CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2 Exhibit)

DATE: **June 2001**

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

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

COST (In Thousands)		FY 2000 Actual	FY 2001 Estimate	FY 2002 Estimate							
	Total Program Element (PE) Cost	90557	81061	125481							
CB2	CHEMICAL BIOLOGICAL DEFENSE (APPLIED RESEARCH)	54117	43717	70156							
TB2	MEDICAL BIOLOGICAL DEFENSE (APPLIED RESEARCH)	23370	23107	36729							
TC2	MEDICAL CHEMICAL DEFENSE (APPLIED RESEARCH)	13070	14237	18596							

A. Mission Description and Budget Item Justification: The use of chemical and biological weapon systems in future conflicts is an increasing threat. 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. 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: June 2001

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

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

B. Program Change Summary:	FY 2000	FY 2001	FY 2002	
FY 2001 President's Budget	97400	73600	83185	
Appropriated Value	99280	80000	0	
Adjustment to Appropriated Value	0	0	0	
a. Congressional General Reductions	0	-560	0	
b. SBIR/STTR	-1409	0	0	
c. Omnibus or Other Above Threshold Reductions	-4697	0	0	
d. Below Threshold Reprogramming	-1587	1800	0	
e. Rescissions	-1030	-179	0	
Adjustments to Budget Years Since FY 2001 PB	0	0	42296	
FY2002/2003 President's Budget	90557	81061	125481	

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 (CB2 $33,443K; TB2 $7,097K; TC2 $3,075K). General reduction to fund higher priority efforts (-$1,931K) and increase for inflation assumptions ($612K).

Schedule:

Technical:

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

DATE: June 2001

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

COST (In Thousands)		FY 2000 Actual	FY 2001 Estimate	FY 2002 Estimate							
CB2	CHEMICAL BIOLOGICAL DEFENSE (APPLIED RESEARCH)	54117	43717	70156							

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: June 2001

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

FY 2000 Accomplishments:

- 728 Biological Point Detection - Completed array and fluidics hardware for the antibody based force differentiation assay (FDA). Demonstrated FDA sensor sensitivity enhancement of 100 fold using ultra filtration membrane. Initiated automation of sample preparation for FDA. Initiated joint effort with DOE CB Non-Proliferation Program to collect ambient background data from multiple U.S. and international sources into a single database and initiated analysis of data.
- 858 Biological Early Warning Detection - Initiated effort to enhance reliability (false detection reduction) and increase discrimination capability of optical analyzers by adding shape/size analysis. Initiated examination of pyrolysis-gas chromatography-ion mobility spectrometry (Py-GC/IMS) as technology to provide improved biological discrimination for early warning and system triggering functions. These approaches are candidate technology solutions for implementation in arrayed detector networks and stand-alone configurations.
- 1409 Biological Genetic Technology - Completed assessment of revised human superlibrary as an approach to recombinant antibody development. Developed recombinant antibody assays for several high priority agents; demonstrated performance exceeds currently available monoclonal antibodies. Initiated evaluation of combinatorial peptides as alternative recognition molecules. Transitioned successful antibodies to Critical Reagents Program for validation.
- 920 Chemical Early Warning Detection - Initiated feasibility studies to develop concepts for use of non-traditional chemical biological (disparate) sensors to cue for early warning.
- 2800 Chemical Point Detection - Completed market survey and downselection of technology for the detection of contaminants in potable water systems (water monitor). Initiated design and build of breadboard for water monitor.
- 1959 Chemical Imaging Sensor (DTO) - Demonstrated a 16-pixel spectrometer operating at 100 Hz with offline processing of data. This speed represents a factor of 20 improvement over current developmental systems.
- 2309 Scanning Airborne Fourier Emission for Gaseous Ultraspectral Analysis & Radiometric Detection (SAFEGUARD) - Upgraded sensors and initiated software and airborne platform integration.

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

DATE: June 2001

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

FY 2000 Accomplishments (Cont):

- 4897 Collective Protection - Conducted side-by-side testing of candidate residual life indicator (RLI) sensors with simulants, and initiated agent testing. Initiated testing of candidate immobilized bed materials to identify the critical properties of those materials. Measured breakthrough and equilibrium data of selected Toxic Industrial Chemicals (TICs). Evaluated candidate adsorbents for use in regenerative filtration applications. Conducted a downselect of best low cost tentage materials. Produced and evaluated a prototype shelter fabricated of the best candidate materials and seals. Transitioned the low cost tentage effort to the Joint Transportable Collective Protection System (JTCOPS) Block I.
- 1747 Individual Protection - Completed a front-end analysis (FEA) and prepared a master plan for individual protection to help focus investment in technologies. Completed the computational fluid dynamics model of the mass/energy transport through protective clothing. Determined dominant factors controlling high permselectivity from membrane structural and chemical studies. Completed a comparison of the finite element/computational fluid dynamic analysis model and the thermal mannequin results. Assessed the ability of nano-fibers to reduce aerosol penetration when applied to the outer-surface of a permeable protective garment. Blended catalysts (enzyme organophosphorus acid anhydrolase) and reactive oxides (MgO) with polymers, and evaluated their efficacy as decontaminants. Evaluated improved seals and closures employed in garment developed under the Advanced Lightweight CB Protection (DTO). Updated and finalized the respiratory encumbrance model. Evaluated integrated near-term mask/helmet concepts for interface and human factors. Completed the evaluation of the Joint Service Aviation Mask (JSAM) early prototype and developed design guidelines. Surveyed technologies and developed initial concepts for application to mask filter end of service life indicators.
- 620 Advanced Lightweight CB Protection (DTO) - Evaluated final concept garment using thermal mannequin, Man In Simulant Test (MIST), and field tests. Potential short-term transitions include JAM (JSLIST Approved Material) Alternate Source Qualification (ASQ) and the Joint Service Protective Aircrew Ensemble (JPACE). The Joint Chemical Ensemble, Block II is the mid-term application of the technology.

