CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2 Exhibit)

DATE **February 2005**

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

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

COST (In Thousands)		FY 2004 Actual	FY 2005 Estimate	FY 2006 Estimate	FY 2007 Estimate	FY 2008 Estimate	FY 2009 Estimate	FY 2010 Estimate	FY 2011 Estimate	Cost to Complete	Total Cost
	Total Program Element (PE) Cost	46946	54056	72533	52701	58910	56734	51911	53167	Continuing	Continuing
CB1	CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)	11847	12241	15707	16290	17324	17648	16160	18471	Continuing	Continuing
TB1	MEDICAL BIOLOGICAL DEFENSE (BASIC RESEARCH)	27067	32437	45966	25528	28470	26363	22306	21532	Continuing	Continuing
TC1	MEDICAL CHEMICAL DEFENSE (BASIC RESEARCH)	8032	9378	10860	10883	13116	12723	13445	13164	Continuing	Continuing

A. <u>Mission Description and Budget Item Justification:</u> This program element (PE) funds the Joint Service core research program for chemical and biological (CB) defense (medical and physical sciences). 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. Moreover, basic research supports a Joint Force concept of an 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.

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

Research areas are aligned 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 government laboratories, industry, and academia to include; Historically Black Colleges and Universities and Minority Institutions (HBCU/MIs). 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 Chemical Biological Defense Program 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 defense-related problems and new-improved military capabilities, and therefore, are correctly placed in Budget Activity 1.

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

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

B. Program Change Summary:	FY 2004	FY 2005	FY 2006	FY 2007
Previous President's Budget (FY 2005 PB)	51380	36769	37839	40913
Current Biennial Budget Estimates (FY 2006)	46946	54056	72533	52701
Total Adjustments	-4434	17287	34694	11788
a. Congressional General Reductions	-59	-962	0	0
b. Congressional Increases	0	18250	0	0
c. Reprogrammings	-3369	0	0	0
d. SBIR/STTR Transfer	-870	0	0	0
e. Other Adjustments	-136	-1	34694	11788

Change Summary Explanation:

Funding: FY05 - Congressional increases to enhance projects within the science and technology base (+$6,000K CB1; +$12,250K TB1). Congressional general reductions and other adjustments (-$172K CB1; -$541K TB1; -$250K TC1).

FY06 - Enhance research efforts in physical sciences and medical biological countermeasures (+$2,000K CB1; +$28,000K TB1). Inflation adjustment (+$232K CB1; +$266K TB1; +$160K TC1). Reprioritization of programs within the Chemical Biological Defense Program to support higher priority efforts (+$5,895K CB1; +$1,053K TB1; -$2,912K TC1).

FY07 - Enhance research efforts in physical sciences (+$4,000K CB1). Inflation adjustment (+$273K CB1; +$428K TB1; +$183K TC1). Reprioritization of programs within the Chemical Biological Defense Program to support higher priority efforts (+$1,563K CB1; +$5,324K TB1; +$17K TC1).

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

Schedule: N/A

Technical: N/A

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

DATE: **February 2005**

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 2004 Actual	FY 2005 Estimate	FY 2006 Estimate	FY 2007 Estimate	FY 2008 Estimate	FY 2009 Estimate	FY 2010 Estimate	FY 2011 Estimate	Cost to Complete	Total Cost
CB1	CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)	11847	12241	15707	16290	17324	17648	16160	18471	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; innovative concepts in modeling and simulation; and information on the chemistry and toxicology of threat agents and related materials.

B. Accomplishments/Planned Program

	FY 2004	FY 2005	FY 2006	FY 2007
Basic Research	6527	0	0	0

FY 2004 Accomplishments:

- 1976 Brooks City Base Biotechnology - Investigated technologies for Brooks City Base Biotechnology.
- 989 Fluorescence Activated Sensing Technology (FAST) - Investigated technologies for FAST.

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

DATE

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

FY 2004 Accomplishments (Cont):

- 1089 Advanced Sensor Design and Threat Detection Facility - Developed sensors and sensory materials that remediate threats to national security as well as public health.
- 1484 Detection of Biological Agents in Water - Investigated technologies for the detection of biological age sources.
- 989 Biodetection Research - Investigated technologies for biodetection.

Total 6527

	FY 2004	FY 2005	
Decontamination	1049	941	

FY 2004 Accomplishments:

- 834 Solution Decontamination - Completed feasibility studies for determination of semi-solid materials che with absorbed CB agents. Completed studies of the decontamination mechanism of secondary catalyti the addition of monovalent salts to a peracid-dioxirane. Completed investigations of the efficacy of art anti-bacterial and anti-viral activity. Completed investigations of the utility of high-field Nuclear Mag (NMR) methodology in conjunction with tandem mass spectrometry to determine structures of biologi Completed investigations of chemical strategies designed for dissolution and deactivation/destruction o organic nanoemulsions.

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DATE: **February 2005**

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

FY 2004 Accomplishments (Cont):

- 215 Sensitive Equipment Decontamination - Completed investigation of efficacy of vaporous dimethyl dioxirane for decontamination of BW agents.

Total 1049

FY 2005 Planned Program:

- 941 Decontamination - Initiate research effort to assess potential of ionic liquids for agent decontamination capability. Initiate research effort to assess potential of metal catalysis for agent decontamination capability.

