CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2 Exhibit)

DATE: **February 2002**

BUDGET ACTIVITY: **RDT&E DEFENSE-WIDE/ BA1 - Basic Research**

PE NUMBER AND TITLE: **0601384BP CHEMICAL/BIOLOGICAL DEFENSE (BASIC 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	38369	45791	64119	36434	37540	38958	42192	Continuing	Continuing
CB1	CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)	8801	10927	6574	6440	6547	7803	10780	Continuing	Continuing
HS1	HOMELAND SECURITY (BASIC RESEARCH)	0	0	25000	0	0	0	0	0	25000
TB1	MEDICAL BIOLOGICAL DEFENSE (BASIC RESEARCH)	19958	25049	23986	20461	21163	20229	20395	Continuing	Continuing
TC1	MEDICAL CHEMICAL DEFENSE (BASIC RESEARCH)	9610	9815	8559	9533	9830	10926	11017	Continuing	Continuing

CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2 Exhibit)	DATE February 2002
BUDGET ACTIVITY **RDT&E DEFENSE-WIDE/** **BA1 - Basic Research**	PE NUMBER AND TITLE **0601384BP CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)**

A. Mission Description and Budget Item Justification: This program element (PE) funds the Joint Service core research program for chemical and biological (CB) defense (medical and non-medical). The basic research program aims to improve the operational performance of present and future Department of Defense (DoD) components by expanding knowledge in relevant fields for CB defense and Homeland Security. Moreover, basic research supports a Joint Force concept of a lethal, integrated, supportable, highly mobile force with enhanced performance by the individual soldier, sailor, airman, or marine. Specifically, the program promotes theoretical and experimental research in the chemical, biological, medical, and related sciences. Research efforts are planned to be initiated in CB defense Homeland Security technologies. This funding supports establishment of a capability for biological terrorism threat assessment research in a Center for Biological Counterterrorism Research. Research areas are determined and prioritized to meet Joint Service needs as stated in mission area analyses and Joint operations requirements, and to take advantage of scientific opportunities. Basic research is executed by academia, including Historically Black Colleges and Universities and Minority Institutions (HBCU/MIs), and government research laboratories. Funds directed to these laboratories and research organizations capitalize on scientific talent, specialized and uniquely engineered facilities, and technological breakthroughs. The work in this program element is consistent with the Joint Service Nuclear, Biological, and Chemical (NBC) Defense Research, Development, and Acquisition (RDA) Plan. Basic research efforts lead to expeditious transition of the resulting knowledge and technology to the applied research (PE 0602384BP) and advanced technology development (PE 0603384BP) activities. This project also covers the conduct of basic research efforts in the areas of real-time sensing and diagnosis and immediate biological countermeasures. The projects in this PE include basic research efforts directed toward providing fundamental knowledge for the solution of military problems and therefore are correctly placed in Budget Activity 1.

CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2 Exhibit)

DATE: **February 2002**

BUDGET ACTIVITY: **RDT&E DEFENSE-WIDE/ BA1 - Basic Research**

PE NUMBER AND TITLE: **0601384BP CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)**

B. Program Change Summary:		FY 2001	FY 2002	FY 2003
Previous President's Budget (FY 2002 PB)		39532	39066	39306
Appropriated Value		39897	46066	0
Adjustments to Appropriated Value		0	0	0
a. Congressional General Reductions		0	-275	0
b. SBIR/STTR		-279	0	0
c. Omnibus or Other Above Threshold Reductions		0	0	0
d. Below Threshold Reprogramming		-1163	0	0
e. Rescissions		-86	0	0
Adjustments to Budget Years Since FY 2002 PB		0	0	24813
Current Budget Submission (FY 2003 PB)		38369	45791	64119

Change Summary Explanation:

Funding: FY02 - Congressional adjustments to support various CBD basic research programs (+$5,000K CB1; +$2,000K TB1). Congressional general reductions (-$275K).