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

DATE: June 2001

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

FY 2000 Accomplishments (Cont):

- 5038 Man-portable Detectors - Developed and optimized polymer coated surface acoustic wave (SAW) and chemiresistive conducting devices which are sensitive and selective to nerve, blister, and blood agent simulants as well as toxic industrial chemicals. Developed impedance and fluorescence-based biosensors employing immunological and DNA detection probes. Integrated hybrid sensor array devices and electronics, neural networks, and other data acquisition and display hardware/software into a prototype detection system for chemical agents. Demonstrated an integrated prototype detector system for CBW agents and toxic industrial chemicals (TIC) under laboratory and field conditions. These efforts were directed toward development of a man transportable detector with low power and no field maintenance requirements.
- 2061 Low Level Chemical Agent Operational Studies - Completed baseline for comparison of historical data for sarin on rats using new methodology and collected data using extended six-hour exposure times with lethality as the endpoint. Initiated planning for determining the potency ratio of the second-generation nerve agents using sarin as the basis. Initiated planning for miosis threshold studies for sarin over extended exposure durations. Initiated planning for multi-species animal studies for toxicological effects of extended exposure duration at low concentrations to validate and verify alarm and warning levels for detector systems.
- 1821 Integrated Detection of Energetic and Hazardous Materials (IDEHM) - Developed integrated detection systems for sensing the presence of CBW agents and explosives utilizing the following technology approaches: ion trap mass spectrometry hardware miniaturization, electromagnetic detection (short range standoff detection of explosives), neutron based detection, and bioanalytical methodologies.
- 930 Advanced Adsorbents for Protection Applications (DTO) - Completed the screening of candidate adsorbent materials for the Joint Service General Purpose Mask (JSGPM). Investigated the effect of carbon fiber and particle size variations on filter bed performance. Initiated investigations of candidate advanced adsorbent materials for protection against TICs.

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

DATE: June 2001

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

FY 2000 Accomplishments (Cont):

- 2994 Biological Sample Preparation System (BSPS) (DTO) - Initiated efforts to develop fully automated two cu ft BSPS concept breadboard coupled with genetic detection sensor and electrospray mass spectrometer. Developed gene-based assays for the Joint Field Trials (JFT). Initiated development of mass spectrometry database for JFT.
- 826 Decontamination (DTO) - Improved enzyme activity on V-agents (persistent nerve agent) 10 fold. Achieved 5-10 fold improvement in production of nerve agent enzymes. Initiated a materials technology approach to HD (mustard) hydrolysis utilizing hyperbranched dendrimeric polymers. The materials were found to be successful in accomplishing hydrolysis of HD in the presence of enzymatic moieties utilized for the decontamination of nerve agents. Initiated new application systems based on emulsions and microemulsions.
- 5038 Decontamination - Incorporated solid adsorbents into the supercritical fluid and non-ozone depleting fluorocarbon solvent systems being developed for sensitive equipment decontamination in order to capture and neutralize removed chemical agents. Demonstrated the validity of the techniques for technical transfer into the Joint Service Sensitive Equipment Decontamination System (JSSED) Block I development program. Performed Front End Analysis (FEA) to identify optimal candidate JSSED Block I technologies. Identified promising approaches to solve JSSED Block II and Block III requirements, such as thermal processes and spot-cleaning technologies. Initiated a new decontamination approach based on oxidative processes. Continued on-going efforts using microemulsions with peracid oxidants. Initiated a further study in the material technology area to expand the capacity of hyperbranched dendrimeric systems based on mono-ethanolamine to perform decontamination operations. Continued efforts in zeolites and high surface area reactive solids as part of the next generation of solid decontaminants. Expanded the scope of this area to include novel reactive nano-particle technology. Conducted studies directed at determining the fate of agents adsorbed on surfaces commonly found at fixed site facilities.

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DATE: June 2001

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

FY 2000 Accomplishments (Cont):

- 2454 Supporting Science and Technology - Identified and technically evaluated emerging chemical threat agents. Designed quantitative toxic powder aerosol generator for use in the first and only U.S. nose-only exposure chamber with adequate containment for studying high-risk (no antidote) chemical aerosol substances. Measured quantitative performance of developmental aerosol collectors and their inlets to establish baseline metrics for future improvements. Initiated design of an advanced aerosol collector using mini-scale-manufacturing technology. Provided controlled biosimulant aerosol challenges for Joint Service, Defense Advanced Research Projects Agency (DARPA), and Department of Energy (DOE) experimental equipment in preparation for the Joint Field Trials (JFT).

- 2816 Modeling and Simulation - Developed High-Level Architecture (HLA) compliant version of Nuclear, Chemical, Biological, and Radiological (NCBR) Simulator for application in Simulation Based Acquisition (SBA) for Joint Service CB defense equipment, and demonstrated capability to support several hardware development programs in distributed simulations of military worth evaluations. Completed Version 3 of the Vapor, Liquid and Solid Tracking (VLSTRACK) Model, which includes the advanced secondary evaporation methodology for chemical agents and the capability to ingest full resolution mesoscale meteorological data fields to more accurately drive atmospheric dispersion. Transitioned coupled CB environment/meteorological model for use with forward-deployed weather forecast operations in Navy's Tactical Environmental Support System (TESS). Demonstrated Initial Operational Capability (IOC) of the Simulation, Training, and Analysis for Fixed Sites (STAFFS) model for simulation of Chemical and Biological Warfare (CBW) effects on operations at a fixed site (AF fighter base).

