CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2 Exhibit)

DATE **February 2006**

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

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

COST (In Thousands)		FY 2005 Actual	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	51998	94366	99182	79149	64565	56330	56314	Continuing	Continuing
CB1	CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)	10710	28808	16082	17130	17874	16271	18154	Continuing	Continuing
TB1	MEDICAL BIOLOGICAL DEFENSE (BASIC RESEARCH)	32308	54902	72356	49050	33805	26521	25222	Continuing	Continuing
TC1	MEDICAL CHEMICAL DEFENSE (BASIC RESEARCH)	8980	10656	10744	12969	12886	13538	12938	Continuing	Continuing

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 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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RDT&E DEFENSE-WIDE/
BA1 - Basic Research

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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DATE: **February 2006**

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

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

B. Program Change Summary:		FY 2005	FY 2006	FY 2007
Previous President's Budget (FY 2006 PB)		54056	72533	52701
Current Biennial Budget Estimate (FY 2007)		51998	94366	99182
Total Adjustments		-2058	21833	46481
a. Congressional General Reductions		-42	-1367	0
b. Congressional Increases		0	23200	0
c. Reprogrammings		-1574	0	0
d. SBIR/STTR Transfer		-442	0	0
e. Other Adjustments		0	0	46481

Change Summary Explanation:

Funding: FY06 - Congressional increases to enhance projects within the science and technology base (+$13,400K CB1; +$9,800K TB1). Congressional general reductions and other adjustments (-$299K CB1; -$864K TB1; -$204K TC1).

FY07 - Increase to enhance Medical Biological research efforts in support of the Transformational Medical Technology Initiative which focuses on broad-spectrum defenses against intracellular bacterial pathogens and hemorrhagic fevers (+$46,500K TB1). Defense-wide directed offsets (-$432K CB1; -$679K TB1; -$289K TC1). Inflation adjustment (+$224K CB1; +$1,007K TB1; +$150K TC1).

Schedule: N/A

Technical: N/A

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

DATE: **February 2006**

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

COST (In Thousands)		FY 2005 Actual	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)	10710	28808	16082	17130	17874	16271	18154	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 detection concepts for chemical and biological agents; advanced concepts in individual and collective protection; new concepts in decontamination; innovative concepts in modeling and simulation; and scientific discovery on the chemistry and toxicology of threat agents and related materials.

B. Accomplishments/Planned Program

	FY 2005	FY 2006	FY 2007
Congressional Interest Items	4959	13269	0

CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2a Exhibit)	DATE February 2006

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

FY 2005 Accomplishments:

- 992 New York Structural Biology Center - Continued a basic research program that leveraged exceptional sensitivity and resolution of high-field Nuclear Magnetic Resonance Spectrometers (NMRS) technology to permit atomic-level structural characterization of chemical compounds. Validated protocols that monitor the fate of chemical and biological warfare agents in battlefield and civilian environments such as concrete, asphalt, soil and water.
- 3967 Fluorescence Activated Sensing Technology (FAST) Integrated Threat Management System - Continued a multi-phased basic research program that will include Deoxyribonucleic acid (DNA) amplification, using multiple displacement amplification (MDA) technology, of anthrax, staph. aureus with the Staph. Enterotoxin B (SEB) gene, tularemia, plague and a smallpox surrogate; evaluated the detection system for the above threat agents using fluorescent probes; evaluated techniques consistent with the FAST process to identify Ribonucleic acid (RNA) viruses, protein toxins and nerve and mustard agents; developed a prototype stand-alone instrument with an integrated air sampler and sonicator and a decision and control system with external communications.

Total 4959

FY 2006 Planned Program:

- 6931 CBDP Basic Research Initiative - Conduct a basic research program that will investigate technologies and methodologies for the rapid detection of, and protection from biological agents.

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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 2006 Planned Program (Cont):

- 1981 Fluorescence Activated Sensing Technology (FAST) Integrated Threat Management System - Continues a multi-phased basic research program that will include Deoxyribonucleic acid (DNA) amplification, using multiple displacement amplification (MDA) technology, of anthrax, staph. aureus with the Staph. Enterotoxin B (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 Ribonucleic acid (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.
- 991 New York Structural Biology Center - Continue a basic research program that leverages exceptional sensitivity and resolution of high-field Nuclear Magnetic Resonance Spectrometers (NMRS) technology to permit atomic-level structural characterization of chemical compounds. Validate protocols that monitor the fate of chemical and biological warfare agents in battlefield and civilian environments such as concrete, asphalt, soil and water.
- 990 Superstructural Particle Evaluation & Characterization with Targeted Reaction Analysis (SPECTRA).
- 990 Photoscrub.
- 1386 Detection of Biological Agents in Water - Investigate technologies for the detection of biological agents in potable water sources.

