CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2 Exhibit)

DATE **February 2008**

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

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

COST (In Thousands)		FY 2007 Actual	FY 2008 Estimate	FY 2009 Estimate	FY 2010 Estimate	FY 2011 Estimate	FY 2012 Estimate	FY 2013 Estimate	Cost to Complete	Total Cost
	Total Program Element (PE) Cost	104830	83132	53191	55484	52990	56651	54348	Continuing	Continuing
CB1	CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)	28959	18885	24424	24350	23167	26836	25681	Continuing	Continuing
CI1	CONGRESSIONAL INTEREST ITEMS (BASIC RESEARCH)	0	16960	0	0	0	0	0	0	16960
TB1	MEDICAL BIOLOGICAL DEFENSE (BASIC RESEARCH)	66140	34951	16388	18131	17480	16942	15616	Continuing	Continuing
TC1	MEDICAL CHEMICAL DEFENSE (BASIC RESEARCH)	9731	12336	12379	13003	12343	12873	13051	Continuing	Continuing

A. Mission Description and Budget Item Justification: This program element (PE) funds the Joint Service fundamental research program for chemical and biological (CB) defense (medical and physical sciences). The basic research program aims to improve the operational performance, reliability, and capability of present and future Department of Defense (DoD) components by expanding knowledge in relevant fields of science and engineering 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, they fully leverage and exploit 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. Where appropriate, scientific discovery and advances are shared within the broader DoD Research, Development, Test and Engineering (RDT&E) Program. 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.

CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2 Exhibit)

DATE: **February 2008**

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

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

B. Program Change Summary:		FY 2007	FY 2008	FY 2009
Previous President's Budget (FY 2008 PB)		104257	72003	59191
FY09 President's Budget (FY 2009 PB)		104830	83132	53191
Total Adjustments		573	11129	-6000
a. Congressional General Reductions		0	-5831	0
b. Congressional Increases		0	16960	0
c. Reprogrammings		1586	0	0
d. SBIR/STTR Transfer		-1013	0	0
e. Other Adjustments		0	0	-6000

Change Summary Explanation:

Funding: FY08 - Congressional increases to enhance projects within the science and technology base (+$16,960K CI1). Congressional general reductions and other adjustments (-$5,439K CB1; -$290K TB1; -$102K TC1).

FY09 - Change proposals that realign funding within the Chemical and Biological Defense Program (CBDP) RDT&E (-$6,000K TB1)

Schedule: N/A

Technical: N/A

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

DATE: **February 2008**

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 2007 Actual	FY 2008 Estimate	FY 2009 Estimate	FY 2010 Estimate	FY 2011 Estimate	FY 2012 Estimate	FY 2013 Estimate	Cost to Complete	Total Cost
CB1	CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)	28959	18885	24424	24350	23167	26836	25681	Continuing	Continuing

A. Mission Description and Budget Item Justification:

Project CB1 CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH): This program supports basic research efforts in nanoscience, bioscience, surface science, information science, and threat agent sciences that focus on detection, protection, and decontamination. The project seeks to broaden knowledge and understanding of the fundamental phenomena observed in these fields. The aim is to foster radically new concepts and directions of research, which could lead to revolutionary innovations and capabilities that can enhance the performance and ensure the safety of the warfighter. Investment strategies are leveraged so as to maximize short-term and long-term gains from different scientific disciplines (chemistry, biology, physics, etc.). Research in synthetic biology, biomimetics for abiotic synthetic receptors and catalysts, and other emerging areas of science lay a foundation for developing novel "smart" materials which combine multiple functionalities into a common autonomous framework or network. Consequently, breakthroughs and advances in functional capabilities gained from these scientific disciplines will be incorporated into an overarching convergence, which will include nanotechnology, biotechnology, information technology, and cognitive science (NBIC). Following the framework envisioned by NBIC convergence, the Transformational Countermeasures Technology Initiative (TCTI) was launched at DTRA in FY2008. The TCTI concept leverages existing research programs and activities within the CBDP, DoD, and other government agencies in order to accelerate revolutionary transformational breakthroughs that can be readily transitioned to applied research or advanced development initiatives. The transformational initiatives were designed to shape the future of research to meet multiple, complex challenges from 21st century threats. Under the TCTI, this basic research program will continue to support world-class scientists whose research serves as pipelines of future breakthroughs. The broad-spectrum, integrated, cross-cutting, macro- and nano-scale technologies developed from these breakthroughs will be an effective countermeasure against traditional, evolving, and emerging chemical and biological threats; this revolutionary approach will gain new knowledge through Basic Research and will enable future CB defenses and countermeasures.