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DATE: June 2001

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

FY 2000 Accomplishments (Cont):

▪	11892	Chemical and Biological (CB) Countermeasure Initiatives - Initiated a broad CB countermeasures program to enhance ability to recognize, prevent, respond to, mitigate, and recover from a CB terrorist incident. Initiated a systems approach to quickly simulate chemical and biological agent dispersal in an urban environment. Modeled the scavenging, degradation, and deposition of CB contaminants in the urban environment. Developed Weapons of Mass Destruction (WMD) supplements to existing healthcare facility plans for biological warfare (BW) events. Initiated program to apply novel biological approaches to quickly develop vaccines and antidotes against selected BW agents. Investigated combinative toxicology of bio toxin mixtures. Developed high affinity antibodies to Yersinia pestis (plague). Developed aptamers with high affinity binding for Ricin A and B. Developed signaling aptamers for optical signal transduction. Engineered hyperstable antibodies that can be stored for months. Initiated program to standardize CB medical databases and communication protocols involved in planning for and response to a CB terrorist attack. Initiated program to integrate various and disparate CB sensor inputs into a central database. Initiated automated database to provide early detection of a CB attack. Developed biosensor assays for rapid detection of microbial pathogens and toxins associated with food and water. Developed base for rapid antibody optical BW sensor. Developed non-woven CB protective clothing with enhanced protection and comfort. Developed rapid methods to perform large surface CB decontamination.
Total	54117	

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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 Planned Program:

- 1648 Biological Point Detection - Complete analysis of accumulated ambient background data and identify gaps for further study as indicated by analysis. Continue generation and screening of recombinant antibodies against select bio agents using biased genetic libraries. Incorporate into Enzyme Linked Immuno Sorbent Assay (ELISA) and biosensors for test/evaluation, and transition best candidates to Critical Reagents Program.
- 319 Biological Standoff Detection (DTO) - Initiate analysis of existing data to identify top candidates for further evaluation to provide improved biological standoff capability. Identify and develop key performance requirements to develop biological standoff capability.
- 2050 Chemical Imaging Sensor (DTO) - Demonstrate a 16-pixel spectrometer in real-time operation at 100 Hz (on-line process of data). This capability will represent the first time use of high performance computers for real-time on-line processing for this application. System will also be capable of being mounted on platforms with objective speeds in excess of 1,000 miles per hour with an imaging capability.
- 2050 Collective Protection - Conduct a Front-End Analysis (FEA) and prepare a Master Plan (MP) for developing integrated NBC protection systems. The FEA/MP will identify and prioritize various DoD user community requirements for Collective Protection. Various filtration and shelter technology approaches will be identified, categorized and prioritized in terms of maturity, risk, applicability, and cost. Complete RLI sensor side-by-side testing. Complete simulant, TIC, and agent testing of candidate sensors. Produce and test immobilized beds for selected applications using optimized materials and processes. Complete the measurement of breakthrough and equilibrium data of current adsorbents against TICs and assess adsorptive/chemisorptive properties. Conduct lab scale testing to validate the Pressure Swing Adsorption model and to help in optimizing the bed/system performance of regenerative filtration systems. Produce and evaluate optimized hermetic seals for shelters, and transition to Joint Transportable Collective Protection System (JTCOPS-Block I).

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

FY 2001 Planned Program (Cont):

- 2750 Biological Sample Preparation System (BSPS) (DTO) - Demonstrate BSPS at JFT. Reduce size of BSPS by 35% while maintaining overall sensitivity on both mass spectrometer and genetic detection platforms against eight bacterial and viral materials. Transition to the Joint Biological Point Detection System (JBPDS) Block II.
- 1050 Chemical Point Detection - Evaluation of alternative technologies, e.g. surface enhanced RAMAN, molecular imprinted polymers, gas chromatograph-ion mobility spectrophotometer, etc. as risk reduction to support the Joint Chemical Biological Agent Water Monitor (JCBAWM).
- 794 Decontamination (DTO) - Produce sufficient V-agent (persistent nerve agent) enzymes and H-agent (blister) reactive polymers to optimize their use in foams, detergents solutions, and other types of dispersion systems. Incorporate conventional chemical approaches into end enzyme formulation.
- 7947 Decontamination - Complete demonstration of sensitive equipment decontamination methodology and finalize transition of technology for Block I of the JSSED program. Select technologies to be demonstrated for the decontamination of sensitive interiors (JSSED Block II) focusing on thermal approaches. Evaluate approaches for operational decontamination of sensitive equipment and interiors on the move (JSSED Block III). Investigate alternative approaches to improve efficiency of V-agent (persistent nerve agent) enzymes. Broaden the scope of enzymatic decontamination processes evaluating potential systems for non-traditional agents. Validate oxidative processes in aqueous and mixed/aqueous/organic solvent systems as solutions, emulsions or microemulsions. Examine dendritic assembly systems incorporating mono-ethanol amine functionality and perform preliminary agent challenges. Continue the evaluation of novel solid matrices. Initiate an effort to determine the fundamental limitations of solid based approaches. Continue efforts to determine the fate of agent on common environmental surfaces associated with fixed site facilities. Conduct study to evaluate the hazard posed by potential reaerosolization of BW materials. Determine an approach to use coating technology to address decontamination and protection of materiel items.

