - Continue to study/validate biological markers for low level CWA exposure in animal models. Investigate the effectiveness of selected pretreatment and treatment countermeasures for low level nerve agent exposure. Determine neurobehavioral deficits resulting from exposure to low levels of nerve agents. Investigate potential therapeutic use of HBuChE for low level nerve agent exposure.

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

DATE: February 2002

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA2 - Applied Research	0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)	TC2

FY 2003 Planned Program (Cont):

- 3500 Fourth Generation Agents (FGAs) - Refine dosing regimen of newly proposed nerve agent countermeasures. Continue search for effective reactivators for acetylcholinesterase (AChE) inhibited by FGAs. Continue synthesis of oximes and other antidotes. Determine mechanism by which oximes bind and reactivate nerve agent-inhibited AChE by use of a library of mutant cholinesterases. Complete evaluation of cardiac pathology. Evaluate topical skin protectants against FGAs. Develop surrogate markers for alternative medical countermeasures in guinea pigs. Determine absorption, distribution, metabolism, and excretion of FGAs using in vivo animal models.

Total 17974

B. Other Program Funding Summary:

	FY 2001	FY 2002	FY 2003	FY 2004	FY 2005	FY 2006	FY 2007	To Compl	Total Cost
TC3 MEDICAL CHEMICAL DEFENSE (ADV TECH DEV)	9968	11302	12156	13423	13773	12907	13011	Cont	Cont