Total 941

	FY 2004	FY 2005	FY 2006	FY 2007
Detection	3443	2430	0	0

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DATE: **February 2005**

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

FY 2004 Accomplishments:

- 2085 Biological Agent Identification Detection - Completed proof-of-principle experimentation; completed theoretical correlations to experimental data for polarization opposition effect. Continued synthesis of candidate stochastic biosensor elements; continued screening testing. Demonstrated proof-of-principle for separation of biological warfare (BW) agent surrogates using optical pressure. Continued investigations of micro-channel mixing via configurable heating and surfaces by comparison of data and model prediction. Initiated investigations of antimicrobial peptides for applicability as bio-detection elements; initiated testing program. Initiated effort to characterize polymorphic regions of B. mallei genome using ribotyping, repetitive sequence polymerase chain reaction, and randomly amplified polymorphic DNAs.
- 1058 Integrated CB Detection - Completed proof of principle investigations of novel materials for selective interactions with CW agent simulants in conjunction with optical amplification to enhance detection. Continued investigations of surface modified gold nanoclusters for detection of chemical warfare (CW) agents. Initiated investigations of modified nanofilaments for detection of CB warfare agents.
- 300 Chemical Stand-off Detection - Completed investigations of the applicability of new techniques to the analysis and processing hyperspectral Fourier Transform Infrared (FTIR) data. Completed investigations of novel two-photon fluorescence spectroscopy method and potential applicability to stand-off CB detection.

Total 3443

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

DATE: **February 2005**

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

FY 2005 Planned Program:

- 1000 Integrated CB Detection - Continue investigations of modified nanofilaments for the detection of CB agents. Initiate novel approaches for improved CB detection. Complete investigations of modified gold nanosensors.
- 1430 Biological Agent Identification Detection - Complete testing of candidate ion channel stochastic sensor elements. Complete investigations of micro-channel mixing via configurable heating and surfaces. Complete development of test articles and procedures. Continue testing of antimicrobial peptides. Continue effort to characterize polymorphic regions of B. mallei genome using ribotyping, repetitive sequence polymerase chain reaction, and randomly amplified polymorphic DNAs. Initiate effort to assess recombinant single-domain antibodies for bio-detection. Initiate effort to assess utility of modified nanowires for biodetection. Initiate effort to assess novel light-scattering method for bio-identification. Initiate effort to enhance utility of microfluidic control for bio-detection. Initiate investigations of bacterial ghosts as simulants for biological warfare agents.

Total 2430

	FY 2004	FY 2005	FY 2006	FY 2007
Modeling and Simulation Battlespace Management	0	302	0	0

FY 2005 Planned Program:

- 302 Modeling and Simulation Battlespace Management - Initiate efforts in support of modeling agent dispersal after release.

Total 302

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DATE: **February 2005**

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

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

PROJECT: **CB1**

	FY 2004	FY 2005	FY 2006	FY 2007
Protection	583	1111	0	0

FY 2004 Accomplishments:

- 157 Respiratory Protection - Completed theoretical and empirical investigations of the mechanisms of interactions of vapors with active surfaces.
- 192 Shelter Protection - Initiated investigations of the interrelationships between the chemical, physical, and transport properties of novel butyl rubber membranes prepared by electrospinning.
- 234 Individual Protection (Clothing) - Evaluated effectiveness of nanofiber-coated fabrics for protection against particulate materials. Completed investigations of protection afforded by a novel surface modified membrane.

Total 583

FY 2005 Planned Program:

- 441 Respiratory Protection - Initiate research into understanding physical adsorption processes for Toxic Industrial Chemicals (TICs) and CW agents on novel adsorbent materials. Initiate effort to develop performance model for the electric-swing adsorption process.

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

FY 2005 Planned Program (Cont):

- 670 Shelter Protection - Continue investigations of the interrelationships between the chemical, physical, and transport properties of novel butyl rubber membranes prepared by electrospinning; expand this effort to include permeation performance evaluations of related polymeric materials. Initiate effort to assess utility of nanoparticle-modified fibers for denaturing CW agents.

Total 1111

	FY 2004	FY 2005	FY 2006	FY 2007
Supporting Science and Technology	245	1406	0	0

FY 2004 Accomplishments:

- 245 Chemical Threat Agents - Continued investigations of CW Blister (HD) agent volatility in humidified air.

Total 245

FY 2005 Planned Program:

- 1406 Chemical Threat Agents - Conduct effort to measure ambient volatility of CW agents.

Total 1406

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DATE: **February 2005**

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

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

PROJECT: **CB1**

	FY 2004	FY 2005	FY 2006	FY 2007
Threat Agent Science	0	0	15707	16290

FY 2006 Planned Program:

- 4057 Threat Agent Science - Conduct basic research to support fourth dimensional contamination plume interpolation, and agent environmental fate and low level toxicity for emerging threat agents.
- 3875 Threat Agent Science - Conduct basic research to investigate nano-technologies for the detection of CB agents, novel light scattering for bio-identification, and predictive models for ambient volatility of agents and simulants.
- 3825 Threat Agent Science - Conduct basic research to investigate theoretical and empirical mechanisms and interactions of vapors with active surfaces for CB protection, utility of nano-particle modified fibers for agent protection.
- 3950 Threat Agent Science - Conduct basic research to investigate ionic liquids and metal catalysts for decontamination, the feasibility of semi-solid material chemical composition with absorbed CB agents and efficacy of vaporous decontaminates.

Total 15707

FY 2007 Planned Program:

- 4000 Threat Agent Science (Detection) - Conduct basic research for innovative concepts in areas such as nanotechnology, hyperspectral imaging, and materials research applicable to detection.
- 3000 Threat Agent Science (Decontamination) - Conduct basic research for innovative concepts in decontamination.
- 3800 Threat Agent Science (Protection) - Conduct basic research for innovative concepts in protection.

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DATE: **February 2005**

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

FY 2007 Planned Program (Cont):

- 5490 Threat Agent Science (Modeling and Simulation) - Conduct basic research for innovative concepts in areas such as modeling and simulation, and threat agent science of CB agents. Continue transitioning of basic research from previous years.