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

FY 2001 Planned Program (Cont):

- 4976 Leap Ahead Technologies - Investigate advanced respiratory and percutaneous protection technologies identified in Individual Protection FEA to reduce thermal load and breathing resistance. Break technology barriers in developing simulants for emerging agents. Complete force differentiation assay (FDA). Refine 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. Complete initial analysis of RADAR multi-mission sensor and identify other disparate sensors. Initiate exploration of chip-based phylogenetic assay for highly multiplexed biological agent detection. Initiate assessment of data gaps in threat agent data and needs for improved simulants in CB defense materiel development. Institute a simulant database for selecting appropriate simulants in materiel development and establish a repository for chemical simulants and a standard biological simulant laboratory.

- 2224 Individual Protection - Select and evaluate permselective membranes to validate the novel permselective membrane model. Investigate mechanisms for more durable nano-fibers; fabricate and test samples of those materials. Investigate nano-fiber bonding/integration methods, and conduct aerosol and challenge tests. Identify methodology for evaluation of suits against TICs. Construct a parametric skeleton model of candidate helmet/mask concepts to help identify those with most potential for long term solutions.

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

FY 2001 Planned Program (Cont):

- 3712 Modeling and Simulation - Develop 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). Improve coupling of CB environment and high resolution meteorological models for incorporation of CBW hazard prediction/tracking into forward-deployed meteorological forecast/nowcast operations. Continue 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. Develop additional models for Joint Service CB defense equipment for application in SBA. Transition current version of the Simulation, Training, and Analysis for Fixed Sites (STAFFS) model to the Center for Army Analysis for evaluation. Enhance development of STAFFS model for simulation of CBW effects on operations at Aerial Ports of Debarkation (APOD) and Sea Ports of Debarkation (SPOD). Complete validation studies and software documentation for VLSTRACK version 3.
- 1206 Advanced Adsorbents for Protection Applications (DTO) - Prepare and evaluate materials and bed compositions according to property/performance correlations, and identify the optimal adsorbent bed composition for masks. Base selection of adsorbents on protection provided against both TICs and CB agents.
- 700 End of Service Life Indicator for Filters (DTO) - Construct and evaluate prototype mask end of service life indicators. Initiate development of advanced concepts in mask air filtration/purification.
- 1300 JCBAWM (DTO) - Complete 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. Develop test protocols for testing system.

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

FY 2001 Planned Program (Cont):

▪	1821	Supporting Science and Technology - Complete initial toxicology study using highly toxic powder in the new nose-only exposure chamber for extremely hazardous aerosols. Measure quantitative performance of candidate aerosol collectors for advanced point biodetection technology. Demonstrate a new aerosol collector using mini-scale manufacturing technology, which substantially reduces power consumption compared to fielded collectors while maintaining high collection efficiency over the respirable particle size range from 1-10 micrometers diameter and operating at the Joint Service low temperature requirement (-28 degrees F). Continue to provide controlled biosimulant aerosol challenges for Joint Service, DARPA, and DOE experimental equipment in preparation for the JFT.
▪	2185	Low Level Chemical Agent Operational Studies - Complete sarin exposure data analysis (lethality endpoint) on rats. Initiate miosis threshold studies using sarin over extended exposure durations. Initiate potency ratio studies of second-generation nerve agents for toxicological effects of extended exposure duration and low concentration exposures to validate and verify alarm and warning levels for detector systems.
▪	4683	Man-portable Detectors - Continue insertion of semi-conductive metal oxide (SMO) technology (and SAWs if required) into a chemical detector brassboard. Based on user inputs, determine the operational parameters of a man-portable detection system. Joint Service requirements will be used to determine the response parameters and operating environment. The sensitivity of the device will be equal to or greater than that required for the Joint Chemical Agent Detector (JCAD) as specified in the JCAD operational requirements document (ORD). Demonstrate an integrated prototype detector system for CW agents under laboratory and field conditions.
▪	1561	Improved CB Detection - Enhance performance of high sensitivity passive stand-off detector by increasing hardware sensitivity, characterizing and removing background variables, and improving system detection software.
▪	741	SBIR
Total	43717	

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FY 2002 Planned Program:

- 6400 Biological Point Detection - Reduce size and logistic burden of optical fluorescence/shape analysis system and Py-GC-IMS sensors. Test against expanded set of biological simulants and interferents. Initiate exploration of new concepts for small, combined chemical and biological identifiers. Develop and test concepts toward automation of chip-based phylogenetic analysis of biological materials. Develop database of multiple gene targets for biological agents. Identify and initiate exploration of other concepts for multiplexed identification/analysis of broad spectrum of biological agents. Continue generation and screening of recombinant antibodies against select biological agents, and transition best candidates to Critical Reagents Program. Initiate biological background data collection efforts to fill data gaps previously identified.
- 2400 Chemical Imaging Sensor (DTO) - Demonstrate a 16-pixel spectrometer operating at 360 Hz with off-line processing of data. Initiate planning for transition of brassboard design and build in support of Joint Service Wide Area Detection (JSWAD) program.
- 1325 Advanced Adsorbents for Protection Applications (DTO) - Continue evaluation of engineered beds and materials and select the optimal bed/material combination for single IP and CP filter pass applications. Select adsorbents for both CP and IP applications against TIC and CB agents.
- 3150 Collective Protection - Determine TIC breakthrough and equilibrium data for advanced and novel adsorbents. Conduct prototype (large diameter bed) regenerative filter bed testing to demonstrate bed improvements and to update the performance model. Develop novel single pass filter concepts using nano-materials and identify absorbents to support that concept. Evaluate shelter materiel using technologies identified to facilitate rapid development of an improved product.
- 2400 Modeling and Simulation of Joint Operability - Expand model development for simulation of CBW effects on joint force operations for incorporation into advanced simulations. Demonstrate operational capability of the STAFFS model for simulation of CBW effects on operations at APODs and SPODs.