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

DATE: February 2008

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

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

PROJECT: CB1

B. Accomplishments/Planned Program

	FY 2007	FY 2008	FY 2009
Congressional Interest Items	10865	0	0

Accomplishments/Planned Program	FY2007	FY2008	FY2009
CBDP Basic Research Initiative - FY 07 - Solicited proposals from degree-granting universities, nonprofit organizations, and commercial concerns, to include small businesses, in support of the CBDP to explore new and innovative ideas to fill identified knowledge gaps. Funded five research proposals that addressed reticular chemistry, microfilters for nano-aerosol filtration, modeling of flow containing nanoparticles through electrostatically charged monolith filters, organ specific blood signatures for host response to infection, and reliable and rapid prediction of agent fate and transport in porous materials.	4951	0	0
Fluorescence Activated Sensing Technology (FAST) Integrated Threat Management System - FY 07 - Enhanced and evaluated the prototype stand-alone instrument with an integrated air sampler and sonicator and a decision and control system with external communications.	991	0	0
Detection of Biological Agents in Water - FY 07 - Refined investigation of the basic techniques required to measure the Raman signature of a wide array of bio-chemical agents, including bacteria, viruses, and biological and chemical toxins, over a full spectra of excitation wave lengths ranging from the deep UV thru the near infrared regions of the electromagnetic spectra in portable water sources.	1486	0	0
New York Structural Biology Center - FY 07 - Refined the basic research program that leverages exceptional sensitivity and resolution of high-yield Nuclear Magnetic Resonance (NMR) technology to permit atomic-level structural characterization of chemical compounds.	1159	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)**	**CB1**

Accomplishments/Planned Program (Cont):	**FY2007**	**FY2008**	**FY2009**
Next Generation Protective Gear Research - FY 07 - Conducted investigative research for an adaptive individual protection system which was described at the Nanotechnology for Chemical & Biological Defense 2030 Workshop by the CB Protection Focus Group.	991	0	0
Organic Light Emitting Receptor Based Nanosensors - FY 07 - Conducted investigative research on multisignal nanosensors for the detection of chemical warfare agents and incorporated the sensors into a prototype of the handheld device capable of measuring the multiple signals generated by the nanosensors.	1287	0	0
Total	**10865**	**0**	**0**

	FY 2007	**FY 2008**	**FY 2009**
Threat Agent Science	18094	0	0

Accomplishments/Planned Program	**FY2007**	**FY2008**	**FY2009**
Threat Agent Science - FY 07 - Continued to investigate genetic and biochemical variability as a potential new source of exploitable signatures and characterized the population dynamics of bacterial germination and migration within the body (toxicokinetics) and infection of target tissue under natural and altered physiological states (toxicodynamics). In FY 08, Threat Agent Science changes to Basic Research Core.	1695	0	0
Integrated Basic Research - FY 07 - Continued to investigate a 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. In FY 08, Threat Agent Science changes to Basic Research Core.	6998	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)**	**CB1**

Accomplishments/Planned Program (Cont):	**FY2007**	**FY2008**	**FY2009**
Detection Science - FY 07 - Continued investigation of nano-technologies as sensors and investigation of a theory-guided approach to the design of molecular sensing devices and systems. In FY 08, Threat Agent Science changes to Basic Research Core.	1698	0	0
Modeling/Simulation Science - FY 07 - Conducted basic research to understand fundamental relationships of atmospheric phenomena, linked equations of motion for terrestrial and space environments, investigated relationships between sensor data and dispersion forecasts, and improved the basic understanding of atmospheric turbulence in the stable boundary level. In FY 08, Threat Agent Science changes to Basic Research Core.	3775	0	0
Special Projects (Nano-technology Initiative) - FY 07 - Continued to leverage identified nano-science and nano-technologies from sources identified by the survey on the $1-Billion federal government's annual investment in nano-technology. In FY 08, Threat Agent Science changes to Basic Research Core.	2913	0	0
Decontamination Science - FY 07 - Continued investigating the growth of hydrophobic polymer chains from enzymes as solvent-soluble decontaminating biocatalysts, and characterized the reactions between vaporous hydrogen peroxide and chlorine dioxide on metallic, metal-oxide and polymeric surfaces. In FY 08, Threat Agent Science changes to Basic Research Core.	1015	0	0
Total	**18094**	**0**	**0**

	FY 2007	**FY 2008**	**FY 2009**
Basic Research Core	0	18682	24424

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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**

Accomplishments/Planned Program	FY2007	FY2008	FY2009
Basic Research in Nanoscience - FY 08 - Initiate research on fundamental phenomena to address opportunities to leverage advances in nanoscience to support chemical and biological defense program requirements. Efforts include investigating: mechanical tools for assessing chemical absorption capacities and rates of chemical absorption for nano-porous materials; atomistic-continuum multi-scale methods for quantum-dot surface growth; silicates as nucleophilic reagents and self-assembling protein nanostructures incorporating active functionality; nano-scale plasmonic and chemical mechanisms of surface enhanced Raman scattering and molecular machines. These developments will prove promising for advanced protection and surface detection of next generation chemical agents. Conduct systematic investigations of biomimetic catalysts in the synthesis of reactive metal oxide nanoparticle networks. Investigate hydrodynamic focusing templated electrochemical fabrication of high density conducting nanowire arrays for nano-sensing technologies for identifying chemical agents. Investigate supramolecular self-assemblies for high-throughput screening of chemical and biological spiral structures, porous carbons using molecular simulations and nonlinear spectroscopy of nanoparticles. Study nanocomposite structures as active and passive barrier materials; and liquid crystalline nanocolloids for sensors and actuators. Analyze molecule-surface encounters relevant to molecular adsorption, size and chemically selective collection and trace identification. Study and elucidate the role of conjugated polyelectrolytes as sensitizers of reactive oxygen species and versatile antimicrobials. FY 09 - Continue research on projects initiated in FY 08. Initiate efforts to investigate ultra-oleophobic textile surfaces, multifunctional nano-structured materials controlled by nanovalves, biomimetic living systems, and bio-nano interfaces of living cells and nanomaterials to provide for future intelligent protection concepts; for example individual protection.	0	3950	6000