FY03 - Increases to the technology base to fund a Homeland Security Support effort identified in the new Project HS1 (+$25,000K). Adjustment for inflation assumptions (-$187K).

Schedule:

Technical:

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

CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2 Exhibit)	DATE February 2002
BUDGET ACTIVITY **RDT&E DEFENSE-WIDE/** **BA1 - Basic Research**	PE NUMBER AND TITLE **0601384BP CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)**

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

Labs/Centers:

TB1 - U.S. Army Medical Research Institute of Infectious Diseases, Ft. Detrick, MD; TC1 - U.S. Army Medical Research Institute of Chemical Defense, Aberdeen Proving Ground, MD; CB1 - U.S. Army Soldier Biological Chemical Command, APG-EA, MD; Naval Research Lab, Washington, DC

Universities: None

FFRDCs: None

Contractors: None

Other: None

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

DATE: **February 2002**

BUDGET ACTIVITY: **RDT&E DEFENSE-WIDE/ BA1 - Basic Research**

PE NUMBER AND TITLE: **0601384BP CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)**

PROJECT: **CB1**

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
CB1	CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)	8801	10927	6574	6440	6547	7803	10780	Continuing	Continuing

A. Mission Description and Budget Item Justification:

Project CB1 CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH): This project funds basic research in chemistry, physics, mathematics, life sciences, and fundamental information in support of new and improved detection technologies for biological agents and toxins; new and improved detection technologies for chemical threat agents; advanced concepts in individual and collective protection; new concepts in decontamination; and information on the chemistry and toxicology of threat agents and related compounds.

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

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA1 - Basic Research	0601384BP CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)	CB1

FY 2001 Accomplishments:

- 4892 Chemical/Biological Agent Detection - Conducted a multidisciplinary project to establish the proof of principle for detection methodologies and to develop detection systems for sensing the presence of chemical and biological warfare (CBW) agents. Produced a design for a point detector to achieve highly specific and rapid detection of the CW agents in air using Cylindrical Ion Trap Mass Spectrometry (CITMS). Investigated Ion Trap Mass Spectrometric (ITMS) methodologies for Biological Warfare (BW) agent detection and a priori identification. Investigated neutron based CW detection.
- 1658 Thin Film Technology Development - Continued development of semiconducting metal oxide (SMO) thin film technology to detect chemical agents. Sought to minimize power requirements, weight, and volume with an overall intent to reduce burden to the individual user. Focused on approaches to maximize selectivity/elimination of false alarms including mixed metal oxide films and nanocluster structures. Examined pre-filtration/preconcentration through chemical vapor deposition (CVD) methods. Continued improvements in signal processing and control.
- 1120 Chemistry and Toxicology of Bio-active Compounds - Continued materials selection for molecular imprinting technique in preparation for integration into a passive thin film chemical detection badge. Continued studies of the percarbonate based decontaminant formulations by determining reaction product distributions and correlate equilibrium concentrations with solvent properties. Completed measurement of requisite adsorption rate data and began development of a continuous adsorption model for filter performance. Continued project to understand the toxicological mechanisms of one or two members of a class of potential new threat agents.

CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2A Exhibit)	DATE February 2002
BUDGET ACTIVITY **RDT&E DEFENSE-WIDE/** **BA1 - Basic Research**	PE NUMBER AND TITLE **0601384BP CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)**
	PROJECT **CB1**

FY 2001 Accomplishments (Cont):

- 694 Bio-sensors - Sequenced and synthesized DNA aptamer recognition elements to Staphylococcal enterotoxin B. Completed conjugate synthesis and integration of specific DNA/fluorescent polymer conjugates; high affinity aptamer for anthrax spores were isolated and cloned and are now being sequenced. Demonstrated separation and identification of dendrimer bound antibody/antigen couples via capillary electrophoresis.
- 437 Aerosol Science - Continued validation of the scattering model theorem by demonstrating imaging of biological cluster particles.

