

UNCLASSIFIED

CBDP BUDGET ITEM JUSTIFICATION SHEET (R-2 Exhibit)	DATE February 2004
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BUDGET ACTIVITY RDT&E DEFENSE-WIDE/ BA2 - Applied Research	PE NUMBER AND TITLE 0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)
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COST (In Thousands)	FY 2003 Actual	FY 2004 Estimate	FY 2005 Estimate	FY 2006 Estimate	FY 2007 Estimate	FY 2008 Estimate	FY 2009 Estimate	Cost to Complete	Total Cost
Total Program Element (PE) Cost	170183	151372	104385	101628	88519	86004	85129	Continuing	Continuing
CB2 CHEMICAL BIOLOGICAL DEFENSE (APPLIED RESEARCH)	104232	81482	63494	66321	52802	49219	50237	Continuing	Continuing
TB2 MEDICAL BIOLOGICAL DEFENSE (APPLIED RESEARCH)	47183	47747	22622	15371	15658	16431	13113	Continuing	Continuing
TC2 MEDICAL CHEMICAL DEFENSE (APPLIED RESEARCH)	18768	22143	18269	19936	20059	20354	21779	Continuing	Continuing

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BUDGET ACTIVITY RDT&E DEFENSE-WIDE/ BA2 - Applied Research	PE NUMBER AND TITLE 0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)	
<p>A. <u>Mission Description and Budget Item Justification:</u> The use of chemical and biological weapon systems in future conflicts is an increasing threat. Funding under this PE sustains a robust program, which reduces the danger of a chemical and/or biological (CB) attack and enables U.S. forces to survive and continue operations in a CB environment. The medical program focuses on development of vaccines, pretreatment, and therapeutic drugs, and on casualty diagnosis, patient decontamination, and medical management. In the non-medical area, the emphasis is on continuing improvements in CB defense materiel, including contamination avoidance, decontamination, and protection systems. This program also provides for conduct of applied research in the areas of real-time sensing and immediate biological countermeasures. This PE also provides concept and technology demonstrations of new system concepts that will shape the development for environmental monitoring, medical surveillance, and data mining/fusion/analysis subsystems. The work in this PE is consistent with the Joint Service NBC Defense Research, Development, and Acquisition (RDA) Plan. Efforts under this PE transition to and provide risk reduction for Advanced Technology Development (PE: 0603384BP), Advanced Component Development and Prototypes (PE: 0603884BP) and System Development and Demonstration (PE: 0604384BP). This project includes non-system specific development directed toward specific military needs and therefore is correctly placed in Budget Activity 2.</p>		
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B. <u>Program Change Summary:</u>		<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
Previous President's Budget (FY 2004 PB)		173362	106451	104385
Current Biennial Budget Estimates (FY 2005)		170183	151372	104385
Total Adjustments		-3179	44921	0
a. Congressional General Reductions		0	-1629	0
b. Congressional Increases		0	46550	0
c. Reprogrammings		-347	0	0
d. SBIR/STTR Transfer		-2542	0	0
e. Other Adjustments		-290	0	0

Change Summary Explanation:

Funding: FY04 - Congressional adjustment for CBD (+\$16,500K CB2; +\$25,550K TB2; +\$4,500 TC2).

Schedule:

Technical:

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BUDGET ACTIVITY RDT&E DEFENSE-WIDE/ BA2 - Applied Research	PE NUMBER AND TITLE 0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)	PROJECT CB2
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COST (In Thousands)	FY 2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	Cost to	Total Cost
	Actual	Estimate	Estimate	Estimate	Estimate	Estimate	Estimate	Complete	
CB2 CHEMICAL BIOLOGICAL DEFENSE (APPLIED RESEARCH)	104232	81482	63494	66321	52802	49219	50237	Continuing	Continuing