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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

Accomplishments/Planned Program (Cont):	FY2007	FY2008	FY2009
Basic Research in Bioscience - FY 08 - Initiate and continue to leverage previous Basic Research efforts in fundamental phenomena to address opportunities to leverage advances in bioscience to support chemical and biological defense program requirements. Investigate multi-variant polymeric substrates for biomolecular adsorption and cell signaling; new hybrid nanomaterials that bridge nanoparticle and metallic surface-biological interfaces; dynamic properties of biological molecules of submillimeter wave-length and integrated micro-resonators; real-time changes in bacterial sizes during germination and growth of standardized preparation of biological agent simulants; recombinant single domain antibodies; immobilized antimicrobial activities in inorganic composites and antibacterial materials and coatings. These developments will prove promising for new and advanced sensing and detection concepts. Study biophysical fluid dynamics near surfaces and interaction of bio-aerosols with shock blast waves on the dispersion, activation, and destruction of airborne threats. Study impedance-based biosensors with tunable sensitivity using micro fluidic flow focusing and three modes of inhibiting a specific target from anthrax. FY 09 - Continue research on projects initiated in FY 08. Initiate efforts to investigate multi-metal ion catalyzed alcoholysis reactions of neutral and anionic organophosphorus compounds in alcohol media, beta-roll peptide structures for allosterically controlled biomolecular recognition and decontamination, investigation of proteomics and bioinformatics approaches for the classification of biological agents and specifically engineered genetics.	0	3860	4800

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RDT&E DEFENSE-WIDE/ BA1 - Basic Research	**0601384BP CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)**	**CB1**

Accomplishments/Planned Program (Cont):	**FY2007**	**FY2008**	**FY2009**
Basic Research in Information Science - FY 08 - Initiate and continue to leverage previous Basic Research efforts in fundamental phenomena to address opportunities to leverage advances in information science to support chemical and biological defense program requirements. Investigate the use of dynamic combinatorial chemistry that enables new host-guest combinations that may result in new approaches in detection, protection, or decontamination. Study the physics of molecules adhered to surfaces under conditions of flow using first principle of computations. Investigate the dynamics of bacterial germination and migration within the body, infection of target tissues and model the results. Conduct an analysis of atmospheric behavior by deriving basic mathematical and physical relationships such as momentum and energy exchanges. Study the fundamental relationships between models and data for moisture in soil, variability in clouds, and characteristics of the wind and turbulence at the boundary layer. Investigate the atmospheric turbulence in the stable boundary layer through theoretical and laboratory studies to further knowledge of dispersion of chemical and biological agents. FY 09 - Continue research on projects initiated in FY 08. Initiate efforts to investigate genetic algorithms to identify optimal material arrangements, quantification and reduction of uncertainty for dispersion models via meteorological predictions through computer experimentation, calculations of the complete electromagnetic response of large macromolecules, new molecular recognition signatures in the electromagnetic spectrum.	0	4680	5925

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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**

Accomplishments/Planned Program (Cont):	**FY2007**	**FY2008**	**FY2009**
Basic Research in Cognitive Science - FY 08 - Initiate efforts in fundamental phenomena to address opportunities to leverage advances in cognitive science to support chemical and biological defense program requirements. Conduct research in cognitive science that draws from many disciplines including cognitive psychology, neuroscience, linguistics, computer science, physics, mathematics, and biology. Initiate research on imaging methods (e.g., modern optical microscopy, functional brain mapping) and their applications to the affects of chemical and biological agents. Leverage data gathered during the study of human cognitive and sensorimotor processes. Conduct research to fill the "gap" between psychological processes and brain functions as they may apply to cause and effect from exposure to chemical and biological agents. FY 09 - Continue research on projects initiated in FY 08. Initiate efforts to investigate the presentation of risk and uncertainty for CB decision making.	0	3174	4199
Integration of Basic Research Science- FY 08 - This is a consolidation of efforts undertaken in Threat Agent Science Basic Research in FY 2007. Initiate a multi-faceted, integrated, and cross-cutting effort involving DoD laboratories, industry, academia, and federally funded research efforts to determine best basic research investment strategies and approach integration of CB basic research findings into applied research. FY 09 - Continue research on projects initiated in FY 08. Initiate research in Abiotic Networked Threat Systems (ANTS) and integrated approach to the NBIC sciences.	0	3018	3500
Total	**0**	**18682**	**24424**