Total 13269

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DATE: **February 2006**

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

	FY 2005	FY 2006	FY 2007
Decontamination	936	0	0

FY 2005 Accomplishments:

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

Total 936

	FY 2005	FY 2006	FY 2007
Detection	2175	0	0

FY 2005 Accomplishments:

- 975 Integrated CB Detection - Completed investigations of modified nanofilaments for the detection of CB agents. Completed investigations of modified gold nanosensors.

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DATE: **February 2006**

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

FY 2005 Accomplishments (Cont):

- 1200 Biological Agent Identification Detection - Completed testing of candidate ion channel stochastic sensor elements. Completed investigations of micro-channel mixing via configurable heating and surfaces. Completed development of test articles and procedures. Continued testing of antimicrobial peptides. Continued effort to characterize polymorphic regions of B. mallei genome using ribotyping, repetitive sequence polymerase chain reaction, and randomly amplified polymorphic DNAs. Initiated effort to assess utility of modified nanowires for bio-detection. Completed effort to assess novel light-scattering method for bio-identification. Completed effort to enhance utility of microfluidic control for bio-detection. Completed initial investigations of bacterial ghosts as simulants for biological warfare agents.

Total 2175

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

FY 2005 Accomplishments:

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

Total 302

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DATE: **February 2006**

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

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

PROJECT: **CB1**

	FY 2005	FY 2006	FY 2007
Protection	1068	0	0

FY 2005 Accomplishments:

- 420 Respiratory Protection - Completed research into understanding physical adsorption processes for Toxic Industrial Chemicals (TICs) and CW agents on novel adsorbent materials. Completed effort to develop performance model for the electric-swing adsorption process.
- 648 Shelter Protection - Completed investigations of the interrelationships between the chemical, physical, and transport properties of novel butyl rubber membranes prepared by electrospinning; expanded this effort to include permeation performance evaluations of related polymeric materials. Completed effort to assess utility of nanoparticle-modified fibers for denaturing CW agents.

Total 1068

	FY 2005	FY 2006	FY 2007
Supporting Science and Technology	1270	0	0

FY 2005 Accomplishments:

- 1270 Chemical Threat Agents - Completed effort to measure ambient volatility of CW agents.

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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 Accomplishments (Cont):
Total 1270

	FY 2005	FY 2006	FY 2007
Threat Agent Science	0	15253	16082

FY 2006 Planned Program:

- 3750 Modeling/Simulation Science - Conduct basic research to understand fundamental relationships of atmospheric phenomena, link equations of motion for terrestrial and space environments, investigate relationships between sensor data and dispersion forecasts, and improve the basic understanding of atmospheric turbulence in the stable boundary level.
- 1155 Detection Science - Investigate nano-technologies as sensors and investigate a theory-guided approach to the design of molecular sensing devices and systems.
- 1140 Threat Agent Science - Investigate genetic and biochemical variability as a potential new source of exploitable signatures and characterize the population dynamics of bacterial germination and migration within the body (toxicokinetics) and infection of target tissue under natural and altered physicological states (toxicodynamics).
- 969 Decontamination Science - Investigate the growth of hydrophobic polymer chains from enzymes as solvent-soluble decontaminating biocatalysts, and characterize the reactions between vaporous hydrogen peroxide and chlorine dioxide on metallic, metal-oxide and polymeric surfaces.

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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 2006 Planned Program (Cont):

- 2470 Special Projects (Nano-technology Initiative) - Survey the $1-Billion federal government's annual investments in nano-technology, develop a knowledge base for nano-technology research relative to chemical-biological defense, and leverage identified nano-science and nano-technologies from sources identified by the survey.
- 5769 Integrated Basic Research - Initiate a multi-faceted, integrated, and cross-cutting program involving industry, academia, and federally funded research efforts to determine best basic research investments and integration into the core applied research program.