Total 16290

	FY 2004	FY 2005	FY 2006	FY 2007
Congressional Increases	0	5951	0	0

FY 2005 Planned Program:

- 992 Biodefense Research
- 992 New York Structural Biology Center
- 3967 Fluorescene Activated Sensing Technology (FAST) Integrated Threat Management System - Integrated Threat Management System - Continue a multi-phased basic research program that will include DNA amplification, using MDA technology, of anthrax, staph. aureus with the SEB gene, tularemia, plague and a smallpox surrogate; evaluation of the detection system for the above threat agents using fluorescent probes; evaluation of techniques consistent with the FAST process to identify RNA viruses, protein toxins and nerve and mustard agents; development of a prototype stand-alone instrument with an integrated air sampler and sonicator and a decision and control system with external communications.

Total 5951

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

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

PROJECT: **CB1**

	FY 2004	FY 2005	FY 2006	FY 2007
SBIR/STTR	0	100	0	0

FY 2005 Planned Program:

- 100 SBIR

Total 100

C. Other Program Funding Summary:

	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	To Compl	Total Cost
CB2 CHEMICAL BIOLOGICAL DEFENSE (APPLIED RESEARCH)	84416	100631	104317	104741	96961	90197	83962	82303	Cont	Cont
CB3 CHEMICAL BIOLOGICAL DEFENSE (ATD)	88011	92075	60787	76897	70670	73260	66155	54853	Cont	Cont
CP3 COUNTERPROLIFERATION SUPPORT (ATD)	4077	5116	0	0	0	0	0	0	0	9193
TT3 TECHBASE TECHNOLOGY TRANSITION	0	0	16207	13978	10783	11077	11523	11857	Cont	Cont

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

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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**

COST (In Thousands)		FY 2004 Actual	FY 2005 Estimate	FY 2006 Estimate	FY 2007 Estimate	FY 2008 Estimate	FY 2009 Estimate	FY 2010 Estimate	FY 2011 Estimate	Cost to Complete	Total Cost
TB1	MEDICAL BIOLOGICAL DEFENSE (BASIC RESEARCH)	27067	32437	45966	25528	28470	26363	22306	21532	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 capability areas (Pretreatments, Diagnostics, and Therapeutics) and directed research efforts. Categories under this project address the Joint Requirements Office (JRO) critical capability gaps identified in the baseline capability assessment performed in FY03. The specific critical capability gaps addressed are Gap #14 (Medical Prophylaxes - Lack of multi-valent vaccines), Gap #15 (Medical Prophylaxes - Lack of prophylaxes for chemical warfare agents), Gap #16 (Medical Prophylaxes - FDA Approval for Radiological prophylaxes), Gap #22 (Medical Therapeutics - Limited anti-viral/ toxin development), Gap #24 (Medical Therapeutics - Lack of FDA Approval for CBRN), Gap #35 (Diagnostics - Lack of portability), Gap #36 (Diagnostics - FDA Approval) and Gap #38 (Diagnostics - Reagent Verification).

B. Accomplishments/Planned Program

	FY 2004	FY 2005	FY 2006	FY 2007
Diagnostics	3501	3913	9778	4577

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RDT&E DEFENSE-WIDE/ BA1 - Basic Research	**0601384BP CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)**	**TB1**

FY 2004 Accomplishments:

- 3501 Diagnostic Technologies - Continued basic research on new diagnostic approaches to the early recognition of infection focusing on technologies compatible with future comprehensive integrated diagnostic systems. Continued to develop reagents and assays for appropriate biological markers for early recognition of infection and identify new host and agent-specific biological markers. Continued research directed toward new technological approaches for diagnosis of biological threat agents and new sample processing technologies.

Total 3501

FY 2005 Planned Program:

- 3913 Diagnostic Technologies - Develop nucleic acid and immunoassays to detect identified threat agents in clinical samples. Perform research on diagnostic approaches to the early recognition of infections. Develop confirmatory tests for toxins. Pursue evaluation of systems compatible with future comprehensive integrated diagnostics. Direct research towards solving the technical problems associated with clinical sample preparation and rapid diagnostics. Evaluate new chemistries for the identification of biological warfare agents.

Total 3913

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RDT&E DEFENSE-WIDE/ BA1 - Basic Research	**0601384BP CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)**	**TB1**

FY 2006 Planned Program:

- 5278 Diagnostic Technologies - Expand nucleic acid and immunoassays for the detection of identified threat agents in clinical samples to additional agents/targets. Improve existing assays, as new genomic data and techniques become available. Continue to perform research on diagnostic approaches to the early recognition of infections and the evaluation of systems compatible with future comprehensive integrated diagnostics. Simplify sample preparation techniques and evaluating rapid diagnostics platforms. Continue to evaluate new chemistries for the identification of biological warfare agents.
- 4500 Multiagent (Broad Spectrum) Medical Countermeasures - Identify common biomarkers for at least four broad classes of Pathogenic Agents (e.g. intracellular facultative bacilli, hemorrhagic viruses, pox viruses, protein neurotoxins).

Total 9778

FY 2007 Planned Program:

- 4577 Diagnostic Technologies - Continue to develop/expand collection of nucleic acid and immunoassays for the detection of identified threat agents in clinical samples to additional agents/targets. Improve sensitivity and specificity of existing assays, as new genomic data and techniques become available. Identify new diagnostic approaches to the early recognition of infections. Continue to evaluate systems compatible with future comprehensive integrated diagnostics. Identify suitable DNA and RNA sample preparation techniques and rapid diagnostics platforms. Expand evaluation of new chemistries for the identification of biological warfare agents to latest state-of-the-art methods.