	FY 2007	**FY 2008**	**FY 2009**
SBIR/STTR	0	203	0

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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**

Accomplishments/Planned Program	FY2007	FY2008	FY2009
SBIR - FY 08 - Small Business Innovative Research.	0	203	0
Total	**0**	**203**	**0**

C. Other Program Funding Summary:

	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	To Compl	Total Cost
CB2 CHEMICAL BIOLOGICAL DEFENSE (APPLIED RESEARCH)	128194	87984	110984	99931	91149	93975	94292	Cont	Cont
CB3 CHEMICAL BIOLOGICAL DEFENSE (ATD)	103420	20499	19242	21745	14112	14178	13695	Cont	Cont
TT3 TECHBASE TECHNOLOGY TRANSITION	15616	7817	8241	8389	8253	9343	9445	Cont	Cont

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BUDGET ACTIVITY	PE NUMBER AND TITLE	PROJECT
RDT&E DEFENSE-WIDE/ BA1 - Basic Research	**0601384BP CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)**	**CI1**

COST (In Thousands)		FY 2007 Actual	FY 2008 Estimate	FY 2009 Estimate	FY 2010 Estimate	FY 2011 Estimate	FY 2012 Estimate	FY 2013 Estimate	Cost to Complete	Total Cost
CI1	CONGRESSIONAL INTEREST ITEMS (BASIC RESEARCH)	0	16960	0	0	0	0	0	0	16960

A. Mission Description and Budget Item Justification:

Project CI1 CONGRESSIONAL INTEREST ITEMS (BASIC RESEARCH):

B. Accomplishments/Planned Program

	FY 2007	FY 2008	FY 2009
Congressional Interest Items	0	16718	0

Accomplishments/Planned Program	FY2007	FY2008	FY2009
CBDP Initiative Fund Basic Research - FY 08 - Solicit proposals from degree-granting universities, nonprofit organizations, and commercial concerns, to include small businesses, in support of the CBDP to explore new and innovative ideas to fill identified knowledge gaps. Upon technical evaluation and selection of proposals, provide a report detailing the number of projects funded and areas of research.	0	3943	0
Detection of Biological Agents in Water - FY 08 - Conduct research to develop a highly sensitive and selective acoustic wave biosensor arrays with signal analysis system to provide a fingerprint for the real-time identification and quantification of a wide array of bacterial pathogens and environmental health hazards.	0	1972	0

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RDT&E DEFENSE-WIDE/ BA1 - Basic Research	0601384BP CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)	CI1

Accomplishments/Planned Program (Cont):	FY2007	FY2008	FY2009
Diamond MEMS Sensors for Real-Time Sensing of Weaponized Pathogens - FY 08 - Research and develop a new class of compact, wearable, real-time chemical and biological point sensors using the unique properties of diamond.	0	986	0
Portable Continuous Monitor for Biodetection - FY 08 - Conduct research to develop a platform capable of performing multiple bioassays for live organisms and toxins simultaneously, efficiently, accurately and extremely fast.	0	1577	0
Rapid Response Database Systems Initiative - FY 08 - Conduct research to develop an exercise system (that can be implemented and replicated throughout the military, guard and the world) that most effectively ensures a rapid response to All Hazards whether natural or man-made.	0	986	0
Garden State Cancer Center Vaccine Development Program - FY 08 - Conduct research to continue the development of a safe vaccine against smallpox that does not require whole or live virus, thereby eliminating the danger of vaccine-associated side effects and transmission for viral infections to immunocompromised individuals.	0	789	0
DNA Safeguard.	0	1341	0
PhotoScrub - FY 08 - Conduct research using PhotoScrub to break down chemical and biological threats into simpler, non-hazardous molecules such as carbon dioxide and water.	0	1578	0
Initiative for Defense Against Bio-Warfare and Bio-Terrorism - FY 08 - Research and develop pharmaceutical drugs with a broad spectrum of action against a range of Categories A and B bacterial pathogens, and emerging drug-resistant bacteria that cause serious, life-threatening infections in the community and health-care facilities.	0	1576	0
Multisignal Nanosensors for Detections of IEDs.	0	1970	0
Total	**0**	**16718**	**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)**	**CI1**

	FY 2007	FY 2008	FY 2009
SBIR/STTR	0	242	0

Accomplishments/Planned Program	FY2007	FY2008	FY2009
SBIR - FY 08 - Small Business Innovative Research.	0	242	0
Total	**0**	**242**	**0**

C. Other Program Funding Summary: N/A

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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**