Total 8801

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

DATE: February 2002

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA1 - Basic Research	0601384BP CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)	CB1

FY 2002 Planned Program:

- 2500 Lightweight Chemical and Biological Sensors - Investigate 3-D imaging of electromagnetic scattering, nanometaloclusters, polymer membranes, dendrimer-based nanodevices, aptmers, and laser based spectroscopy technologies for next generation, lightweight CB sensor.
- 2500 Magnetic Resonance Spectrometer - Effort will purchase a 900 MHz magnetic resonance spectrometer for a university structural biology center.
- 1798 Biological Detection - Complete investigations of aptamer-based bio detection for anthrax strains; complete initial evaluations of Multiplex Electronic/Photonic Sensor (MEPS) technology. Initiate investigations of novel technologies to detect and identify BW simulants and agents in environmental matrices. Complete project to identify aerosol materials by analysis of scattering.
- 1876 Chemical Detection - Complete investigation of dendrimer-based detection tickets; complete investigations of molecular imprinting for chemical detection. Initiate efforts to detect CW agents using solid-state nano-arrays and analysis of degradation products.
- 770 Decontamination - Continue efforts to develop advanced decontamination materials to allow treatment of sensitive equipment, phase transfer materials, and solution chemistry.
- 375 Information Technology - Initiate effort to directly couple information into warning system by neural coupling.
- 475 Protection - Complete investigations of rate and equilibrium properties of adsorbents for filtration modeling. Initiate investigations of self-assemblies for protective materials.
- 448 Supporting Science - Initiate investigation of volatility and material interactions of CW agents and simulants under ambient environmental conditions.

CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2A Exhibit)	DATE February 2002
BUDGET ACTIVITY **RDT&E DEFENSE-WIDE/** **BA1 - Basic Research**	PE NUMBER AND TITLE **0601384BP CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)**
	PROJECT **CB1**

FY 2002 Planned Program (Cont):

- 185 SBIR - Small Business Innovative Research.

Total 10927

FY 2003 Planned Program:

- 1469 Biological Detection - Continue investigations of novel technologies to rapidly and definitively detect and identify BW simulants and agents in environmental matrices. Initiate new effort based on light scattering approach.
- 1500 Chemical Detection - Continue efforts to detect CW agents using solid-state nano-arrays and analysis of degradation products.
- 1000 Decontamination - Complete investigations of environmentally benign decontamination materials based on peroxycarbonates; transition to development program. Initiate new efforts to develop advanced decontamination materials to allow treatment of sensitive equipment, phase transfer materials, and solution chemistry.
- 1000 Information Technology - Continue efforts to directly couple information into warning system by neural coupling.
- 605 Protection - Continue investigations of self-assemblies for protective materials. Initiate effort to investigate agent interactions with microporous surfaces at the molecular level using Magic-Angle Spinning Nuclear Magnetic Resonance (MAS-NMR) spectrometry, Xray Photoelectron Spectroscopy (XPS), and thermal desorption methods.
- 1000 Supporting Science - Continue investigations of the behavior of CW agents and simulants under ambient environmental conditions. Make available to the 6.2 agent fate program preliminary volatility and environmental adsorption data from new techniques that extend previous methods in dry air only to measure agent vapor concentrations in the presence of relative humidity and contact with porous materials including silica and soil.

Total 6574

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

DATE: **February 2002**

BUDGET ACTIVITY: **RDT&E DEFENSE-WIDE/ BA1 - Basic Research**

PE NUMBER AND TITLE: **0601384BP CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)**

PROJECT: **CB1**

B. Other Program Funding Summary:

	FY 2001	FY 2002	FY 2003	FY 2004	FY 2005	FY 2006	FY 2007	To Compl	Total Cost
CB2 CHEMICAL BIOLOGICAL DEFENSE (APPLIED RESEARCH)	56925	91432	68817	54007	52828	56281	54451	Cont	Cont
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/ BA1 - Basic Research	**0601384BP CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)**	**HS1**