Total 15253

FY 2007 Planned Program:

- 3775 Modeling/Simulation Science - Continue basic research to understand fundamental relationships of atmospheric phenomena, link equations of motion for terrestrial and space environments, investigate relationships between sensor data and dispersion forecasts, and improve the basic understanding of atmospheric turbulence in the stable boundary level.
- 1180 Detection Science - Continue investigating nano-technologies as sensors and investigate a theory-guided approach to the design of molecular sensing devices and systems.
- 1165 Threat Agent Science - Continue investigating genetic and biochemical variability as a potential new source of exploitable signatures and characterize the population dynamics of bacterial germination and migration within the body (toxicokinetics) and infection of target tissue under natural and altered physicological states (toxicodynamics).

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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 2007 Planned Program (Cont):

- 1015 Decontamination Science - Continue investigating the growth of hydrophobic polymer chains from enzymes as solvent-soluble decontaminating biocatalysts, and characterize the reactions between vaporous hydrogen peroxide and chlorine dioxide on metallic, metal-oxide and polymeric surfaces.
- 2495 Special Projects (Nano-technology Initiative) - Continue to leverage identified nano-science and nano-technologies from sources identified by the survey.
- 6452 Integrated Basic Research - Continue a multi-faceted, integrated, and cross-cutting program involving industry, academia, and federally funded research efforts to determine best basic research investments and integration into the core applied research program.

Total 16082

	FY 2005	FY 2006	FY 2007
SBIR/STTR	0	286	0

FY 2006 Planned Program:

- 286 SBIR

Total 286

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DATE: **February 2006**

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

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

PROJECT: **CB1**

C. Other Program Funding Summary:

	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	To Compl	Total Cost
CB2 CHEMICAL BIOLOGICAL DEFENSE (APPLIED RESEARCH)	104707	134222	103092	95674	91186	84402	80623	Cont	Cont
CB3 CHEMICAL BIOLOGICAL DEFENSE (ATD)	87033	110219	78236	72496	75429	67855	56786	Cont	Cont
CP3 COUNTERPROLIFERATION SUPPORT (ATD)	4869	0	0	0	0	0	0	0	4869
TT3 TECHBASE TECHNOLOGY TRANSITION	0	11127	11087	7879	8340	8688	8627	Cont	Cont

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DATE: **February 2006**

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 2005 Actual	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)	32308	54902	72356	49050	33805	26521	25222	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 #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 2005	FY 2006	FY 2007
Transformational Medical Technology Initiative	0	27205	51416

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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 2006 Planned Program:

- 27205 Multiagent (Broad Spectrum) Medical Countermeasures - Identify common biomarkers for several broad classes of Pathogenic Agents (e.g. intracellular facultative bacilli, hemorrhagic viruses, pox viruses). Develop a systematic evaluation of pathogen biomarkers for categories of Biological Warfare (BW) Pathogenic Agents that tie to commonality in pathogenic mechanisms(s) of action. Develop collaborations to 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 sequences. 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 27205

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

FY 2007 Planned Program:

- 51416 Multiagent (Broad Spectrum) Medical Countermeasures - This effort is part of the Quadrennial Defense Review (QDR) "leading edge" investment to develop broad spectrum medical countermeasures against future genetically-engineered bio-terror threats, for which there are no current defenses. Continue to identify common biomarkers for several broad classes of Pathogenic Agents (e.g. intracellular facultative bacilli, hemorrhagic viruses, pox viruses). Develop problem solving approach that 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 further a systematic evaluation of pathogen biomarkers for categories of Biological Warfare (BW) Pathogenic Agents that tie to commonality in pathogenic mechanisms(s) of action. 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. Pursue collaborations and continue development of in silico and other methodologies to predict three-dimensional structure and comparative assessment of virulence moieties on important protein virulence molecules from genetic sequences. Build on knowledge of 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 51416

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

	FY 2005	FY 2006	FY 2007
Congressional Interest Items	13142	9709	0

FY 2005 Accomplishments:

- 992 Biodefense Research - Used the Reverse Phase Protein Microarrays (RPPA) technique to discover and characterize the signaling pathways of bio-threat microorganism proteins.
- 5951 Bug-to-Drug - Developed a consortium structure with key industry performers to augment innovative, rapid drug development approaches. Identified a rapid strategy to form Biorosettex.
- 992 National Center for Biodefense - Investigated mechanisms of pathology in disease caused by biological warfare agents and identified effective broad spectrum treatments against major biological threat agents.
- 248 Research to Discover Neutralizing Antibodies to Mycotoxin - Generated monoclonal antibodies for the treatment of aflatoxin exposure targeting the respiratory and gastrointestinal system.
- 1984 Therapeutic Approaches to Anthrax and Ricin Toxins - Designed antisense oligomers to block transcription and translation of critical proteins involved in the pathogenesis of biowarfare pathogens such as bacterial (anthrax), viral or toxin (ricin) threats; demonstrate utility in either cell culture (in vitro) systems or small mammal animal models.
- 2975 Therapeutic Phosphorodiamidate Morphilino Oligomers (PMO) - Conducted animal studies to demonstrate proof of principle of patented technology for antisense molecule protection against viral pathogens.

Total 13142

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

FY 2006 Planned Program:

- 2773 Biomarker Molecular Toxicology Initiative.
- 991 Monoclonal Antibody Manufacturing for the Treatment of Emerging Infections.
- 991 Northeast Biodefense Center.
- 991 Selective Biological Center.
- 1981 Ricin & Anthrax Countermeasures.
- 991 Vaccine Development Program.
- 991 DNA Safeguard Project at Boise State University.

Total 9709

	FY 2005	FY 2006	FY 2007
Diagnostics	3704	5129	4518

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

FY 2005 Accomplishments:

- 3704 Diagnostic Technologies - Designed new nucleic acid and immunoassays specific for different bacterial and viral targets in order to enhance current detection capabilities. Assessed novel methods to develop immunodiagnostic assays. Initiated study to identify biomarkers of immunity in individuals vaccinated against biological warfare agents. Evaluated new chemistries for the identification of biological warfare agents. Identified host biomarkers of early infection resulting from exposure to biological agents. Evaluated the utility of novel technologies such as nucleic acid microarrays for biological agent detection.

Total 3704

FY 2006 Planned Program:

- 5129 Diagnostic Technologies - Improve the sensitivity and specificity of existing nucleic acid and immunodiagnostic assays. Design new nucleic acid and immunodiagnositic assays to augment pathogen detection as new genomic data and cutting edge techniques become available. Simplify DNA and RNA (Ribonucleic Acid) extraction methods for field use. Continue study to identify biomarkers of immunity in individuals vaccinated against biological warfare agents. Pursue new chemistries for the identification of biological warfare agents. Verify host response markers correlating with early recognition of infections caused by selected biological warfare agents.

Total 5129

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

FY 2007 Planned Program:

- 4518 Diagnostic Technologies - Expand assay design for nucleic acid and immunoassays to additional agents/targets. Continue to improve sensitivity and specificity of existing assays, as new genomic data and techniques become available. Direct research towards increasing sample concentration and extending sample viability prior to nucleic acid testing.

Total 4518

	FY 2005	FY 2006	FY 2007
Pretreatments	6624	7300	9437

FY 2005 Accomplishments:

- 1200 Multiagent Vaccines - Identified bacterial multiagent vaccine target antigens. Cloned and expressed chimeric vaccine constructs for multivalent toxin and bacterial vaccines by protein engineering. Initiated effort on anthrax-plague combined vaccine development. Established new animal efficacy models. Explored genomics/proteomics-based high throughput approaches for identifying potential vaccine target antigens. Explored use of Virus-Like Particles (VLP) for multiagent vaccine development. Evaluated DNA-based immunization against viral and bacterial threat agents.

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

FY 2005 Accomplishments (Cont):

- 4624 Vaccine Research Support - Initiated project to develop a generic Bacillus vaccine, including identification of target antigens. Facilitated and consolidated research efforts in Brucella/Burkeholderia/Tularemia to include identification of potential intracellular pathogen target antigens. Characterized novel virulence genes and gene products of selected bacterial threat agents to support discovery of new medical countermeasures. Identified new Staphylococcal Enterotoxin A/Staphylococcal Enterotoxin B (SEA/SEB) structural determinants as potential immunogens to protect against multiple SE serotypes. Began investigating the role of cytotoxic T cells in the higher animal model of filovirus infection. Expanded development of animal models of aerosol infection with filoviruses. Determined the use of viral-like particles (VLP) and adenoviruses as antigen delivery platforms for vaccines against filoviruses.
- 800 Vaccine Technology Development - Used high throughput gene expression and sequencing technologies for a genomics/proteomics-based approach toward rapid vaccine development. Began studies in anthrax/plague molecular vaccine development and evaluation. Initiated Bacillus generic molecular vaccine construction.