Total 4577

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RDT&E DEFENSE-WIDE/ BA1 - Basic Research	**0601384BP CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)**	**TB1**

	FY 2004	FY 2005	FY 2006	FY 2007
Emerging Threats	0	0	19500	0

FY 2006 Planned Program:

- 19500 Multiagent (Broad Spectrum) Medical Countermeasures - Convene expert committee of nationally prominent biologists, biochemists, geneticists, pharmaceutical development experts to assist in overseeing an encompassing technical strategy and roadmap development for development of broad-spectrum countermeasures that focus on common host-response mechanisms of defense to develop means to defeat emerging/engineered threats. Approach will focus on four major modules of broad-spectrum effort (pathogen science; host response systems biology; adaptive technology to speed drug approval process; next-generation break-through technology. Develop a systematic evaluation of pathogen Biomarkers for categories of Biological Warfare (BW) Pathogenic Agents that tie to commonality in pathogen mechanism(s) of action (pathodeme concept - diverse pathogens that effect similar types of pathology in a host, e.g. hemorrhage, liver disease, etc.). Identify primary or common host pathways/networks that respond to pathogenesis events to uncover promising intervention points for broad-spectrum therapeutic approaches. Exploit advances in genomics, proteomics and systems biology studies to identify pathogenesis pathways and networks for at least three broad classes of pathogenic mechanisms. Develop collaborations and initiate a program to develop in silico and other methodologies to predict three-dimensional structure and comparative assessment of virulence moieties on important protein virulence molecules from genetic sequence.

Total 19500

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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 2004	FY 2005	FY 2006	FY 2007
Medical Biological Warfare Defense	4610	0	0	0

FY 2004 Accomplishments:

- 4610 Medical Biological Warfare Defense, Engineered Pathogen Identification and Countermeasures Program (Bug to Drug) - Identified the impact of biowarfare pathogens on the human body using computer models and direct protein analysis. Continued to develop counteracting drugs based on a comprehensive understanding of how the potential drug candidates impact the human body, outside of their desired effect against the pathogen.

Total 4610

	FY 2004	FY 2005	FY 2006	FY 2007
Pretreatments	10610	7020	7511	9560

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RDT&E DEFENSE-WIDE/ BA1 - Basic Research	**0601384BP CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)**	**TB1**

FY 2004 Accomplishments:

- 3058 Vaccines, Bacterial - Continued studies on the molecular mechanisms of pathogenesis of selected BW threat agents. Identified additional virulence determinants of Brucella species. Initiated a study to identify and characterize novel virulence proteins of F. tularensis.
- 1701 Vaccines, Toxin - Conducted computational chemistry studies to develop next generation botulinum neurotoxin and recombinant ricin toxin A-chain (rRTA) vaccines. Evaluated theoretical feasibility of multivalent vaccines by protein engineering. Evaluated the role of glycosylation or other structural modifications in reducing efficacy of botulinum neurotoxin vaccines.
- 1701 Vaccines, Viral - Completed investigating the role of cytotoxic T cells in the Ebola virus-mouse model. Examined the use of virus-like particles (VLP) as antigen for vaccines for filoviruses. Initiated research to investigate the role of cytotoxic T cells in the filovirus model in non-human primates.
- 3228 Vaccines, Plant Vaccine Development - Developed plant-based subunit vaccines as countermeasures against biological warfare agents.
- 922 Vaccines, Plant Derived Vaccine Against Anthrax and Smallpox - Developed plant-based subunit vaccines against anthrax and smallpox as countermeasures against agents of biological warfare. Expressed both proposed vaccines in edible plants using a constitutive expression system based on transgenic plants. Expressed in spinach functionally important epitopes of the anthrax recombinant Protective Antigen (rPA) and the B5R protein of the smallpox virus, using a transient expression system based on plant virus vectors. Evaluated immunogenicity of plant-based vaccines in animal models.

Total 10610

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RDT&E DEFENSE-WIDE/ BA1 - Basic Research	**0601384BP CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)**	**TB1**

FY 2005 Planned Program:

- 1200 Multiagent Vaccines - Identify bacterial multiagent vaccine target antigens. Clone and express chimeric vaccine constructs for multivalent toxin and bacterial vaccines by protein engineering. Initiate effort on anthrax-plague combined vaccine development. Establish new animal efficacy models. Explore genomics/proteomics-based high throughput approaches for potential vaccine target antigens. Explore use of Virus-Like Particles (VLP) for multiagent vaccine development. Evaluate DNA-based immunization against viral threat agents.
- 5020 Vaccine Research Support - Initiate project to develop a generic Bacillus vaccine, including identification of target antigens. Facilitate and consolidate research efforts in Brucella/Burkeholderia/Tularemia to include identification of potential intracellular pathogen target antigens. Characterize novel virulence genes and gene products of selected bacterial threat agents to support discovery of new medical countermeasures. Identify new Staphylococcal Enterotoxin A/Staphylococcal Enterotoxin B (SEA/SEB) structural determinants as potential immunogens to protect against multiple SE serotypes. Begin investigating the role of cytotoxic T cells in the higher animal model of filovirus infection. Expand development of animal models of aerosol infection with filoviruses. Determine the use of VLP and adenoviruses as antigen delivery platforms for vaccines against filoviruses.
- 800 Vaccine Technology Development - Use high throughput gene expression and sequencing technologies for a genomics/proteomics-based approach toward rapid vaccine development. Begin studies in anthrax/plague molecular vaccine development and evaluation. Initiate Bacillus generic molecular vaccine construction.