COST (In Thousands)		FY 2007 Actual	FY 2008 Estimate	FY 2009 Estimate	FY 2010 Estimate	FY 2011 Estimate	FY 2012 Estimate	FY 2013 Estimate	Cost to Complete	Total Cost
TB1	MEDICAL BIOLOGICAL DEFENSE (BASIC RESEARCH)	66140	34951	16388	18131	17480	16942	15616	Continuing	Continuing

A. Mission Description and Budget Item Justification:

Project TB1 MEDICAL BIOLOGICAL DEFENSE (BASIC RESEARCH): This project area funds basic research which seeks to promote the development of vaccines and therapeutic drugs to provide effective medical defense against validated biological threat agents including bacteria, toxins, and viruses. These Basic Research efforts advance promising biotechnology with the potential to rapidly identify, diagnose, prevent, and treat disease due to exposure to biological threat agents. Categories for this project area include core science and technology program areas in medical biological defense capability areas (Pretreatments, Diagnostics, Therapeutics) and directed research areas such as the Transformational Medical Technologies Initiative (TMTI). The TMTI was launched in FY06 as a key Quadrennial Defense Review initiative to respond to the threat of emerging or intentionally bioengineered biological threats. It augments the core science and technology area by expanding the novel programs currently funded under the core Therapeutics program and introducing new technologies for developmental focus. TMTI is a novel experiment to develop drugs that are broad spectrum in nature by using non-traditional and high risk approaches to accelerate the development and licensure of new medicines. The basic research supported by the TMTI is focused on delineating the pathogenic mechanisms of intracellular bacterial pathogens and hemorrhagic fever viruses. Teaming the core program and TMTI provides a complementary strategy (single agent versus broad spectrum, conventional versus emerging threats and established model systems versus expanded integration of novel technology, respectively) towards the development of effective medical countermeasures against biothreat agents.

B. Accomplishments/Planned Program

	FY 2007	FY 2008	FY 2009
Congressional Interest Items	9410	0	0

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

Accomplishments/Planned Program	FY2007	FY2008	FY2009
Northeast Biodefense Center - FY 07 - Increased laboratory capacity so that urgent local, national and global needs can be met without compromising ongoing research programs. Key research objectives include: establishing new technologies for producing monoclonal antibodies for passive administration; establishing new technologies for rapid active immunization employing dendritic cell, macrophage and B-cell interactions; discovering novel therapeutic preventive and immunomodulatory targets and molecules for bacterial and viral pathogens.	991	0	0
FY 07 - Anthrax Vaccine Research.	496	0	0
FY 07 - Mismatch Repair Derived Medicines to treat Clostridium, Staphylococcus and Bacillus Bioweapons.	1981	0	0
FY 07 - UCLA High Speed, High Volume Laboratory Network for Infectious Diseases - Initiated development of a high speed, high volume (high-throughput) laboratory capability that links into a network and is operated by several premier institutions.	5942	0	0
Total	**9410**	**0**	**0**

	FY 2007	FY 2008	FY 2009
Transformational Medical Technologies Initiative	32273	22510	6211

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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

Accomplishments/Planned Program	FY2007	FY2008	FY2009
Multiagent (Broad Spectrum) Medical Countermeasures -	32273	22510	6211
FY 07 - Identified common biomarkers for several broad classes of Pathogenic Agents with specific applications to intracellular bacterial pathogens and hemorrhagic fever viruses. Developed a problem solving approach that focused on four major modules of broad-spectrum effort (host immune response, small molecule therapeutics, nucleotide therapeutics, protein based therapeutics) with the emphasis on developing adaptive technology to speed drug approval process and next generation break-through technology. Accelerated a systematic evaluation of pathogen biomarkers for categories of Biological Warfare (BW) Pathogenic Agents that tie to commonality in pathogenic mechanism(s) of action. Identified primary common host pathways/networks that respond to pathogenesis events to uncover promising intervention points for broad-spectrum therapeutic approaches. Exploited advances in genomics, proteomics and systems biology studies to identify pathogenesis pathways and networks using two classes of agents (hemorrhagic fever viruses and intracellular bacterial pathogens) as model systems. Built on knowledge of host cellular response patterns that have been compromised by pathogen-directed shifts in pathways.			
FY 08 - Apply knowledge on common biomarkers for broad classes of Pathogenic Agents to specific species of intracellular bacterial pathogens and hemorrhagic fever viruses. Validate problem solving approach focusing on four major modules of broad-spectrum effort (host immune response, small molecular therapeutics, nucleotide therapeutics, protein based therapeutics). Assess the systematic evaluation of pathogen biomarkers for categories of BW Pathogenic Agents that tie to commonality in pathogenic mechanisms(s) of action. Relate primary or common host pathways/networks that respond to pathogenesis events to uncover promising intervention points for broad-spectrum therapeutic approaches. Continue to mine advances in genomics, proteomics and systems biology studies. Initiate collaborations 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. Collate 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.).			