Total 6624

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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 2006 Planned Program:

- 1311 Multiagent Vaccines - (Formerly under Animal Models and Resuscitative Intervention) Continue to investigate the development of a trivalent anthrax-plague vaccine, to include a 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. Continue to evaluate the use of virus-like particles (VLP) to induce an immune response against targeted antigens and characterize the nature of the response. Continue evaluation of DNA-based immunization platforms. Explore the use of novel approaches including recombinant protein and/or fusion protein constructs.
- 4489 Vaccine Research Support - Continue development and construction of initial generic Bacillus vaccine candidates and begin initial immunogenicity studies. Identify and evaluate new target antigens for intracellular pathogens. Evaluate the role of cytotoxic T-cell immune response in higher animal models against filovirus infection. 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 (VEE) 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.

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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 2006 Planned Program (Cont):

- 1500 Vaccine Technology Development - Improve DNA-based immunization platforms against multiagent targets that stimulate protective immunity following minimal dosing. Evaluate high throughput gene expression systems for immune responses against selected bio-threat agents including Bacillus spore antigens and tularemia. Explore alternate immunization platforms for efficacy against selected biothreat agent pathogens. Evaluate bioinformatics-based approach to identify common Bacillus-specific spore target antigens. Evaluate the application of Toll-Like Receptors (TLR) agonists in vaccine construction and enhancement. Explore the use of human genome sequence analysis to determine genetics of host response to vaccination. Explore aspects of the innate immune response with respect to vaccine enhancement strategies.

Total 7300

FY 2007 Planned Program:

- 1760 Multiagent Vaccines - Evaluate trivalent vaccine formulations using anthrax/plaque and the third component such as ricin or staphylococcal enterotoxin A/B, as well as other possible components. Identify additional valid target antigens for different bio-threat pathogens and the use of genetic engineering approaches to construct unique gene fusions encoding multi-epitope protein antigens to optimize multiagent vaccine delivery systems. Expand effort in multiagent vaccine development to include the evaluation of novel immunization platforms and therapeutic immunization strategies for post-exposure treatment. Continue to develop the use of Virus-Like Particles (VLP) for multiagent vaccine development. Continue to evaluate DNA-based immunization strategies against bio-threat agents.

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

FY 2007 Planned Program (Cont):

- 5677 Vaccine Research Support - Proceed with generic Bacillus vaccine construction/evaluation. Establish broad spectrum vaccine strategy to target the four major facultative intracellular bacterial 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 information in the genomics/bioinformatics database 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). 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.
- 2000 Vaccine Technology Development - Evaluate generic Bacillus molecular vaccine in animal studies. Explore additional user friendly alternate immunization platforms/modalities that confer rapid protection following minimal dosing. Continue refinement and development of approaches to identify potential vaccine target antigens. Continue evaluation of gene expression technologies for in vitro analysis of host responses to bacterial pathogens. Comparison of genomics/bioinformatics database information analysis for the design of unique target antigens. Design studies to evaluate cell-mediated immune targeting of antigens for intracellular pathogens. Evaluate the genetic basis of the human immune response to immunization through genomic analysis. Evaluate the T-cell response against selected target antigens (analysis of cell-mediated immune response). Assess human immunodominant epitopes of selected bio-threat target antigens.

Total 9437

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

DATE: **February 2006**

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

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

PROJECT: **TB1**

	FY 2005	FY 2006	FY 2007
Therapeutics	8838	5031	6985

FY 2005 Accomplishments:

- 1243 Therapeutics, Bacterial - Evaluated efficacy of selected licensed and investigational products for efficacy in mice against bacterial threat agents. Maintained surveillance of new products in the U.S. so that these products can be evaluated for efficacy in vitro and in vivo. Initiated efficacy studies of Investigational New Drug (IND) antibiotics for inhalational anthrax in non-human primates (NHPs). Evaluated Heat Shock Proteins (HSPs) with candidate vaccines. Evaluated immunoglobulin therapies for bacterial threat agents.
- 5110 Therapeutics, Toxin - Assessed structural analogs of lead therapeutic compounds using high-throughput screening assays for toxins. Refined X-ray data for toxin-inhibitor co-crystal structures of most promising botulinum neurotoxin inhibitors. Initiated modeling time course of inhibitor effects. Performed computational chemistry studies to refine lead compound co-crystal structures. Tested FDA-approved drugs for septic shock as adjunct Staphylococcal Enterotoxin (SE) therapeutics in vivo. Continued development of lead monoclonal antibody systems against toxins as passive immunotherapeutics in vivo. Performed testing of lead compounds using cell-based model systems for assessment of therapeutic efficacy.

CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2a Exhibit)	DATE February 2006

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

FY 2005 Accomplishments (Cont):

- 2485 Therapeutics, Viral - Developed high throughput in vitro drug screening assays for lethal human pathogenic viruses. Identified several lead small molecule therapeutics which protected animals against Ebola and Marburg lethal infections. Found that virus-like particles of Ebola activated the innate immune responses through natural killer cells and elicited protection against lethal Ebola challenge. Developed assays by identification of a suitable therapeutic target, cloning, expression and characterization of the therapeutic target proteins. Developed quantitative assays for variola and other orthopox viruses using dried-down chemistry to detect and discriminate the variola virus from other orthopox viruses simultaneously (in the same reaction tube). Developed heterologous virus like particles (VLPs) containing viral proteins GP and VP40 from Ebola and Marburg for testing them as therapeutic agents for treating filovirus infections in murine and guinea pig model systems.

Total 8838

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.
- 2454 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.

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

DATE: **February 2006**

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 (Cont):

- 1300 Therapeutics, Viral - Perform drug discovery assays to identify and test leading antivirals with in vitro assays, small animal models, and authentic threat agents. 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.

Total 5031

FY 2007 Planned Program:

- 491 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.
- 4894 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.

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

DATE: **February 2006**

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):

- 1600 Therapeutics, Viral - Continue drug discovery to identify and test antivirals. Test leading antivirals in appropriate, existing animal models and worst-case scenarios such as viral challenge dose, route, and variation in viral challenge strain. Optimize key dosing, administration, and pharmacological characteristics of leading antivirals in non human primate 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 6985

	FY 2005	FY 2006	FY 2007
SBIR/STTR	0	528	0

FY 2006 Planned Program:

- 528 SBIR

Total 528

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

DATE: **February 2006**

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

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

PROJECT: **TB1**

C. Other Program Funding Summary:

	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	To Compl	Total Cost
TB2 MEDICAL BIOLOGICAL DEFENSE (APPLIED RESEARCH)	42987	88779	145073	76474	54837	43864	41114	Cont	Cont
TB3 MEDICAL BIOLOGICAL DEFENSE (ATD)	67899	88830	96736	143039	200722	229218	131723	Cont	Cont

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

DATE: **February 2006**

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

COST (In Thousands)		FY 2005 Actual	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)	8980	10656	10744	12969	12886	13538	12938	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 #15 (Medical Prophylaxes - Lack of prophylaxes for chemical warfare agents), 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 2005	FY 2006	FY 2007
Diagnostics	362	298	301

CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2a Exhibit)	DATE February 2006

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

FY 2005 Accomplishments:

- 362 Diagnostic Technologies - Conducted basic research experiments aimed at developing detection methods in clinical samples for metabolites, adducts and/or relevant biomarkers resulting from chemical warfare exposure. Performed study examining the potential for detecting sulfur mustard exposure by cleavage of adducts formed with blood proteins. Initiated assessment of a non-invasive immunodiagnostic test detecting sulfur mustard skin exposure before the onset of vesication. Performed initial assessment of gas chromatography mass spectrometry (GC-MS)/solid phase micro-extraction as a simple and quick clinical screen to verify exposure to Chemical Warfare Agent (CWA).

Total 362

FY 2006 Planned Program:

- 298 Diagnostic Technologies - Continue basic research experiments aimed at developing detection methods in clinical samples for metabolites, adducts and/or relevant biomarkers resulting from chemical warfare exposure. Report on the potential for detecting sulfur mustard exposure by cleavage adducts formed with blood proteins.

Total 298

FY 2007 Planned Program:

- 301 Diagnostic Technologies - Accelerate basic research experiments aimed at developing detection methods in clinical samples for metabolites, adducts and/or relevant biomarkers resulting from chemical warfare exposure.