Total 7020

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RDT&E DEFENSE-WIDE/ BA1 - Basic Research	**0601384BP CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)**	**TB1**

FY 2006 Planned Program:

- 1311 Multiagent Vaccines - Continue to develop anthrax-plague vaccine, including third component. Evaluate specific combinations of target antigens and vaccine platforms such as adenovirus delivery vectors for vaccine development. Continue to explore genomics/proteomics-based high throughput approaches to identify potential vaccine target antigens. Evaluate use of VLP for vaccine development. Continue to evaluate DNA-based immunization against viral threat agents.
- 4700 Vaccine Research Support - Develop construction of initial generic Bacillus vaccine candidates and begin initial immunogenicity studies. Identify and evaluate new target antigens for intracellular pathogens. Evaluate T-cell immune response against intracellular pathogens. Continue basic studies in anthrax and plague pathogenic mechanisms. Continue development of alternative delivery platform strategies for immunization. Continue the development of recombinant vaccine candidates for botulinum neurotoxins. Evaluate various platforms for compatibility with the V3526 vaccine candidate. Analyze Western and Eastern Equine Encephalitis (WEE/EEE) mutants with various engineered attenuating mutations. Evaluate additional target antigens for Ebola virus vaccine development. Continue to evaluate adenovirus-based immunization approaches for vaccination against filoviruses.
- 1500 Vaccine Technology Development - Improve DNA-based immunization platforms as a multiagent anthrax-plague vaccine strategy, including evaluation of a third component. Continue studies in Bacillus molecular vaccine development and evaluation. Explore alternate immunization platforms for efficacy against selected biothreat agent pathogens.

Total 7511

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RDT&E DEFENSE-WIDE/ BA1 - Basic Research	**0601384BP CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)**	**TB1**

FY 2007 Planned Program:

- 1760 Multiagent Vaccines - Continue anthrax/plague/third component trivalent vaccine research. Identify valid target antigens for different biothreat pathogens and the use of genetic engineering approaches to construct unique gene fusions encoding multi-epitope protein antigens to optimize multiagent vaccine delivery. Expand effort in multiagent vaccine development to include the evaluation of novel immunization platforms and therapeutic immunization strategies for post-exposure treatment. Develop use of VLP for multiagent vaccine development. Continue to evaluate DNA-based immunization against viral threat agents.
- 5800 Vaccine Research Support - Proceed with generic Bacillus vaccine construction/evaluation. Establish broad spectrum vaccine strategy to target the four major facultative intracellular bacteria threats using genetic immunization and/or phagosome-lysosome based approaches. Continue evaluation of gene expression technologies for in vitro (inside a test tube) analysis of host responses to bacterial pathogens. Continue the comparative analysis of the genomics/bioinformatics database information for the design of unique target antigens. Continue basic pathogenicity studies of selected biothreat agents. Evaluate next generation SEA/SEB immunogens as vaccine candidates to protect against multiple SE serotypes in vivo (inside the organism). Conduct stability analysis and immunogenicity of SEB toxin vaccine in support of clinical trial. Develop and refine in vitro correlates of immunity for new antigens. Continue B and T cell epitope mapping of lead antigen candidates. Evaluate filovirus cellular immunity parameters. Develop animal models for Ebola-Sudan strain of virus infections.

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

DATE: **February 2005**

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

FY 2007 Planned Program (Cont):

- 2000 Vaccine Technology Development - Evaluate studies in anthrax/plague molecular vaccine development. Evaluate generic Bacillus molecular vaccine. Explore additional alternate immunization platforms for efficacy against selected biothreat agent pathogens. Continued refinement and development of approaches to identify potential vaccine target antigens. Continued evaluation of gene expression technologies for in vitro analysis of host responses to bacterial pathogens. Comparison of genomics/bioinformatics database information for the design of unique target antigens. Design and evaluation of cell-mediated immune targeting of antigens for intracellular pathogens.

Total 9560

	FY 2004	FY 2005	FY 2006	FY 2007
Therapeutics	8346	9089	9177	11391

FY 2004 Accomplishments:

- 5018 Therapeutics, Toxin - Continued custom synthesis of structural analogs of lead compounds identified by high-throughput screening assays for botulinum and SE toxins. Refined x-ray data for toxin-inhibitor co-crystal structures of most promising botulinum neurotoxin and SE inhibitors. Performed computational chemistry studies to refine lead compound co-crystal structures.

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DATE: **February 2005**

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

FY 2004 Accomplishments (Cont):

- 2120 Therapeutics, Viral - Continued research for development of intervention strategies for filovirus-induced shock and therapeutic approaches that combine antiviral and anti-shock drug therapy. Completed research for development of in vitro assays utilizing filovirus polymerase as a potential antiviral drug target. Generated baculovirus-expressed Ebola virus proteins for use in research studies. Identified sequences within Ebola virus genes that are highly susceptible to short interfering RNA-mediated degradation.
- 1208 Therapeutics, Bacterial - Evaluated novel lead antimicrobial compounds in small animal models for anthrax and plague.

Total 8346

FY 2005 Planned Program:

- 1243 Therapeutics, Bacterial - Evaluate efficacy of selected licensed and investigational products for efficacy in mice against bacterial threat agents. Maintain surveillance of products in the U.S. so that new products can be evaluated for efficacy in vitro and in vivo. Initiate efficacy studies of Investigational New Drug (IND) antibiotics for inhalational anthrax in non-human primates (NHPs). Evaluate Heat Shock Proteins (HSPs) with candidate vaccines. Evaluate immunoglobulin therapies for bacterial threat agents.