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

Bullet Text (cont)	**FY2007**	**FY2008**	**FY2009**
FY 09 - Validate knowledge on common biomarkers for broad classes of Pathogenic Agents beyond intracellular bacterial pathogens hemorrhagic fever viruses. Continue to follow a systematic/problem solving approach towards the broad-spectrum development effort by mining advances in genomics, proteomics and systems biology studies and applying them to pathogen science; host response systems biology; adaptive technology to speed drug approval process; and next generation break-through technology. Pursue promising intervention points for broad-spectrum therapeutic approaches. 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. Continue to collate knowledge of host cellular response patterns that have been compromised by pathogen-directed shifts in pathways. Continue to mine advances in genomics, proteomics and systems biology studies.	32273	22510	6211
Total	**32273**	**22510**	**6211**

	FY 2007	**FY 2008**	**FY 2009**
Diagnostics	7541	4875	3210

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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**

Accomplishments/Planned Program	FY2007	FY2008	FY2009
Diagnostic Technologies - FY 07 - Expanded assay design for nucleic acid and immunoassays to additional agents/targets. Continued to improve sensitivity and specificity of existing assays, as new genomic data and techniques became available. Directed research towards increasing sample concentration and extending pathogen viability prior to nucleic acid testing. Collated/analyzed microarray data on host response to immunization from biowarfare vaccine recipients and made recommendations for follow-on studies. Directed research towards development of a microfluidic card to automate sample preparation. Investigated surface amplification methods to enhance microarray sensitivity. Investigated novel method to produce improved immunodiagnostic reagents. FY 08 - Explore new avenues for assay design and application, focusing on those that enhance sensitivity and specificity. Validate microfluidic card to automate sample preparation. Optimize surface amplification methods for selected microarrays. Accelerate development of a novel method to produce improved immunodiagnostic reagents. Assess the applicability of novel technology platforms as new genomic techniques become available. Pursue identification of novel biomarkers identifying exposure to biological pathogens. FY 09 - Continue to seek novel avenues for assay design and application. Investigate cutting edge technologies as new genomic techniques become available. Accelerate identification of novel biomarkers of biological warfare agent (BWA) infection and apply to assay development.	7541	4875	3210
Total	**7541**	**4875**	**3210**

	FY 2007	FY 2008	FY 2009
Pretreatments	8062	2261	3339

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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

Accomplishments/Planned Program	FY2007	FY2008	FY2009
Pretreatments, Multiagent Vaccines - FY 07 - Expanded the identification of potential vaccine target antigens for multiple agents using genomics/proteomics-based high throughput approaches. Further assessed the use of novel approaches for vaccine construction and delivery including recombinant protein and/or fusion protein constructs. FY 08 - Identify conserved genes required for the survival and/or virulence of intracellular pathogens (i.e., those considered potential biological threats), that could serve as potential targets in the design of multi-agent vaccines. FY 09 - Utilize novel technologies to define target antigens for different bio-threat pathogens. Explore DNA-based vaccine formulations against multiple agents. Incorporate novel adjuvants and/or delivery systems in the design of a multi-agent vaccine.	1728	504	345
Pretreatments, Vaccine Technology Development - FY 07 - Evaluated cell-mediated immune targeting of antigens for intracellular pathogens. Investigated the T-cell response against selected target antigens (analysis of cell-mediated immune response). Continued to investigate Toll-Like Receptor (TLR) agonists and other aspects of the innate immune system for vaccine construction and enhancement. Examined multiple T-cell agonists in the induction/enhancement of immune responses against biothreat agents. FY 08 - Identify common pathogenic mechanisms to subvert TLR signaling. Explore the manipulation of TLR signaling pathways in vaccine design for enhanced immunity. FY 09 - Vaccine technology development efforts transition to Vaccine Research Support in FY 09.	2000	481	0

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

Accomplishments/Planned Program (Cont):	**FY2007**	**FY2008**	**FY2009**
Pretreatments, Vaccine Research Support - FY 07 - Explored additional intracellular pathogen target antigens using animal model systems including the use of alternative delivery platforms. Evaluated gene expression technologies for in vitro analysis of host responses to bacterial pathogens. Analyzed information in the genomics/bioinformatics database to aid in the design of unique target antigens. Conducted basic pathogenicity studies of selected biothreat agents. Continued B and T-cell epitope mapping of lead antigen candidates. Characterized in vitro correlates of immunity for biothreat agents. FY 08 - Expand evaluation of human immune response to bacterial pathogens. Continue basic pathogenicity studies of selected biothreat agents. Develop and refine in vitro correlates of immunity for vaccines under development. Identify and evaluate new target antigens for intracellular pathogens. Expand B and T cell epitope mapping to additional lead antigen candidates. FY 09 - Further conduct basic pathogenicity studies of selected biothreat agents. Develop and refine in vitro correlates of immunity for new antigen in relation to vaccines under development. Pursue the identification and evaluation of novel target antigens for intracellular pathogens by studying the innate and adaptive immune responses to pathogens. Optimize epitope mapping of lead antigen candidates.	4334	1276	2994
Total	**8062**	**2261**	**3339**