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FY 2002 Planned Program (Cont):

- 2300 Modeling and Simulation of CBW Environment - Expand development of advanced CB weapons models (Lagrangian particle and complex fluid dynamics methodologies) for more accurate, higher-resolution atmospheric transport and fate predictions in complex and urban terrain for battlespace awareness and contamination avoidance. Extend development of high-altitude CB agent behavior for application in Tactical Ballistic Missile (TBM) intercept analysis. Begin development of the capability to accurately model the interaction (evaporation and persistence) of chemical agents with materials and the reaerosolization of biological agents.

- 9800 Supporting Science and Technology - Continue assessment of gaps in threat agent data, and identify needs for improved simulants in CB defense materiel development. Initiate a program of synthesis, toxicology screening, and characterization of new threat materials (to include Fourth Generation Agents (FGAs)) identified as urgent needs while continuing assessment of long-term needs. Initiate development of improved simulants for chemical aerosols, microencapsulated viruses, stabilized bacteria, and proteinaceous and nonproteinaceous toxins/bioregulators. 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 and collectors using micro-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 JFT. Assemble a database on agent fate on surfaces incorporating prior year's findings. Complete BW reaerosolization studies.

- 2650 Detection of Contaminants on Surfaces - 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.

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

FY 2002 Planned Program (Cont):

- 1750 Biological Standoff Detection (DTO) - 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 stand off system.
- 1600 Chemical Point Detection - Test/demonstrate the capabilities of the high potential alternative technologies from the technical evaluation of technology conducted in FY01 for the JCBAWM effort.
- 2100 Modeling and Simulation of CB Defense Equipment - Expand development of models for Joint Service CB defense equipment for application in Simulation Based Acquisition (SBA) training, distributed simulations, war-gaming, and military-worth evaluations.
- 800 End of Service Life Indicator for Filters (DTO) - Construct and evaluate proof of principle for end of service life indicator (ESLI) model.
- 2000 JCBAWM (DTO) - Complete construction of initial breadboard. Complete testing to identify shortfalls. Transition technologies to Advanced Technology Development.
- 2100 Early Warning Detection - Demonstrate concept and technology of a test representative RADAR system for queuing of stand off systems. Investigate options for linking disparate sensors to battlespace management systems.

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

FY 2002 Planned Program (Cont):

- 4550 Individual Protection - Incorporate aerosol threat mediation techniques in the fabrication of concept garments. Initiate testing of concept garments. Identify and incorporate color transition materials into nano-fiber membranes and test for response to agent simulants. Evaluate fielded and developmental clothing materials for the protection they provide against TICs. Produce trial membranes using ion implantation techniques, and evaluate their material physical properties and agent protection capabilities. Conduct a study of adsorbent fabric placement in semi-permeable membrane garments for added vapor and aerosol protection. Fabricate and evaluate a proof of concept model of the helmet/mask concept using the parametric skeleton model. Construct and evaluate prototype mask end of service life indicators. Initiate development of advanced concepts in mask air filtration/purification.
- 900 Decontamination (DTO) - Complete development of enzymatic formulations and transition to either the Joint Service Fixed Site Decontamination System program as a product improvement or to follow-on efforts under the Superior Decontamination System program.
- 7431 Decontamination - Continue developmental efforts to address JSSED Block II and III approaches focusing on thermal technology and spot cleaning methodology. Develop solution approaches for Superior Decontamination Systems combining novel chemical and biochemical technologies into a unified approach. Complete the evaluation determining the physical limitations of novel solid technology and implement findings into the program. Determine best future uses for these materials.
- 5000 Low Level Chemical Agent Operational Studies - Complete miosis threshold studies for sarin over extended exposure durations. Continue G agent potency ratio studies on rats. Initiate multi-species animal studies for G agents. Initiate planning for third generation nerve agents studies in rats. Initiate physiological modeling efforts to understand the dependence of toxicological effects on the route of exposure to low level nerve agents.

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

DATE: June 2001

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):

▪	2500	FGA (non-medical) - 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.
▪	4000	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 LIDAR, millimeter wave spectroscopy. Investigate potential applicability of UV and IR imaging.
▪	3000	Agent Fate - Identify standard construction and natural environmental materials and study interactions of these materials with chemical agents using novel in situ methods. 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 relate to chemical hazard evolution.
▪	2000	CB Modeling/Simulation - Enhance spatial resolution of hazard prediction codes through physical models that incorporate resolution improvements in radiation, turbulence, and precipitation physics. Initiate coupling of numerical weather prediction models with existing CBW dispersion codes.
Total	70156	

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

DATE: June 2001

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 2000 Actual	FY 2001 Estimate	FY 2002 Estimate							
TB2	MEDICAL BIOLOGICAL DEFENSE (APPLIED RESEARCH)	23370	23107	36729							

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 tc exposure to biological threat agents. Categories for this project include Defense Technology Objectives (DTO); current Science and Technology Plans in medical biological defense (diagnostic technology, bacterial therapeutics, toxin therapeutics, viral therapeutics, bacterial vaccines, toxin vaccines, and viral vaccines); and directed research efforts (chemical/biological hazard detection and protocols to enhance biological defense).

FY 2000 Accomplishments:

- 600 Common Diagnostic Systems (DTO) - Evaluated alternative approaches, devices, and reagents for the portable nucleic acid analysis of a broad range of biological threat agents in clinical specimens that will lead to an enhanced diagnostic capability by field medical laboratories. Established methods and prepared documentation for preparing standards and controls for regulatory-compliant evaluation trials. Evaluated alternative methods for rapid medical specimen-processing compatible with the integrated specimen processing and gene amplification system that will be evaluated for further refinement and transition.
- 500 Medical Countermeasures for Encephalitis Viruses (DTO) - Defined a common vaccine platform for development of a multivalent equine encephalitis vaccine using a full-length cDNA recombinant vaccine for Venezuelan equine encephalitis (VEE) virus types 1A/B/C.