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DATE: **February 2005**

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

FY 2005 Planned Program (Cont):

- 5361 Therapeutics, Toxin - Identify custom synthesis of structural analogs of lead compounds by high-throughput screening assays for toxins. Continue to refine X-ray data for toxin-inhibitor co-crystal structures of most promising botulinum neurotoxin inhibitors. Perform computational chemistry studies to refine lead compound co-crystal structures. Perform test of lead compounds using in vivo model systems for assessment of therapeutic efficacy. Standardize in vivo concept model systems for assessment of therapeutic efficacy and surrogate endpoints of human clinical efficacy. Standardize in vivo concept model systems for assessment of therapeutic efficacy and surrogate endpoints of human clinical efficacy for toxins. Test FDA-approved drugs for septic shock as adjunct Staphylococcal Enterotoxin (SE) therapeutics in vivo. Develop lead monoclonal antibody systems against toxins as passive immunotherapeutics in vivo.
- 2485 Therapeutics, Viral - Develop high throughput in vitro drug screening assays and identify new molecular targets and develop assays by identification of a suitable target, cloning, expression and characterization of the target protein. Perform drug discovery assays to identify and test leading antivirals with in vitro assays. Identify compounds that demonstrate antiviral activity in small animal models and in vitro assays using authentic filoviruses and orthopox viruses. Develop a strategic plan for advanced development of compounds in regards to manufacturing and licensure. Identify potential mediators of shock or toxemia and determine the basis for the pathogenesis of shock or toxemia in appropriate animal models. Develop, characterize and evaluate the ability of monoclonal antibodies to viral specific proteins to neutralize the specific virus in vitro and in vivo and map protective monoclonal antibodies to distinct epitopes and to determine affinity and the importance of isotype. Develop appropriate small animal model to study Marburg virus infection.

Total 9089

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DATE: **February 2005**

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

FY 2006 Planned Program:

- 1277 Therapeutics, Bacterial - Evaluate if cellular immune response against the F1-V fusion protein of plague can be screened for potential therapeutics approaches, particularly through cytokine mediated pathways or expression of heat shock proteins.
- 2600 Therapeutics, Toxin - Define and validate essential indicators of therapeutic efficacy against selected toxins; establish conceptual framework for protocol screening for therapeutic candidates that demonstrate threshold efficacy; define and develop the key linking technologies (peptide binding design, candidate delivery systems) that have relevance to eventual human clinical efficacy trials for toxins.
- 1300 Therapeutics, Viral - Identify and test leading antivirals in appropriate animal models and worst-case scenarios such as viral challenge dose, route, and variation in viral challenge strain. Validate potential mediators of shock or toxemia and determine the basis for the treatment of shock or toxemia in appropriate animal models. Evaluate the utility of combining approaches that target different aspects of viral replication and/or disease pathogenesis. Standardize leading antivirals in appropriate animal models. Continue to develop a strategic plan for licensure and manufacturing with lead compounds.
- 4000 Multiagent (Broad Spectrum) Medical Countermeasures - Determine feasibility of re-engineering host cellular response patterns that have been compromised by pathogen-directed shifts in pathways (e.g. override of host apoptosis (programmed cell death) pathways, immune down-regulation, signal transduction agonists / antagonists, etc.)

Total 9177

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

DATE: **February 2005**

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

FY 2007 Planned Program:

- 1991 Therapeutics, Bacterial - Begin evaluation of therapeutic strategies for naturally occurring antibiotic-resistant strains of anthrax, plague, and other validated threat agents. Finalize studies of non-specific immune response factors (CpG, heat-shock proteins, etc.) as an adjunct to plague therapy.
- 6100 Therapeutics, Toxin - Refine planned therapeutic animal models, to conclude development in vivo model instrumentation, and its interface with the developed screening protocol for lead toxin therapeutics studies. Demonstrate clinical correlates for targeted endpoints that have been developed for in vivo models. Investigate and develop additional resuscitative technologies that integrate established and emerging toxin therapeutic modalities into suitable candidate therapies in humans.
- 3300 Therapeutics, Viral - Optimize key dosing, administration, and pharmacological characteristics of leading antivirals in appropriate animal models. Establish threshold therapeutic effects for candidate viral therapeutics, as to various parameters such as dose, route, and area under the curve. Investigate and develop additional resuscitative technologies that integrate established and emerging viral therapeutic modalities into suitable candidate therapies in humans.

Total 11391

	FY 2004	FY 2005	FY 2006	FY 2007
Congressional Increases	0	12150	0	0

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)**	**TB1**

FY 2005 Planned Program:

- 5951 Bug to Drug - Develop a Consortium structure with key industry performers to augment innovative rapid drug development approaches. Identify detailed rapid strategy to form BioRosettex.
- 992 National Center for Biodefense -
- 248 Research to Discover Neutralizing Antibodies to Mycotoxins -
- 1984 Therapeutic Approaches to Anthrax and Ricin Toxins - Design antisense oligomers to block transcription and translation of critical proteins involved in the pathogenesis of biowarfare pathogens such as a bacterial (anthrax), viral or toxin (ricin) threats. Demonstrate utility in either cell culture (in vitro) systems or small mammal animal models.
- 2975 Therapeutic Phosphorodiamidate Morpholino Oligomers (PMOs) - Demonstrate proof-of-principle of patented technology for antisense molecules by conducting and assisting in animal model studies designed to protect against viral biodefense pathogens.

Total 12150

	FY 2004	FY 2005	FY 2006	FY 2007
SBIR/STTR	0	265	0	0

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

DATE: **February 2005**

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

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

PROJECT: **TB1**

FY 2005 Planned Program:

- 265 SBIR

Total 265

C. Other Program Funding Summary:

	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	To Compl	Total Cost
TB2 MEDICAL BIOLOGICAL DEFENSE (APPLIED RESEARCH)	44784	43678	61654	42401	35344	29153	31017	31606	Cont	Cont
TB3 MEDICAL BIOLOGICAL DEFENSE (ATD)	44353	68272	63124	37131	31339	32232	41281	41147	Cont	Cont

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

DATE: **February 2005**

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 2004 Actual	FY 2005 Estimate	FY 2006 Estimate	FY 2007 Estimate	FY 2008 Estimate	FY 2009 Estimate	FY 2010 Estimate	FY 2011 Estimate	Cost to Complete	Total Cost
TC1	MEDICAL CHEMICAL DEFENSE (BASIC RESEARCH)	8032	9378	10860	10883	13116	12723	13445	13164	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 in medical chemical defense capability areas (Diagnostics, Therapeutics and Emerging Threats). Categories under this project address the Joint Requirements Office (JRO) critical capability gaps identified in the baseline capability assessment performed in FY03. The specific critical capability gaps addressed are Gap #14 (Medical Prophylaxes - Lack of multi-valent vaccines), Gap #15 (Medical Prophylaxes - Lack of prophylaxes for chemical warfare agents), Gap #16 (Medical Prophylaxes - FDA Approval for Radiological prophylaxes), Gap #22 (Medical Therapeutics - Limited anti-viral/ toxin development), Gap #24 (Medical Therapeutics - Lack of FDA Approval for CBRN), Gap #35 (Diagnostics - Lack of portability), Gap #36 (Diagnostics - FDA Approval) and Gap #38 (Diagnostics - Reagent Verification).