	FY 2007	**FY 2008**	**FY 2009**
Therapeutics	8854	4873	3628

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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**

Accomplishments/Planned Program	FY2007	FY2008	FY2009
Therapeutics, Viral - FY 07 - Identified host cell and viral proteins that may be susceptible to broad spectrum therapeutics. Investigated additional technologies that may integrate established and novel viral therapeutic modalities into suitable candidate therapies in humans. FY 08 - Delineate the host cell response to viral infection to enhance the current understanding of viral pathogenesis, in support of therapeutic development against orthopox, filovirus, and other category A and B viral threat agents of interest. Focus on host cell responses common to infection with multiple viral threats. FY 09 - Delineate the mechanisms of pathogenesis of conventional threats to support the progression of therapeutics to advanced development. Compare the host response of well characterized threats with that of poorly characterized category A and B threats to identify new therapeutic targets.	799	595	435

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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**

Accomplishments/Planned Program (Cont):	**FY2007**	**FY2008**	**FY2009**
Therapeutics, Toxin - FY 07 - Refined therapeutic animal models, to include in vivo model instrumentation, and its interface with the developed screening protocol for lead toxin therapeutics studies. Demonstrated clinical correlates for targeted endpoints that have been developed for in vivo models. Optimized aerosol models of disease to support toxin therapeutic development. Studied the pathogenesis associated with aerosol exposure to ricin toxin. Initiated development of a mouse model for inhalational exposure to Staphylococcal enterotoxin B (SEB) using microinstillation technology. Conducted advanced structural analysis of botulinum neurotoxin (BoNT) serotypes, focusing on catalytic sites and substrate binding. FY 08 - Continue to develop a mouse model for inhalational exposure to SEB using microinstillation technology. Initiate studies to investigate the process of intracellular targeting of BoNT, with application to the development of an intracellular assay system for evaluating potential therapeutics. Investigate the restoration of synaptic activity following neuroparalysis due to BoNT intoxication. Utilize in silico modeling techniques and in vitro and in vivo assays to provide structural and molecular data to facilitate the design and development of therapeutic countermeasures against BoNT, SEB, and ricin toxin. FY 09 - Improve in silico, in vitro, and in vivo modeling systems that will assist in defining responses to threat agent toxins. Complete development of a mouse model for inhalational exposure to SEB using microinstillation technology. Characterize the process of intracellular targeting of BoNT, and initiate intracellular assay model development. Define the cellular factors responsible for the BoNT translocation inside cells. Determine the structural requirements of potential restorative therapeutics for neuroparalysis following BoNT intoxication.	5272	3386	2540

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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

Accomplishments/Planned Program (Cont):	FY2007	FY2008	FY2009
Therapeutics, Bacterial - FY 07 - Completed development of a mouse model to study anthrax toxin function. Identified virulence factors and biochemical pathways as potential targets for therapeutic countermeasures. FY 08 - Delineate host cell response to bacterial pathogens to identify new therapeutic targets for broad spectrum therapeutics. Demonstrate and confirm the role for selected common pathways and factors in bacterial virulence. FY 09 - Characterize new potential targets for therapeutic countermeasures, focusing on those identified for poorly characterized threats.	2783	892	653
Total	**8854**	**4873**	**3628**

	FY 2007	FY 2008	FY 2009
SBIR/STTR	0	432	0

Accomplishments/Planned Program	FY2007	FY2008	FY2009
SBIR - FY 08 - Small Business Innovative Research.	0	432	0
Total	**0**	**432**	**0**

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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**

C. Other Program Funding Summary:

	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	To Compl	Total Cost
TB2 MEDICAL BIOLOGICAL DEFENSE (APPLIED RESEARCH)	93501	100935	54738	51114	50205	52457	52506	Cont	Cont
TB3 MEDICAL BIOLOGICAL DEFENSE (ATD)	87067	95527	252331	227287	128222	121096	112771	Cont	Cont

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DATE: **February 2008**

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 2007 Actual	FY 2008 Estimate	FY 2009 Estimate	FY 2010 Estimate	FY 2011 Estimate	FY 2012 Estimate	FY 2013 Estimate	Cost to Complete	Total Cost
TC1	MEDICAL CHEMICAL DEFENSE (BASIC RESEARCH)	9731	12336	12379	13003	12343	12873	13051	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 biological mechanisms and bodily 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 (Pretreatments, Diagnostics, and Therapeutics).