A. Mission Description and Budget Item Justification:

Project CB2 CHEMICAL BIOLOGICAL DEFENSE (APPLIED RESEARCH): This project addresses the urgent need to provide all services with defensive materiel to protect individuals and groups from threat chemical-biological (CB) agents in the areas of detection, identification and warning, contamination avoidance via reconnaissance, individual and collective protection, and decontamination. The project provides for special investigations into CB defense technology to include CB threat agents, operational sciences, modeling, CB simulants, and Nuclear, Biological, Chemical (NBC) survivability. Of special interest are two Defense Technology Objectives described as follows: (1) The fate of CW agents following deposition onto natural and man-made materials found in operation environments including battlefields and air bases and (2) toxicological effects resulting from low-level exposure to CW agents, e.g., less than 0.1 ECt-50, as well as the relationships between concentration and total exposure as measured by the product of concentration and time. This project focuses on horizontal integration of CB defensive technologies across the Joint Services. The Defense Technology Objectives (DTOs) provide a means to shape the development of selected technologies within this project.

B. Accomplishments/Planned Program

	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
Detection	56557	16724	16800

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<p>FY 2003 Accomplishments:</p> <ul style="list-style-type: none"> • 4540 Stand-off Biological Aerosol Detection (DTO CB35) - Initiated construction and characterization of breadboards to demonstrate the capability to detect and discriminate between biological and non-biological agents at a concentration of 1,000 agent containing particles per liter of air (ACPLA) at a range of 1 km based on the results of the downselect and user input. • 1824 Wide Area Aerial Reconnaissance for Chemical Agents (DTO CB53) - Performed airborne phenomenology tests to adopt existing hyperspectral imaging sensors (100-Hz, 2x8 TurboFT and 0.3-Hz, 128x128 Adaptive Infrared Imaging System (AIRIS)) as next generation chemical stand-off sensors. Completed engineering designs for a 30-Hz, 64-pixel TurboFT, and a 3-Hz, 128x128 AIRIS. • 3344 Integrated CB Stand-off Detector (DTO CB49) - Conducted initial downselection of potential technologies based on market survey and user input. Downselection process involved user community as well as internal and external technical experts and included performance, logistics, platform, operational concerns, maturity, and cost factors. Downselection process determined that efforts within DTO CB35 were needed as a basis to further development of integration concepts at an acceptable risk. DTO CB49 was merged into DTO CB35 in FY04. • 1419 Biological Sample Preparation System (BSPS) for Biological Identification (DTO CB20) - Continued development of new taggant chemistry for multi-agent, multiplexing PCR assays. Conducted a feasibility analysis of what is required to make multiplex and multi-agent assays cost effective. Conducted an analysis of alternatives (AoA) based on feasibility study to design an optimized platform using multi-agent, multiplexing PCR assays. Analysis of alternatives determined that this approach was not cost effective to field. This effort was terminated at the end of FY03. 		
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<p>FY 2003 Accomplishments (Cont):</p> <ul style="list-style-type: none"> • 2736 Chemical/Biological Agent Water Monitor (DTO CB37) - Completed downselection of technology for the detection of chemical agents in potable water. Continued technology development of detection of biological agents in potable water to include sample processing and preparation. Initiated the process for a Milestone A decision, transitioned effort to Advanced Technology Development. • 3485 Point Detection, Biological Identification - Continued development of Force Discrimination Assay (FDA). Continued development and testing on automated chip-based phylogenetic analysis of biological materials. Continued development and testing of quantum dot technology for application to enhance antibody ticket technology for improved stability and sensitivity. Conducted evaluation and continued development of database for protein markers from biological agents for mass spectroscopy based systems. Evaluated the potential of aptamers as substitutes for antibodies in current platforms. • 3699 Lightweight Integrated CB Detection (DTO CB 50) - Developed and partially populated database on technological parameters for downselection criteria. Initiated an AoA to downselect best technologies to meet the requirements of the Joint Modular CB Detector. Focused on physical methodologies like optical spectroscopy and pyrolysis gas chromatography ion mobility spectroscopy to address the requirements. • 1280 Point Detection, Integrated CB - Initiated exploration of new concepts for small, combined chemical and biological sensors. Continued evaluation and development of millimeter wave spectroscopy and data fusion techniques to combine chemical and biological detection requirements. 		