B. Accomplishments/Planned Program

	FY 2004	FY 2005	FY 2006	FY 2007
Chemical Warfare Agent Defense	4715	0	0	0

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

FY 2004 Accomplishments:

- 1575 Chemical Warfare Agent Defense, Inhalation Therapeutics - Investigated enzymatic targets of HD. Conducted a dose-response assessment of early acute lung injury in rodents administered intravascular HD. Determined the biochemical effects in male and female guinea pigs following exposure to chemical warfare agents.
- 265 Chemical Warfare Agent Defense, Medical Diagnostics - Identifed molecular intracellular proteomic changes following HD exposure.
- 1775 Chemical Warfare Agent Defense, Low Level Chemical Warfare Agent Exposure - Identifed biomarker(s) to indicate low level chemical exposure. Continued studies of neurotoxic effects of low dose chemical agent exposure. Examined potential for immunological deficits following nerve agent exposures. Identifed potential medical countermeasures for low level chemical warfare nerve agent and HD exposure.
- 1100 Chemical Warfare Agent Defense, Non-Traditional Agents (NTAs) - Investigated changes to pulmonary airway resistance and permeability of pulmonary microvessels induced by exposure to various concentrations of NTA. Identifed changes in the global gene expression profile of cultured human epidermal keratinocytes (HEK) in response to NTA exposure using DNA microarrays and genomics techniques to aid in considering strategies leading to medical countermeasures.

Total 4715

	FY 2004	FY 2005	FY 2006	FY 2007
Diagnostics	0	195	305	305

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DATE: **February 2005**

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

FY 2005 Planned Program:

- 195 Diagnostic Technologies - Perform basic research experiments aimed at developing detection methods in clinical samples for metabolites, adducts and/or other relevant biomarkers resulting from Chemical Warfare Agent (CW agents) exposure. Conduct experiments focusing on detecting sulfur mustard exposure by cleavage of adducts formed with blood proteins. Assess lab based Ellman cholinesterase assay for automation and increased throughput. Explore alternate sample collection/extraction technology to standard hydrolysis product assays.

Total 195

FY 2006 Planned Program:

- 305 Diagnostic Technologies - Continue basic research experiments aimed at developing detection methods in clinical samples for metabolites, adducts and/or other relevant biomarkers resulting from CW agent exposure. Focus on developing assays for detecting sulfur mustard exposure. Develop automation/high throughput strategy for cholinesterase assay. Continue development of alternate sample collection/extraction technology. Assess the development of a genomics-based diagnostic screening test for chemical warfare agent exposure.

Total 305

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DATE: **February 2005**

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

FY 2007 Planned Program:

- 305 Diagnostic Technologies - Continue basic research experiments aimed at developing detection methods in clinical samples for metabolites, adducts and/or other relevant biomarkers resulting from CW agent exposure. Complete assessment of alternate sample collection/extraction technology. Pursue development of a genomics-based diagnostic screening test for chemical warfare agent exposure. Initiate lab based studies to assess the development of a genomics-based diagnostic screening test for chemical warfare agent exposure.

Total 305

	FY 2004	FY 2005	FY 2006	FY 2007
Emerging Threats	0	2415	2131	1729

FY 2005 Planned Program:

- 966 Chemical Warfare Agent Defense, Low Level Chemical Warfare Agent Exposure - Examine multiple biomarkers as confirmatory for low level chemical exposure. Study possible immunological deficit following low level chemical nerve agent exposure. Examine physiological parameters that may alter sensitivity to low level CW agents. Identify potential medical countermeasures for low level CW agent exposures.
- 1449 Chemical Warfare Agent Defense, Non-Traditional Agents (NTAs) - Compare the direct effects of NTA on smooth muscle, hematic constituents, and lung to determine role in toxicity. Continue to identify changes in the global gene expression profile of cultured human epidermal keratinocytes (HEK) exposed to NTAs using DNA microarrays and genomic techniques to aid in considering strategies leading to medical countermeasures.

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DATE: **February 2005**

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

FY 2005 Planned Program (Cont):
Total 2415

FY 2006 Planned Program:

- 531 Chemical Warfare Agent Defense, Low Level Chemical Warfare Agent Exposure - Complete studies of medical countermeasures that minimize the effects of low level chemical exposure. Determine the effects of repeated exposure to chemical agents on CNS gene and protein expression in rodents.
- 1600 Chemical Warfare Agent Defense, Non-Traditional Agents (NTAs) - Study the oxidative metabolism of non-traditional convulsive agents. Study the pathophysiology of more classes of NTAs.

Total 2131

FY 2007 Planned Program:

- 1729 Non-Traditional Agents - Study the medical effects of additional classes of NTAs including ion channel blockers and convulsive agents.