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

DATE: June 2001

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

FY 2000 Accomplishments (Cont):

- 1000 Multiagent Vaccines for Biological Threat Agents (DTO) - Evaluated prior studies performed with individual and combined vaccine components (antigens, DNA, viral vectors, etc.) and identified several components to test in multiagent vaccine delivery platforms.
- 2343 Diagnostic Technologies - Prepared new diagnostic reagents by using recombinant biotechnologies and designed devices that will enhance the diversity and depth of the medical diagnostic capability. Optimized processing methods for selected clinical specimen formats, including swabs, whole blood, sera, and tissues that will enhance current capabilities for the rapid recognition of infections by biological threat agents. Prepared evaluation criteria and standardized reagents that are compatible with regulatory guidelines prior to comprehensive evaluation trials of portable nucleic acid analysis systems for the identification of biological threat agents in clinical laboratories. Optimized new medical diagnostic approaches, reagents, and devices for the rapid recognition of infections by Bacillus anthracis (B. anthracis), Yersinia pestis (Y. pestis), Francisella tularensis (F. tularensis), Brucella sp., alphaviruses, filoviruses, and orthopox viruses that will enhance medical care and force protection. Evaluated preclinical models for assessing diagnostic approaches that will enhance identification of anthrax and alphavirus infections prior to transition to regulatory-compliant medical laboratories.
- 589 Therapeutics, Bacterial - Evaluated selected antimicrobial compounds for treatment of respiratory infection caused by B. mallei, the causative agent of glanders. Initiated a study of cellular mediators (cytokines, chemokines, and cell surface receptors) during glanders infection and immunomodulation as a potential countermeasure approach.
- 1771 Therapeutics, Toxin - Developed approaches to the generation of therapeutics (peptides and synthetic compounds) for Staphlyococcal enterotoxins (SEs), botulinum neurotoxin, and ricin toxin based on rational drug design and molecular structure of the toxins. Synthesized a short polypeptide that is the most potent inhibitor known (2 uM) for type A botulinum neurotoxin. Developed high-throughput assays, suitable for screening large numbers of compounds for inhibitors of botulinum toxin proteolytic activity. Completed therapeutic proof-of-concept experiments in nonhuman primate and mouse SE incapacitation models.

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

DATE: June 2001

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

FY 2000 Accomplishments (Cont):

- 2326 Therapeutics, Viral - Developed at the Centers for Disease Control & Prevention, an aerosol variola nonhuman primate model for future bridging studies to monkeypox as a surrogate model in support of the U.S. Government Research Plan for smallpox. Demonstrated protection from lethal challenge in the Ebola virus mouse model using antibody therapy.
- 3603 Vaccines, Bacterial - Further characterized selected plague virulence factors as vaccine antigen candidates; identified two surrogate markers of protection against plague in an animal model; established the correlation of surrogate markers of immunity with efficacy of the candidate plague vaccine in the mouse model; established an improved animal (rabbit) model for anthrax. Explored in vitro correlates of immunity using novel gene microarray technology and found increases in messenger RNA expression for over 30 genes in murine spleen cells cultured with Brucella antigens.
- 2015 Vaccines, Toxin - Completed vaccine candidate cloning of botulinum toxin serotypes D and G in anticipation of future requirements for vaccine candidates. Initiated studies focused on increasing the immunogenicity for botulinum toxin serotype vaccines for E and F. Characterized candidate vaccines for SEs C1 and D. Demonstrated that the T-lymphocyte assay is useful in predicting the probability of survival in rhesus monkeys vaccinated with recombinant SEB vaccine and challenged by the aerosol route. Developed new surrogate immune assay based on dendritic cell cultures for evaluating human immune responses.
- 1979 Vaccines, Viral - Established and refined a nonhuman primate model for filoviruses. Determined aerosol LD50 and characterized pathology of the disease.
- 1821 Chemical/Biological Hazard Detection - Requested full proposal to develop custom cellular DNA and protein arrays designed to detect cellular responses to infectious agents to support the development of rapid quantitative devices to measure exposure and response to validated and emerging biological threat agents, thus enabling appropriate triaging and medical intervention.

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

DATE: June 2001

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

FY 2000 Accomplishments (Cont):

- 4823 Protocols to Enhance Biological Defense - Initiated review of proposal to examine innovative methodologies for treatment of anthrax infection to include endolymphatic administration of antibiotics, use of microencapsulated antibiotics, development of therapeutics to protect the phagocytic system from destruction by anthrax lethal toxin, and the use of proinflammatory cytokine inhibitors.

Total 23370

FY 2001 Planned Program:

- 600 Common Diagnostic Systems (DTO) - Establish preclinical models for the evaluation of rapid nucleic acid analysis options that will enhance the recognition of infections caused by a broad range of biological threat agents. Prepare and optimize new molecular diagnostic reagents, controls, and protocols that are compatible with emerging portable nucleic acid analysis systems for the identification of biological threat agents before the conduct of comprehensive evaluation trials.
- 400 Medical Countermeasures for Brucella (DTO) - Continue to develop and validate in vitro systems in mice and nonhuman primates to reliably quantitate the intensity of potentially protective immune responses and determine the immune system components that eliminate infection with candidate live vaccines. Determine stability of live, attenuated vaccine strain over time, using the mouse model. Develop additional live vaccine candidates with multiple attenuating mutations.
- 700 Medical Countermeasures for Encephalitis Viruses (DTO) - Develop nonhuman primate models for VEE virus type 1E and for western equine encephalitis virus. Complete the development of vaccine candidates for eastern equine encephalitis virus.
- 500 Multiagent Vaccines for Biological Threat Agents (DTO) - Improve vaccine delivery platforms (naked DNA and VEE replicon systems) to optimize their efficiency for use as multiagent vaccines.