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
HS1	HOMELAND SECURITY (BASIC RESEARCH)	0	0	25000	0	0	0	0	0	25000

A. Mission Description and Budget Item Justification:

Project HS1 HOMELAND SECURITY (BASIC RESEARCH): This basic research project emphasizes a better understanding of the threats and risks posed by future bioterrorism activities against the U.S. The proliferation of weapons of mass destruction, to include biological weapons and scientific expertise necessary to develop biological weapons capability, has become one the greatest new threats our nation faces today. Recent terrorism incidents in the U.S. demand a greater emphasis on research to assess the threat potential of classic, emerging and genetically engineered biological threats. Funding for this project supports establishment of a capability for biological terrorism threat assessment research in a Center for Biological Counterterrorism Research. Currently there is no single, coherent DoD or national scientific program focused on assessment of the classical and emerging biological threats from the perspective of counterterrorism. Risk assessment and threat assessment studies of certain biological agents will require dedicated facilities, equipment and personnel, and will ultimately involve some degree of classified work in order not reveal or create defense vulnerabilities. Such a program is not suitable, nor is laboratory capacity available, for placement within existing biodefense programs or facilities.

FY 2001 Accomplishments: None

FY 2002 Planned Program: No planned program

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

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BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA1 - Basic Research	**0601384BP CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)**	**HS1**

FY 2003 Planned Program:

- 25000 Microbial Threat Assessment Basic Research - Conduct technology survey and identify knowledge gaps with respect to biological threat agents; initiate extramural research contract awards for expanded study of basic biology and molecular biology of biological threat agents, with emphasis on identification of virulence factors, pathogenic mechanisms, and structural biology.

Total 25000

B. Other Program Funding Summary:

	FY 2001	FY 2002	FY 2003	FY 2004	FY 2005	FY 2006	FY 2007	To Compl	Total Cost
HS2 HOMELAND SECURITY (APPLIED RESEARCH)	0	0	137000	0	0	0	0	0	137000
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/ BA1 - Basic Research	**0601384BP CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)**	**TB1**

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
TB1	MEDICAL BIOLOGICAL DEFENSE (BASIC RESEARCH)	19958	25049	23986	20461	21163	20229	20395	Continuing	Continuing

A. Mission Description and Budget Item Justification:

Project TB1 MEDICAL BIOLOGICAL DEFENSE (BASIC RESEARCH): This project funds basic research on the development of vaccines and therapeutic drugs to provide effective medical defense against validated biological threat agents including bacteria, toxins, and viruses. This project also funds basic research employing biotechnology to rapidly identify, diagnose, prevent, and treat disease due to exposure to biological threat agents. Categories for this project include current science and technology program areas in medical biological defense (diagnostic technology, bacterial therapeutics, toxin therapeutics, viral therapeutics, bacterial vaccines, toxin vaccines, and viral vaccines) and directed research efforts (anthrax studies and bug to drug identification and countermeasures program).

FY 2001 Accomplishments:

- 2976 Diagnostic Technologies - Investigated new medical diagnostic technologies based upon state-of-the-art biotechnological approaches for the enhanced recognition of infections by validated biological threats (bacteria, viruses, and toxins) of military interest including new gene analysis chemistries and immunodiagnostics. Identified new biological markers and host responses that can be used for early recognition of infections including new primer and probe sets against new gene targets. Identified unique host immune markers using in vitro and in vivo models and developed primer and probe sets for these markers.