B. Accomplishments/Planned Program

	FY 2007	FY 2008	FY 2009
Diagnostics	140	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**

Accomplishments/Planned Program	**FY2007**	**FY2008**	**FY2009**
Diagnostic Technologies - FY 07 - Accelerated basic research experiments aimed at developing detection methods in clinical samples for metabolites, adducts and/or relevant biomarkers resulting from chemical warfare agent (CWA) exposure. Evaluated the hypothesis that analysis of hair samples can be used to verify exposure to CWA. Applied results of basic research to develop a sample extraction technique and test method to detect the presence of chemical warfare analytes from hair samples in FY 08, supported by TB2 investment.	140	0	0
Total	**140**	**0**	**0**

	FY 2007	**FY 2008**	**FY 2009**
Therapeutics	9591	12186	12379

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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**

Accomplishments/Planned Program	FY2007	FY2008	FY2009
Therapeutics, Respiratory and Systemic - FY 07 - Utilized exposure/effects models to further delineate the mechanisms of injury following chemical warfare agent exposure. Pursued additional technologies that address both the direct pulmonary injury and systemic effects of chemical warfare agents, with a focus on identifying common sites for therapy at the tissue, cellular, and sub-cellular levels of injury. Initiated research into the molecular basis of injury (pulmonary) in small (rat) and large (swine) animal models. Isolated and cultured non-commercial human lung tissue to improve upon existing human tissue models. FY 08 - Develop additional in vitro and in vivo model systems to identify new therapeutic targets, based on findings from mechanism of injury studies and focusing on common injury pathways. Investigate long term effects of pulmonary injury in large and small animal models, collecting toxicological, physiological, and biochemical data. FY 09 - Expand efforts to elucidate common injury pathways due to multiple agents and routes of exposure, to maximize application to the development of broad-based therapeutics. Establish definitive correlation between simulants and live agent effects at the molecular level.	3055	4723	4952

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

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

PROJECT: TC1

Accomplishments/Planned Program (Cont):	FY2007	FY2008	FY2009
Therapeutics, Cutaneous and Ocular -	2582	2446	2422
FY 07 - Developed animal models for cutaneous, percutaneous and ocular exposure. Optimized in vitro tissue assays with application to identifying potential therapeutic compounds. Conducted studies to correlate gene expression and histopathology of sulfur mustard exposure. Investigated the genotoxicity of agent exposure in ocular cells. Initiated toxicogenomic studies to characterize the phases of wound healing. Identified the location of dermal and sub-dermal reservoirs of chemical agents.			
FY 08 - Optimize animal models for cutaneous, percutaneous and ocular exposure. Explore novel cellular biochemical pathways as potential targets for therapeutic intervention. Maximize strategies to extend "latency" period between exposure and certain injury. Expand the study of genotoxicity of agent exposure to cutaneous cells.			
FY 09 - Extrapolate the results of genotoxicity studies to the development of cancerous conditions using the appropriate in vivo models. Investigate the effects of solvent vehicles on percutaneous transmission to normalize past, present, and future research endeavors. Investigate new tissue engineering technologies to reduce reliance on grafts.			

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

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

PROJECT: TC1

Accomplishments/Planned Program (Cont):	FY2007	FY2008	FY2009
Therapeutics, Neurologic - FY 07 - Improved molecular modeling capabilities, coupled with X-ray crystallographic analysis and site directed mutagenesis, for rational drug design of new neurologic therapeutics. Optimized in vitro and in vivo laboratory techniques that may be applied to develop neuroprotectants, anticonvulsants, and broad spectrum reactivators to reduce or prevent injury from nerve agents. Studied known mechanisms of cell death to identify potential therapeutic targets. Developed strategies for medical intervention to prevent seizures and minimize related neuronal injury in animal models. Evaluated therapeutic delivery systems targeting the central nervous system. FY 08 - Exploit data from structure activity relationship (SAR) studies to delineate commonality between agents and oximes. Delineate general mechanism of action for oxime reactivation as required to support FDA submissions for improved reactivators under the animal rule. FY 09 - Research mechanisms of action of nerve agents and therapeutic interventions using whole animal models, with a focus on data required to support FDA submissions under the animal rule. Initiate research into the development of therapeutic alternatives to atropine, with reduced impact on visual performance.	1173	1286	1291
Therapeutics, Medical Toxicology - Non Traditional Agents (NTAs) and Other Agents - FY 07 - Conducted exploratory and comparative studies of emerging non-traditional chemical nerve agents. Focused on structure, function, and mechanism of action. FY 08 - Collect mechanistic and kinetic data derived from chemical agent exposure studies. Initiate exploratory studies to determine the mode/mechanism of action of NTAs. Develop appropriate animal model systems for non-traditional modes of toxicity. FY 09 - Demonstrate the biological equivalency of NTA toxicity mechanisms across relevant species.	2781	3731	3714
Total	**9591**	**12186**	**12379**

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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 2007	FY 2008	FY 2009
SBIR/STTR	0	150	0

Accomplishments/Planned Program	FY2007	FY2008	FY2009
SBIR - FY 08 - Small Business Innovative Research.	0	150	0
Total	**0**	**150**	**0**

C. Other Program Funding Summary:

	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	To Compl	Total Cost
TC2 MEDICAL CHEMICAL DEFENSE (APPLIED RESEARCH)	29057	36627	36034	34726	33021	37927	38257	Cont	Cont
TC3 MEDICAL CHEMICAL DEFENSE (ATD)	15740	28726	26567	28961	30493	31539	31836	Cont	Cont