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

DATE: June 2001

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

FY 2001 Planned Program (Cont):

- 573 Needleless Delivery Methods for Recombinant Protein Vaccines (DTO) - Identify assays for toxin-specific antibodies/other indicators of immunity. Identify commercial or proprietary devices for vaccine delivery.
- 160 Recombinant Plague Vaccine Candidate (DTO) - Complete the development of assays and reagents for determining correlates for immunity for the recombinant plague vaccine candidate.
- 500 Recombinant Protective Antigen (rPA) Anthrax Vaccine Candidate (DTO) - Perform comparative biochemical and biophysical characterization of recombinant protective antigen (rPA) vaccine candidate and licensed anthrax vaccine (AVA).
- 2737 Diagnostic Technologies - Prepare 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. Evaluate 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. Identify field sites for the comprehensive validation of rapid diagnostic methods that will provide performance data prior to transitioning to advanced development.
- 565 Therapeutics, Bacterial - Optimize animal models for therapeutic indices; evaluate in vivo activity of selected antimicrobials in established in vitro biochemical assays. Evaluate next generation antibiotics for therapeutic efficacy against bacterial threat agents.
- 5143 Therapeutics, Toxin - Standardize assays for high-throughput screening of small molecule inhibitors of botulinum and SE toxin ligand-receptor interaction.

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

DATE: June 2001

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

FY 2001 Planned Program (Cont):

- 3786 Therapeutics, Viral - Develop a rabbitpox-rabbit animal model for analysis and characterization of candidate antiviral compounds for therapeutic activity. Investigate mechanisms of Ebola and Marburg virus (MBGV) pathogenesis in nonhuman primate models to define likely targets in agent pathogenesis and identify potential mediators of shock.
- 5123 Vaccines, Bacterial - Evaluate previously identified virulence factors as vaccine candidates for Y. pestis. Optimize the animal model for aerosol exposure to B. mallei (glanders) for use in assessing vaccine candidates. Complete research on existing surrogate markers of protection against plague; identify surrogate markers for anthrax and additional markers for plague.
- 1184 Vaccines, Toxin - Express recombinant vaccine candidates for botulinum toxin serotypes D and G in the Pichia yeast system and initiate efficacy studies.
- 745 Vaccines, Viral - Explore the addition of cytokine gene co-delivery with Ebola viral genes to achieve protective immunity. Determine the components required in a vaccine that will protect against the most divergent isolates of MBGV.
- 391 SBIR

Total 23107

FY 2002 Planned Program:

- 600 Common Diagnostic Systems (DTO) - Complete validation 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.

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

DATE: June 2001

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):

- 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 nonhuman primates to reliably quantitate 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) - Develop nonhuman primate models for VEE virus type 3 and for eastern equine encephalitis virus. Complete the development of vaccine candidates for VEE virus type 3.
- 300 Multiagent Vaccines for Biological Threat Agents (DTO) - Complete final improvements to the vaccine delivery platforms for their use as multiagent vaccines.
- 593 Needleless Delivery Methods for Recombinant Protein Vaccines (DTO) - Evaluate formulations for intranasal, inhalation and transdermal application of recombinant proteins intended for use as vaccines. Determine the optimal mode of vaccine delivery using animals.
- 230 Recombinant Plague Vaccine Candidate (DTO) - Determine the range of protection of the recombinant plague vaccine candidate against other virulent strains of Y. pestis in animals.
- 500 Recombinant Protective Antigen (rPA) Anthrax Vaccine Candidate (DTO) - Perform passive transfer studies with AVA-immune human sera in mice and rabbits. Initiate a challenge study employing human sera passively transferred to monkeys.
- 5241 Diagnostic Technologies - Prepare 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.

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

DATE: June 2001

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):

- 1853 Therapeutics, Bacterial - Optimize and correlate in vitro assays with animal models for selected antibiotic and nonantibiotic therapeutics for bacterial threat agents; examine effects of selected therapies on multiple agent exposures in an animal model.
- 7995 Therapeutics, Toxin - Initiate structural stabilization and formulation studies on lead inhibitors of botulinum and SE toxin activity. Refine in vivo and standardize in vitro screening models for botulinum toxin and SE intoxication.
- 3706 Therapeutics, Viral - Assess the potential for immunotherapy against Ebola virus in nonhuman primate models. Complete investigation of mechanisms of Ebola and MBGV pathogenesis in nonhuman primate models to characterize promising surrogate markers of efficacy for therapies.
- 4530 Vaccines, Bacterial - Optimize in vitro correlate assays for candidate vaccines against various bacterial threat agents; 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.
- 2023 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.
- 2608 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.
- 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.
- 1500 Medical Countermeasures - Enhance applied research efforts toward the development of broad-spectrum therapeutic countermeasures for exposure to broad classes of biological threats.