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BUDGET ACTIVITY **RDT&E DEFENSE-WIDE/** **BA1 - Basic Research**	PE NUMBER AND TITLE **0601384BP CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)**
	PROJECT **TB1**

FY 2001 Accomplishments (Cont):

- 312 Therapeutics, Bacterial - Analyzed host cellular and subcellular responses to Bacillus anthracis, Burkholderia mallei, and Yersinia pestis exposure and evaluated cloned heat shock genes as potential targets for therapeutic intervention. Developed methodologies utilizing biochemical (metabolic) processes for assaying in vivo antibiotic activity. Initiated studies to optimize a mouse model for testing established and investigational antibiotics against anthrax.
- 5452 Therapeutics, Toxin - Identified sites of molecular action and mechanisms of intervention for therapies for botulinum toxin and staphylococcal enterotoxin B (SEB) threats; developed models for therapeutic intervention. Defined endpoints for in vivo assessment of efficacy of therapeutic intervention for botulinum toxin and SEB and surrogate endpoints of human clinical efficacy. Generated candidate therapeutic moieties for botulinum and SEB toxins using combinatorial chemistry.
- 2722 Therapeutics, Viral - Humanized mouse monoclonal antibodies specific for Ebola virus to test as an immunotherapeutic. Investigated mechanisms of filovirus transcription and replication focusing on polymerase as potential target for antiviral therapy.

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BUDGET ACTIVITY **RDT&E DEFENSE-WIDE/** **BA1 - Basic Research**	PE NUMBER AND TITLE **0601384BP CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)**
	PROJECT **TB1**

FY 2001 Accomplishments (Cont):

- 4652 Vaccines, Bacterial - Investigated pathogenesis (cellular and molecular) and host immune responses; characterized additional virulence factors; continued to define strain diversities; and established correlates of immunity for plague (Y. pestis), glanders (B. mallei), and anthrax (B. anthracis). Identified potential host cell targets for a plague virulence factor and demonstrated mechanism of action in vitro of protective immunity against this virulence factor. Continued to evaluate live attenuated plague strains for their ability to elicit protective immunity. Demonstrated the importance of antibodies to an anthrax virulence protein in protecting host cells against killing by anthrax spores early in the infectious process. Investigated in vivo ability of licensed anthrax vaccine to protect against additional anthrax strains representing geographically diverse isolates. Characterized virulence genes in glanders strains that are responsible for encoding the organism's capsular virulence factor. Developed an in vitro model to examine interactions between Brucella and human monocyte cells. Compared the ability of Brucella lipopolysaccharide (LPS) to that of E. coli LPS for induction of cytokines.
- 982 Vaccines, Toxin - Initiated studies to identify potential neutralizing epitopes in the translocation domains of the botulinum neurotoxins. Investigated the variability of Clostridium botulinum strains in terms of their neurotoxic isoforms and the presence of other toxins produced by various strains. Initiated structural and biophysical characterization studies of recombinant protein vaccine antigens. Constructed enzymatically inactivated mutant of ricin A-chain for evaluation as a potential vaccine candidate. Initiated evaluation of adjuvants that may enhance the host immune response to aerosol-administered vaccines and assessed delivery vehicles that may enhance the uptake of aerosol-administered vaccines.

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	PROJECT **TB1**

FY 2001 Accomplishments (Cont):

- 2862 Vaccines, Viral - Demonstrated a role of cytotoxic T cells in conferring protection against Ebola virus in the mouse model. Initiated investigation into poxvirus immunity to determine feasibility of replacing vaccinia immune globulin (VIG) with monoclonal antibodies and to construct a safe and effective vaccine to replace the vaccinia virus vaccine for variola. Confirmed hypothesis that vaccination with intracellular mature virus particles and extracellular enveloped virus immunogens is required for protection.

Total 19958

FY 2002 Planned Program:

- 3444 Diagnostic Technologies - Continue investigation of new medical diagnostic technologies based upon state-of-the-art biotechnological approaches for the enhanced recognition of infections by potential biological threats (bacteria, viruses, and toxins) of military interest including new gene analysis chemistries and immunodiagnostics. Continue to identify new biological markers and host responses that can be used for early recognition of infections including new primer and probe sets against new gene targets. Continue to identify unique host immune markers using in vitro and in vivo models and developed primer and probe sets for these markers.
- 1094 Therapeutics, Bacterial - Evaluate therapeutic indices for new (investigational) antibiotic agents identified by in vitro assays in mouse models. Study the effect of immunomodulators on the host response to B. mallei and Y. pestis candidate vaccines and identify those modulators that are effective in enhancing candidate vaccines. Conduct studies on the effects of established and Investigational New Drug (IND) therapeutic compounds on Brucella in vitro.