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<p>FY 2003 Accomplishments (Cont):</p> <ul style="list-style-type: none"> • 1926 Polymer Based Chemical and Biological Sensors - Developed a technique for processing carbon based MEMS for use in biosensors. The carbon based MEMS are in the form of a micro-bridge array fabricated using standard integrated circuit methods to detect the presence of a biological agent through the use of low frequency resonance (i.e. vibration) of a freestanding bridge structure. • 964 Bioinformatics - Extended the CYTOSCAPE software architecture and relational databases to allow the easy manipulation of data from disparate sources in order to incorporate the higher-order information from proteomic and metabolomic data to give a holistic view of any organism. • 1923 Bio-Compact Disk Application Development - Demonstrated the feasibility of rapid, real time molecular detection and identification of a panel of biological warfare agents (BWA) on a modified compact disc system. The system will be automated, have a low unit cost, and require little training or expertise to employ. • 16966 Chem-Bio Defense Initiatives Fund - Identified proteomic biomarkers for the expansion of national database; enhanced a stand-off sensor to detect agents on surfaces; enhanced a field portable nucleic acid based biodetector; evaluated novel concepts for a lightweight, miniature chemical stand-off detector; evaluated concepts for a hand held biological agent detector; assessed novel materials for biological decontamination capabilities. • 4717 National Consortium for Countermeasures to Biological and Chemical Threats - Assessed an aptamer based high throughput sensor for rapid screening and detection of biological agents; evaluated an integrated system to detect bioterrorist events and natural epidemics; assessed the capabilities of synthetic, aptamer based antiviral vaccines; investigated novel countermeasures to selected viral diseases including encephalitis. 		
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<p>FY 2003 Accomplishments (Cont):</p> <ul style="list-style-type: none"> • 5102 Anthrax Bio Defense Technologies - Initiated development and commercialization of an inexpensive and robust hand-held sensor that can be used by military field personnel with minimal training to detect low levels of bio warfare (BW) agents. The technology is based on antibodies supported on Love Shear horizontal acoustic wave devices. Preliminary data has shown that this technology has the potential to provide biological identification at an enhanced sensitivity of 10 to 100 times over current systems, within a few minutes, in a hand-held unit. • 2632 Detection of CB Contamination on Surfaces (DTO CB52) - Performed preliminary downselection of technologies to include factors such as performance, logistics, platform, operational concerns, maturity, and cost. Initiated construction of breadboards to demonstrate the capability to detect chemical agents at a deposition of 0.5 g/m² and operationally significant biological agent contamination levels to be determined. <p>Total 56557</p> <p>FY 2004 Planned Program:</p> <ul style="list-style-type: none"> • 4901 Stand-off Biological Aerosol Detection (DTO CB35) - Complete construction and characterization of breadboards to demonstrate the capability to detect and discriminate biological and non-biological agents at a concentration of 1,000 agent containing particles per liter of air (ACPLA) at a range of 1 km. • 1634 Wide-Area Aerial Reconnaissance for Chemical Agents (DTO CB53) - Complete the development a 30-Hz frame rate, 64-pixel Fourier transform infrared (FTIR) hyperspectral imager (TurboFT). Continue the development of AIRIS. Characterize the sensor performance on the TurboFT for downselection of technology in FY06. Initiated development of off-line algorithms and signal processing techniques. 		
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<p>FY 2004 Planned Program (Cont):</p> <ul style="list-style-type: none"> • 400 Detection of CB Contamination on Surfaces (DTO CB52) - Collect data on three surfaces for four surety agents using laser enhanced Raman spectroscopy to detect the presence of the chemical agents. Effort reduced due to FY04 funding adjustments. • 4139 Point Detection, Biological Identification - Complete development and demonstration of Force Discrimination Assay (FDA). Complete development and testing automation of chip-based phylogenetic analysis of biological materials. Identify engineering/manufacturing issues for the transition of quantum dot technology to the Critical Reagent Program for application to enhance antibody ticket technology for improved stability and sensitivity. Continue development of database for protein markers from biological agents for mass spectroscopy based systems. • 1634 Lightweight Integrated CB Detection (DTO CB50) - Complete the population of the technical parameter database. Transition the analysis of alternatives to advance development for downselection for best technology to meet the requirements of the Joint Modular CB Detector. • 816 Point Detection, Integrated CB - Continue exploration of novel concepts in small, combined chemical and biological sensors. Continue development of millimeter wave spectroscopy. • 3200 Laser Induced Surface Analysis (LISA) Prototype - Construct and demonstrate a laser enhanced Raman system that can detect the presence of chemical agent on surfaces at a contamination level of 0.5 g/m² and suitable for integration into a recon vehicle to demonstrate on the move capability. <p>Total 16724</p>		
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FY 2005 Planned Program:

- 4600 Stand-off Biological Aerosol Detection (DTO CB35) - Evaluate breadboards via field testing and demonstrate the capability to detect and discriminate biological vs non-biological agents at concentration of 1,000 ACPLA at a range of 1 km. Initiate feasibility studies to integrate chemical and biological capabilities with the objective of maintaining demonstrated capabilities.
- 1500 Wide-Area Aerial Reconnaissance for Chemical Agents (DTO CB53) - Complete the development a 3-Hz, 128x128 tunable hyperspectral imager (AIRIS). Characterize the sensor performance of the AIRIS for technology downselection in FY06. Complete off-line algorithms and signal processing techniques.
- 4500 Detection of CB Contamination on Surfaces (DTO CB52) - Reinitiate breadboard construction and characterization due to FY04 funding adjustments. Initiate feasibility studies to determine the ability to detect biological agents on surfaces.
- 2700 Point Detection, Integrated CB - Complete exploration of novel, small, chemical and biological sensors. Initiate exploration and concept development for new concepts for small, combined chemical and biological identifiers. Conduct feasibility studies and perform a cost benefit analysis on "low consumable or reagentless" concepts. Complete first generation breadboard based on millimeter wave spectroscopy.
- 3500 Point Detection, Biological Identification - Initiate development of micro-array concepts to meet high throughput and reduce logistical burden on biological identification requirements. Complete mass spectroscopy database development and transition to advanced technology development to populate database to extend biological material information.

Total 16800

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	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
Protection	10123	5262	7928

FY 2003 Accomplishments:

- 912 End-of-Service-Life Indicators (ESLI) for NBC Mask Filters (DTO CB36) - Completed baseline evaluations of candidate technologies. Performed analysis of battlefield interferences. Conducted a value-added analysis to assess benefits of the ESLI to the warfighter. Downselected to top three candidate technologies. Fabricated and evaluated ESLI/filter concept models. Optimized baseline design and determine optimum ESLI location.
- 1520 Self-Detoxifying Materials for Clothing Applications (DTO CB45) - Continued to assess new reactive compounds and treatments for improved detoxification in membranes. Developed concepts for nanoreactors and surface-migrating phases for improved agent breakdown within membranes and coatings. Selected relevant reactive nanoparticles and polymeric materials for subsequent processing and testing studies. Characterized the reaction kinetics and loading capacity of N-halamines treated materials with CWA simulants.

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FY 2003 Accomplishments (Cont):

- 2027 Collective Protection, Filtration - Completing database and model of adsorption equilibrium and rate processes for high priority TICs. Optimized candidate adsorbents for use in regenerative filtration applications that are effective against a wide spectrum of TIC and Chemical Warfare Agents (CWA). Completed development of initial pressure, temperature, and electrical swing adsorption (P/T/E/SA) regeneration models and fabrication of test stands. Completing proof of principle testing and evaluation of 50 CFM pressure temperature swing adsorption filter to validate model. Completing evaluation of electrostatic and biocidal filter enhancement for aerosol and particulate capture and deactivation. Evaluated degradation effects of TICs on HEPA filters and proposed mitigation concepts. Completed initial literature review for developing hybrid air purification systems incorporating technologies providing broad protection. Finished trade study assessing feasibility and application of open and closed circuit air supply and rebreather technologies. Completed chemical and physical residual life indicators (RLI) sensor testing and developed RLI prototype concept.