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

DATE: **June 2001**

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):

▪	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 research efforts such as curating the genetic information base, evaluating mechanisms of pathophysiology associated with toxin threats and developing critical proteomics capability.
Total	36729	

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

DATE: June 2001

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

COST (In Thousands)		FY 2000 Actual	FY 2001 Estimate	FY 2002 Estimate							
TC2	MEDICAL CHEMICAL DEFENSE (APPLIED RESEARCH)	13070	14237	18596							

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 Plans (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: June 2001

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

FY 2000 Accomplishments:

- 1300 Chemical Agent Prophylaxis II (DTO) - Identified best candidates of genetically engineered scavengers as next generation pretreatments for nerve agents.
- 3898 Medical Countermeasures for Vesicant Agents (DTO) - Assessed the efficacy of new, improved countermeasure technologies to vesicant exposure in several model systems, both in vitro and in vivo. Prepared supporting documentation for Milestone A technical data package for lead countermeasures for vesicant agents.
- 680 Diagnostics - Identified promising analytical procedures for diagnosis of vesicant-induced inflammation. Assessed the efficacy of far-forward, rapid diagnostic tests for blister and nerve agents for real-time analysis of clinical samples on the battlefield.
- 3693 Pretreatments - Developed in vivo transgenic animal models for use as test beds for evaluating scavengers. Expanded the evaluation of human protein catalytic scavengers to include enzymes and human butyrylcholinesterase. Initiated development of an animal model capable of producing large quantities of recombinant enzyme scavenger. Identified several delivery platforms for exploration of administration of bioscavenger genetic material for transient induction of nerve agent scavengers.
- 1934 Therapeutics - Evaluated potential phosgene injury treatments using mouse lung model. Discovered a highly effective wetting solution for a reusable polyurethane sponge that significantly increased survival rates for guinea pigs whose skin was wiped after epidermal organophosphate exposure. Determined that cholinesterase enzymes could be impregnated on the polyurethane sponge and maintain activity for one year at 37 degrees C. Discovered that triamicinolone/cefazolin combination provides considerable protection against sulfur mustard (HD)-induced ocular damage. Identified a therapeutic mixture (Varma mixture) as a promising treatment for HD-induced ocular injury.

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

DATE: June 2001

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

FY 2000 Accomplishments (Cont):

- 1565 Low Level Chemical Warfare Agent Exposure - Identified pharmacological, physiological, and toxicological methods for monitoring long term, low level effects of chemical warfare agents. Developed animal models and exposure limits for chronic exposures to chemical warfare nerve agents. Investigated physiological markers for long term neuroanatomical effects of exposures to chemical warfare nerve agents.

Total 13070

FY 2001 Planned Program:

- 1200 Chemical Agent Prophylaxis II (DTO) - Test best candidates of genetically engineered scavengers using appropriate model systems. Expand 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. Explore approaches for evaluating the human safety of human protein scavengers. 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.
- 4000 Medical Countermeasures for Vesicant Agents II (DTO) - Define in vitro/in vivo models for safety and efficacy studies that can be extrapolated to humans. Determine best route of administration for candidate therapies. Begin physicochemical data acquisition for therapy candidates. Determine in vivo efficacy of candidate therapies for prevention of mustard-induced pathology. Begin downselect process.
- 591 Diagnostic - Evaluate commercial off-the-shelf products for potential for use as pretreatments or therapeutics for nerve agent, vesicant agent, blood agent, or respiratory agent exposure.
- 2728 Pretreatments - Extend molecular modeling and site-directed mutagenesis research to develop next generation nerve agent bioscavenger.

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DATE: June 2001

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

FY 2001 Planned Program (Cont):

▪	3477	Therapeutics - Optimize formulations for sponges, towelettes, and surgical pads containing scavenger enzymes for use in wound decontamination. Begin efforts to acquire human butyrylcholinesterase enzyme in bulk. Screen anticholinergic compound candidates for improvement of effectiveness of anticonvulsant, midazolam.
▪	1000	Low Level Chemical Warfare Agent Exposure - Determine pharmacological, physiological, and toxicological effects of long term, low level chemical warfare agents. Investigate new sensitive biochemical and histological assay technologies for use in low level chemical warfare agent exposures. Investigate the use of biological markers to indicate prior low dose chemical warfare agent exposure.
▪	1000	Fourth Generation Agents - Assess the efficacy against Fourth Generation Agents of countermeasures currently fielded or in advanced or exploratory development against nerve agents.
▪	241	SBIR
Total	14237	

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

DATE: June 2001

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) - Complete testing of various vector/gene combinations to validate in an animal model the concept of gene therapy for delivery of bioscavengers.
3000	Medical Countermeasures for Vesicant Agents II (DTO) - Evaluate improved animal models for screening candidate combination therapies for HD exposure. Define side effects and establish adversity levels; collate available industrial documentation.
1448	Diagnostics - Modify currently fielded cholinesterase testing kit to more efficiently test a large sample load.
4971	Pretreatments - Develop animal models to test scavenger candidates efficacy. Conduct characterization studies. Begin preliminary efficacy studies with next generation nerve agent scavengers. Continue development of potential transgenic/bioengineered sources of next generation nerve agent.
2677	Therapeutics - Assess candidate agents in suitable animal models of soman-induced status epilepticus for efficacy in saving vulnerable neurons and improving neurobehavioral outcome. Develop criteria for evaluating neuronal salvage after status epilepticus. Determine the essential ingredients for a rinse solution to optimally treat HD-induced ocular injury. Evaluate improved animal models for screening candidate combination therapies.
1000	Low Level Chemical Warfare Agent Exposure - Study biological markers for indicating prior low dose exposures and investigate selectivity of the markers for chemical warfare agents.
4500	Fourth Generation Agents - Assess the efficacy of new proposed nerve agent countermeasures. Prioritize potential approaches for improving effectiveness of new nerve agent countermeasures. Evaluate oxime effectiveness against Fourth Generation Agents. 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.
Total 18596	

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

DATE: June 2001

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