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BUDGET ACTIVITY **RDT&E DEFENSE-WIDE/** **BA1 - Basic Research**	PE NUMBER AND TITLE **0601384BP CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)**
	PROJECT **TB1**

FY 2002 Planned Program (Cont):

- 4720 Therapeutics, Toxin - Refine and standardize in vivo screening models for assessment of efficacy of therapeutic intervention in botulinum toxin and SEB intoxication and standardize in vitro assays for neutralizing activity of lead inhibitors. Conduct high-output generation of candidate therapeutic moieties for botulinum and SEB toxins using combinatorial chemistry. Evaluate inhibitor delivery strategies and demonstrate in vitro proof-of-concept. Initiate high-throughput screening technology to investigate therapeutic candidates for exposure to ricin toxin.
- 2188 Therapeutics, Viral - Determine the therapeutic potential of candidate drugs for treatment of disease caused by filovirus or orthopox infections. Characterize filovirus polymerases as potential antiviral drug targets and incorporate into in vitro assays.
- 3099 Vaccines, Bacterial - Obtain genetic sequencing data and establish a database for plague (Y. pestis), glanders (B. mallei), anthrax (B. anthracis) and brucellosis (Brucella species). Evaluate the data for potential for genetic engineering and genetic modification and determine genetic fingerprints (genetic identifiers) of various isolates of the organisms. Evaluate genetically modified strains of these pathogens for their level of virulence in animals and identify genes that encode for novel virulence factors. Expand and characterize strain collections of bacterial threat agents to identify strains that may be resistant to existing vaccines and/or those under advanced development. Characterize in vitro host cell gene expression during infection with plague, glanders, anthrax, and Brucella and identify novel bacterial genes expressed. Test multiagent vaccine constructs in avirulent anthrax and Brucella platforms for immunogenicity in mice.
- 1540 Vaccines, Toxin - Complete experiments involving the crystallization of toxins and vaccine candidates for structural studies and biophysical characterization. Complete assessment of novel adjuvants and delivery vehicles for aerosol-administered vaccines. Investigate potential neutralizing epitopes in the translocation domains of botulism neurotoxins.

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BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA1 - Basic Research	0601384BP CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)	TB1

FY 2002 Planned Program (Cont):

- 1540 Vaccines, Viral - Continue investigating poxvirus immunity to determine the feasibility of replacing VIG with monoclonal antibodies and to construct a safe and effective vaccine to replace the vaccinia virus vaccine for variola (smallpox).
- 5000 Anthrax studies - Initiate development and testing of new approaches for the treatment of inhalational anthrax. Focus on two classes of compounds that inhibit the activity of the lethal toxin produced during anthrax infection and on an enzyme target critical for the germination and vegetative life cycle of B. anthracis.
- 2000 Bug to Drug Identification and Countermeasures Program - Conduct research directed toward decreasing the time required to identify and counter biological threats. Focus on rapidly identifying host proteins that are altered by BW pathogens and rapidly developing countermeasures based on how the countermeasures affect the host, outside of their desired effect against the pathogen. This research will utilize structure-based small molecule design, microfluidics-based bioassays, and computational molecular biology and pathway modeling.
- 424 SBIR - Small Business Innovative Research Efforts.

Total 25049

FY 2003 Planned Program:

- 4389 Diagnostic Technologies - Apply new diagnostic approaches to the early recognition of infections. Technologies will be compatible with future comprehensive integrated diagnostic systems.