- 1135 Collective Protection, Shelters - Continued development and evaluation of advanced CB shelter materials (shell, support, airlocks, liner, seams, and seals). Two new hermetic seals for shelters were fabricated and tested. Four new CB shell materials were developed to include constructed shelter systems. Completed initial computational fluid dynamic modeling of one airlock system. Continuing development and testing of chemistries for self decontaminating shelter materials. Completed initial assessment and modeling of shelter materials failure mechanisms to conventional weapons blast pressure effects and proposed transition to JCPE.

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FY 2003 Accomplishments (Cont):

- 1393 Individual Protection, Clothing - Completed testing of fielded and developmental protective garment materials to evaluate their effectiveness against TICs, and to provide recommendations to the user community. Characterized the surface phenomena occurring in ion implanted polymers and determined the transport properties of moisture and chemicals of those polymers. Completed transport and physical characterization of selected candidate permselective membranes, and initiated detailed analysis of structure property relationships. Optimized materials and material treatment solutions for overgarments to improve protection against NTA aerosols. Identified sampling techniques and assessed clothing air velocities as an initial step in evaluating the effects of atmospheric temperature and wind on agent penetration of IPE. Validated recent research which indicates that intermittent cooling to various body regions can provide as much cooling benefit (in terms of core temperature reduction) as cooling continuously, but at a fraction of the MCS capacity. Inadequate funding to continue development of this area during FY04. Funding to resume in FY05.

- 1216 Advanced Adsorbents for Protection Applications (DTO CB08) - Completed database and model of adsorption equilibrium and rate processes for four agent classes. Identified adsorbent bed compositions that provide the level of protection required by the JSGPM, JCPE, and JTCOPS programs for all CW agents and the highest priority toxic industrial chemicals (TICs). For single pass applications several adsorbent compositions were transitioned to Joint Program Manager for Individual Protection for use in the JSGPM and for regenerative applications several proposed bed compositions were identified for full spectrum protection capability (light to heavy TIC/CWA).

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FY 2003 Accomplishments (Cont):

- 1920 Individual Protection, Masks - Initiated development of advanced mask concepts focusing on lightweight system integration, a wider range of protection, and reduced thermal load. Assembled advanced mask concept prototypes for preliminary human factor studies. Initiated optimization of candidate sorbent media structures by the testing of media properties and the modification of that media to improve performance. Optimized candidate lens materials through the evaluation of chemical and physical properties and the modification of that material to enhance performance. Developed and evaluated new and improved mask technologies to improve protection through novel sealing and pressurization options. Identified appropriate aerosol generation and detection equipment, developed and validated test procedures.

Total 10123

FY 2004 Planned Program:

- 850 Collective Protection, Shelters - Continue development and testing of advanced CB shelter materials and prototype shelter system components (shell, liner, support, airlocks, seams and seals). Identify and test optimal chemistries for self decontaminating shelter materials and applications. Conduct airflow modeling of airlock and contamination control area configurations to optimize designs to reduce dwell time, increase entry/exit rate, and facilitate dual entry and exit of personnel, patients and supplies.
- 900 End-of-Service-Life Indicators for NBC Mask Filters (DTO CB36) - Fabricate and conduct demonstration testing of ESLI filter concept models to verify ESLI is a reliable indicator of gas life depletion for key target agents (i.e., GB, HD, CK, AC and CG). Assessments will include determining the effects of common environmental factors (heat and humidity) that may impact ESLI performance and evaluating the effects of long term storage.