Total 1729

	FY 2004	FY 2005	FY 2006	FY 2007
Therapeutics	3317	6691	8424	8849

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DATE: **February 2005**

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

FY 2004 Accomplishments:

- 410 Nerve Agent Defense, Neuroprotection - Evaluated drug treatment strategies and combinations of therapies for nerve agent-induced seizures.
- 2907 Vesicant Agent Defense, Vesicant Medical Countermeasures - Identified mechanism of action of vesicant pretreatment compounds. Determined effects of sulfur mustard (HD) on cell structure using multiphoton laser scanning microscopy. Analyzed in vitro effects of HD on cellular energy metabolism. Studied in vitro (inside the test tube) biochemical changes induced by HD.

Total 3317

FY 2005 Planned Program:

- 821 Nerve Agent Defense, Neuroprotection - Test putative neuroprotectants in at least one and possibly more than one animal species.
- 3938 Vesicant Agent Defense, Vesicant Medical Countermeasures - Characterize pathophysiological endpoints. Continue elucidation of pathophysiological schema. Identify points in schema for potential pharmaceutical intervention.
- 1932 Chemical Warfare Agent Defense, Inhalation Therapeutics - Identify and solicit for scientifically plausible animal and non-animal exposure models to investigate mechanisms of toxicity on pulmonary related function and to establish in-house and collaborative research programs within the confines of the approach.

Total 6691

CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2a Exhibit)	DATE February 2005
BUDGET ACTIVITY **RDT&E DEFENSE-WIDE/** **BA1 - Basic Research**	PE NUMBER AND TITLE **0601384BP CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)**
PROJECT **TC1**	

FY 2006 Planned Program:

- 2200 Nerve Agent Defense, Neuroprotection - Compare these events to what is known of mechanisms of cell death in other forms of status epilepticus and to stroke. As candidates emerge, priority may be given to studies which attempt to characterize the mechanism of protection seen with successful candidates. Develop and refine screening protocol for candidate down-select. The mechanisms with various classes of candidates may differ. Refine planned therapeutic animal models, to conclude development in vivo (inside the organism) model instrumentation, and its interface with future screening protocols for lead therapeutics studies. Demonstrate clinical correlates for targeted endpoints that have been developed for in vivo models. Investigate and develop additional resuscitative technologies that integrate established and emerging toxin therapeutic modalities into suitable candidate therapies in humans.
- 4100 Vesicant Agent Defense, Vesicant Medical Countermeasures - Continue to explore purification and delivery strategies of vesicant pretreatments, to include percutaneous, ocular, and pulmonary exposures. Continue to analyze in vitro effects of sulfur mustard agent (HD) on cellular energy metabolism. Continue to study in vitro biochemical changes induced by HD. Initiate efforts to develop biological tissue assays for selected compounds. Refine planned therapeutic animal models, to conclude development in vivo model instrumentation, and its interface with future screening protocols for lead therapeutics studies. Demonstrate clinical correlates for targeted endpoints that have been developed for in vivo models. Investigate and develop additional resuscitative technologies that integrate established and emerging anti-vesicant therapeutic modalities into suitable candidate therapies in humans.

CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2a Exhibit)	DATE February 2005
BUDGET ACTIVITY **RDT&E DEFENSE-WIDE/** **BA1 - Basic Research**	PE NUMBER AND TITLE **0601384BP CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)**
	PROJECT **TC1**

FY 2006 Planned Program (Cont):

- 2124 Chemical Warfare Agent Defense, Inhalation Therapeutics - Initiate experimentation in the areas of interest by establishing exposure/effects models from in vitro to in vivo systems by addressing a commonality of response/effects, i.e., identify a common response effect regardless of inhaled toxicant. Refine planned therapeutic animal models, to conclude development in vivo model instrumentation, and its interface with future screening protocols for lead therapeutics studies. Demonstrate clinical correlates for targeted endpoints that have been developed for in vivo models. Investigate and develop additional resuscitative technologies that integrate established and emerging toxicant therapeutic modalities into suitable candidate therapies in humans.

Total 8424

FY 2007 Planned Program:

- 2600 Nerve Agent Defense, Neuroprotection - Finish initial conceptual framework of known mechanisms of cell death in other forms of status epilepticus and to stroke. Relate events to known mechanisms of propagation of status epilepticus in well-studied animal models, and plan to begin to develop suitable refinement to established animal models with demonstrated clinical correlation to humans.
- 4100 Vesicant Agent Defense, Vesicant Medical Countermeasures - Determine in animal models the safety and efficacy of selected compounds for percutaneous, ocular and pulmonary exposure. Complete efforts to develop biological tissue assays for selected compounds and design screening protocol to down-select these candidate compounds. Refine planned therapeutic animal models, to conclude development in vivo model instrumentation, and its interface with future screening protocols for lead therapeutics studies.

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DATE: **February 2005**

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

FY 2007 Planned Program (Cont):

- 2149 Chemical Warfare Agent Defense, Inhalation Therapeutics - Initiate studies largely (in vivo when possible) based on data gathered in the previous study year, to address the administration of a medical countermeasure(s) therapy(ies) against multiple agent exposures. Refine planned therapeutic animal models, to conclude development in vivo model instrumentation, and its interface with future screening protocols for lead therapeutics studies. Demonstrate clinical correlates for targeted endpoints that have been developed for in vivo models. Investigate and develop additional resuscitative technologies that integrate established and emerging toxicant therapeutic modalities into suitable candidate therapies in humans.

Total 8849

	FY 2004	FY 2005	FY 2006	FY 2007
SBIR/STTR	0	77	0	0

FY 2005 Planned Program:

- 77 SBIR

Total 77

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

DATE: **February 2005**

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

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

PROJECT: **TC1**

C. Other Program Funding Summary:

	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	To Compl	Total Cost
TC2 MEDICAL CHEMICAL DEFENSE (APPLIED RESEARCH)	21698	24518	21516	31172	39449	40969	40384	39952	Cont	Cont
TC3 MEDICAL CHEMICAL DEFENSE (ATD)	10097	13129	24363	19222	32238	31302	32460	34454	Cont	Cont