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	PROJECT **TB1**

FY 2003 Planned Program (Cont):

- 1061 Therapeutics, Bacterial - Correlate metabolic measurements as a rapid and sensitive means to detect antibiotic activity with conventional susceptibility determinations and appropriate animal models of infection. Establish collaborative research and development agreements with interested pharmaceutical companies to test new and investigational antibiotics. Initiate evaluation of selected therapeutic compounds against Brucella in vivo.
- 5186 Therapeutics, Toxin - Complete high-output generation of candidate therapeutic moieties for botulinum and SEB toxins using combinatorial chemistry. Demonstrate in vivo proof-of-concept for integrated therapeutic approaches in botulinum toxin and SEB intoxication. Select lead ricin inhibitor and prepare toxin-inhibitor crystals for x-ray diffraction analysis.
- 2225 Therapeutics, Viral - Develop intervention strategies for filovirus-induced shock and for therapeutic approaches that combine antiviral and anti-shock drug therapy.
- 3001 Vaccines, Bacterial - Develop mutations 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 B. mallei vaccines. Evaluate differences in the course of Brucella infection in different mouse strains. Test multiagent vaccine constructs for immunogenicity in higher animal species.
- 1001 Vaccines, Toxin - Compare efficacy of constructs with neutralizing epitopes in other domains of botulinum neurotoxin serotypes E and F with the current subunit vaccine candidates. Evaluate vaccine candidates specifically designed to address host vulnerabilities identified in the lung. Develop vaccine candidates that protect against inhalationally induced incapacitation by selected toxin threat agents.

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PE NUMBER AND TITLE: **0601384BP CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)**

PROJECT: **TB1**

FY 2003 Planned Program (Cont):

- 2123 Vaccines, Viral - Complete investigating poxvirus immunity and determine the feasibility of replacing VIG with monoclonal antibodies and constructing a new vaccine to replace vaccinia.
- 5000 Anthrax studies - Continue extramural research efforts toward the development and testing of new approaches for the treatment of inhalational anthrax. Focus will continue on two classes of compounds that inhibit the activity of the lethal toxin produced during anthrax infection and on an enzyme target critical for the germination and vegetative life cycle of B. anthracis.

Total 23986

B. Other Program Funding Summary:

	FY 2001	FY 2002	FY 2003	FY 2004	FY 2005	FY 2006	FY 2007	To Compl	Total Cost
TB2 MEDICAL BIOLOGICAL DEFENSE (APPLIED RESEARCH)	22428	36513	38386	24085	25097	17826	18148	Cont	Cont
TB3 MEDICAL BIOLOGICAL DEFENSE (ADV TECH DEV)	22394	29919	34200	50789	45560	40585	40675	Cont	Cont

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BUDGET ACTIVITY: **RDT&E DEFENSE-WIDE/ BA1 - Basic Research**

PE NUMBER AND TITLE: **0601384BP CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)**

PROJECT: **TC1**

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
TC1	MEDICAL CHEMICAL DEFENSE (BASIC RESEARCH)	9610	9815	8559	9533	9830	10926	11017	Continuing	Continuing

A. Mission Description and Budget Item Justification:

Project TC1 MEDICAL CHEMICAL DEFENSE (BASIC RESEARCH): This project emphasizes understanding of the basic action mechanisms of nerve, blister (vesicating), blood, and respiratory agents. Basic studies are performed to delineate mechanisms and sites of action of identified and emerging chemical threats to generate required information for initial design and synthesis of medical countermeasures. In addition, these studies are further designed to maintain and extend a science base. Categories for this project include science and technology program areas (Pretreatments, Therapeutics, and Diagnostics) and directed research efforts (Low Level Chemical Warfare Agent Exposure and Fourth Generation Agents).