Total 301

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

DATE: **February 2006**

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

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

PROJECT: **TC1**

	FY 2005	FY 2006	FY 2007
Emerging Threats	2283	2071	0

FY 2005 Accomplishments:

- 966 Chemical Warfare Agent Defense, Low Level Chemical Warfare Agent Exposure - Examined multiple biomarkers as confirmatory for low level chemical exposure. Studied possible immunological deficit following low level chemical nerve agent exposure. Examined physiological parameters that may alter sensitivity to low level CW agents.
- 1317 Chemical Warfare Agent Defense, Non-Traditional Agents (NTAs) - Compared the direct effects of NTA on smooth muscle, hematic constituents, and lung to determine role in toxicity. Continued 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.

Total 2283

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 Central Nervous System gene and protein expression in rodents.
- 1540 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.

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

DATE: **February 2006**

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):

Total 2071

	FY 2005	FY 2006	FY 2007
Therapeutics	6335	8183	10443

FY 2005 Accomplishments:

- 821 Nerve Agent Defense, Neuroprotection - Identified and tested various potential neuroprotectant agents in both rat and guinea pig nerve agent seizure models.
- 3582 Vesicant Agent Defense, Vesicant Medical Countermeasures - Characterized pathophysiological endpoints. Continued elucidation of pathophysiological schema. Identified points in schema for potential pharmaceutical intervention.
- 1932 Chemical Warfare Agent Defense, Inhalation Therapeutics - Identified and solicited 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 6335

CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2a Exhibit)	DATE February 2006

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

FY 2006 Planned Program:

- 2200 Nerve Agent Defense, Neuroprotection - Investigate novel pharmacologic measures to protect against organophosphate injury, using animal neurobehavioral, physiological, and neuroanatomic measures. Characterize the mechanism of protection seen with successful candidates, develop additional resuscitative technologies into suitable candidate therapies in humans.
- 3859 Vesicant Agent Defense, Vesicant Medical Countermeasures - Continue to explore pharmacological strategies of vesicant pretreatments and therapeutics, to include percutaneous, ocular, and pulmonary exposures. Analyze in vitro effects of sulfur mustard agent (HD) on cellular energy metabolism, and apoptotic (cell death) pathways. Continue to study in vitro biochemical changes induced by HD.
- 2124 Chemical Warfare Agent Defense, Inhalation Therapeutics - Establish exposure/effects models from the whole sequence of in vitro to in vivo systems, to identify common injury responses which may serve as broad targets for therapeutic intervention. Investigate and develop additional resuscitative technologies that integrate established and emerging toxicant therapeutic modalities into suitable candidate therapies in humans.

Total 8183

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

DATE: **February 2006**

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:

- 2322 Therapeutics, Neurologic - Develop neuroprotectants, anticonvulsants, and broad spectrum reactivators to reduce or prevent injury from nerve agents using molecular modeling as well as in vitro/in vivo laboratory techniques. Continue studies of known mechanisms of cell death and molecular interventions. Develop strategies for medical intervention to prevent seizures, minimize related neuronal injury in animal models, screen and adapt existing compounds/approaches to nerve agent protection strategies.
- 4265 Therapeutics, Cutaneous and Ocular - Develop animal models for percutaneous, ocular and pulmonary exposure. Complete efforts to develop in vitro tissue assays for potential therapeutic compounds, design screening protocols to down-select these candidate compounds.
- 2149 Therapeutics, Respiratory and Systemic - Investigate and develop additional resuscitative technologies that address both the direct pulmonary injury and systemic effects of chemical warfare agents, focus on identifying common sites for therapy at the tissue, cellular, and sub-cellular levels of injury.
- 1707 Therapeutics, Medical Toxicology - NTAs and Other Agents - Exploratory and comparative studies of emerging non-traditional chemical nerve agents. Focus on structure, function, and mechanism of action.

Total 10443

	FY 2005	FY 2006	FY 2007
SBIR/STTR	0	104	0

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

DATE: **February 2006**

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:

- 104 SBIR

Total 104

C. Other Program Funding Summary:

	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	To Compl	Total Cost
TC2 MEDICAL CHEMICAL DEFENSE (APPLIED RESEARCH)	24426	23657	30682	38927	41418	40598	39136	Cont	Cont
TC3 MEDICAL CHEMICAL DEFENSE (ATD)	12125	23863	18893	31812	31656	32621	33785	Cont	Cont