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DATE: **February 2002**

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA1 - Basic Research	**0601384BP CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)**	**TC1**

FY 2001 Accomplishments:

- 2540 Pretreatment - Evaluated catalytic scavengers designed by site-directed mutagenesis. Developed candidate next generation pretreatments using knowledge gained from studies in molecular modeling and site-directed mutagenesis. Identified new candidate compounds with potential as pretreatments for vesicant injury based on current research strategies.
- 1399 Therapeutics - Developed science base to identify specific factors leading to and/or preventing neuronal death in status epilepticus caused by nerve agents. Identified potential synergistic interactions of midazolam with anticholinergic drugs in rodent species.
- 4164 Low Level Chemical Warfare Agent Exposure - Identified data gaps relevant to the pathological and behavioral effects of low level chemical warfare nerve agent exposures. Investigated possible cellular mechanisms of low level chemical warfare agent injury. Explored highly sensitive diagnostic techniques to determine exposure to low levels of chemical warfare agents and subsequent physiological and toxicological effects.
- 1507 Fourth Generation Agents - Determined mechanism by which Fourth Generation Agents produce toxicity, which is not responsive to current nerve agent countermeasure pretreatments, using the knowledge gained from studies in molecular modeling and site-directed mutagenesis.

Total 9610

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

DATE: **February 2002**

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA1 - Basic Research	**0601384BP CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)**	**TC1**

FY 2002 Planned Program:

- 2082 Pretreatments - Evaluate organophosphate anhydrolase enzyme for potential use as catalytic nerve agent scavenger. Utilize in vitro screening of identified compounds for potential use as pretreatments for vesicant exposure.
- 1476 Therapeutics - Identify target sites for neuroprotection. Identify therapeutic targets for candidate compound combination therapies. Initiate determination of the optimal hypochlorite concentration for use in decontaminating chemical agent-exposed skin and agent-contaminated wounds.
- 4500 Low Level Chemical Warfare Agent Exposure - Continue studies on identification of chronic pathological and behavioral effects of low level chemical warfare agent exposures. Investigate putative mechanisms of low level toxicity. Develop consensus for a coherent methodology for studies across endpoints and model species to permit integration of disparate endpoints, post-hoc analysis of research results, and extrapolation to higher animal species.
- 1000 Fourth Generation Agents - Develop strategies to improve efficacy of current medical countermeasures against Fourth Generation Agents.
- 591 Diagnostics - Develop new assays for sulfur mustard adducts and for diagnosing cyanide exposure.
- 166 SBIR - Small Business Innovative Research Efforts.

Total 9815

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

DATE: **February 2002**

BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA1 - Basic Research	**0601384BP CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)**	**TC1**

FY 2003 Planned Program:

- 2091 Pretreatments - Develop next generation pretreatments using knowledge gained from studies in molecular modeling and site-directed mutagenesis. Continue delineation of pathways of injury and potential pretreatment pharmaceutical intervention sites.
- 1618 Therapeutics - Incorporate biomarker panels into screening modules. Evaluate combination therapies for neuroprotection efficacy. Screen antidotes representing new strategies to improve medical countermeasures against conventional and emerging agents.
- 4000 Low Level Chemical Warfare Agent Exposure - Continue studies of chronic neurological and/or behavioral effects of chronic low level chemical warfare agent exposures. Identify potential toxic endpoints in low dose chemical warfare agent exposures. For verified endpoints, identify the mechanism(s) and biochemical pathway(s) involved in the generation of endpoint pathology.
- 850 Diagnostics - Continue development of leading edge assays for sulfur mustard adducts and for diagnosing cyanide exposure. Initiate studies for a far-forward diagnostic capability.

Total 8559

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

DATE: **February 2002**

BUDGET ACTIVITY: **RDT&E DEFENSE-WIDE/ BA1 - Basic Research**

PE NUMBER AND TITLE: **0601384BP CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)**

PROJECT: **TC1**

B. Other Program Funding Summary:

	FY 2001	FY 2002	FY 2003	FY 2004	FY 2005	FY 2006	FY 2007	To Compl	Total Cost
TC2 MEDICAL CHEMICAL DEFENSE (APPLIED RESEARCH)	13819	18486	17974	17150	16569	18421	18572	Cont	Cont
TC3 MEDICAL CHEMICAL DEFENSE (ADV TECH DEV)	9968	11302	12156	13423	13773	12907	13011	Cont	Cont