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<p>FY 2004 Planned Program (Cont):</p> <ul style="list-style-type: none"> • 1500 Self-Detoxifying Materials for Chemical/Biological Protective Clothing (DTO CB45) - Demonstrate ability to produce materials employing self detoxification chemistries for G-agents, VX, and HD by commercial electrospinning. Demonstrate improved reactivities for hyperbranched surface migrating compounds. Demonstrate agent deactivation chemistry of fiber bound catalysts through solution and vapor challenge testing for a target reactivity level of 2 mg agent/cm²/day. Demonstrate effectiveness of scaled up N-halamine treated materials against significant biological. Demonstrate nanoparticle reactivities in excess of 2 mg agent/cm²/day in both fiber and coating form. Downselect most reactive, cost effective nanoparticle compositions and optimize those materials for reactivity rates and range of materials they detoxify • 522 Individual Protection, Masks - Refine advanced mask system concepts using actual technologies to the maximum extent possible. Optimize candidate mask sealing options and assess antifogging and moisture control technologies. Prepare human use bio-aerosol protection factor assessment protocol, establish and validate test procedures, and conduct human PF study with monodisperse inert aerosols. • 890 Advanced Adsorbents for Protection Applications (DTO CB08) - Complete validation of single-pass and regenerative filtration adsorption models. Complete performance verification of adsorbents for use in NBC filtration systems with emphasis on regenerative materials. Selected adsorbent beds will undergo performance verification testing to fully assess the performance constraints expected in the host filter system. These evaluations will consider adsorbent bed performance under a wide range of agent challenge concentration scenarios and environmental conditions. Selection of the best adsorbent bed composition for regenerative filtration application will be made. If temperature swing adsorption and pressure swing adsorption are both considered viable regenerative filter technologies, at least two different adsorbent bed compositions will be selected. 		
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FY 2004 Planned Program (Cont):

- 600 Collective Protection, Filtration - Characterize constraints of mature candidate adsorbent compositions against a wide range of TIC and CWA including aging, chemical reaction regeneration cycles, relative humidity, temperature, and material compatibility. Optimize regenerative process (including, temperature, pressure, ECS, cycle time) using verified candidate adsorbent materials. This task will mature the technology for future consideration as an advanced technology demonstrator. Complete literature review and database of unit processes for developing hybrid air purification systems. Downselect anti-microbial aerosol/particulate filter media, complete initial testing and develop enhanced prototype.

Total 5262

FY 2005 Planned Program:

- 800 End-of-Service-Life Indicators for NBC Mask Filters (DTO CB36) - Assess the effects of common battlespace interferences on ESLI performance. Optimize ESLI design and complete demonstration testing on ESLI filter prototype(s). Investigate new indicators (or optimize existing indicators as required) to detect sorbent depleting battlefield contaminants., or optimize existing indicators as required, to detect sorbent depleting battlefield contaminants.
- 1200 Advanced Air Purification System Model (DTO CB61) - Develop model for hybrid air purification systems that incorporate mature unit processes for the purpose of providing broader protection than current single pass filter technology. Develop a matrix model for hybrid air purification systems that can address wide application requirements by providing the optimal mix of technologies.

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FY 2005 Planned Program (Cont):

- 1528 Individual Protection, Clothing - Optimize ion implantation conditions for maximum permselectivity and demonstrate optimized membranes. Complete analysis of membrane structure property relationships, optimize the most promising membranes, evaluate the properties of modified membranes, and produce and evaluate fabric systems which include the optimized membranes. Investigate selectively permeable membranes and new reactive membranes for addressing NTA aerosols, and conduct agent testing of optimized NTA protective systems. Develop swatch test technology for assessing role of wind speed, temperature in challenge penetration of individual protection equipment. Initiate development of advanced ensemble closure technologies to reduce/prevent aerosol penetration. Identify thermal management technologies for protective ensemble applications.
- 1000 Collective Protection, Shelters - Continue development and testing of advanced CB shelter materials and prototype shelter systems (shell, liner, support, airlocks, seams, seals and self decontaminating materials). Perform testing of shelter components incorporating self decontaminating materials.
- 300 Collective Protection, Filtration - Characterize and optimize performance of advance aerosol/particulate removal processes providing enhanced protection. Develop regenerative filtration advanced technology demonstrator.

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<p>FY 2005 Planned Program (Cont):</p> <ul style="list-style-type: none"> • 1400 Self-Detoxifying Materials for Chemical/Biological Protective Clothing (DTO CB45) - Demonstrate reactivity stability to realistic time, temperature, and use conditions. Optimize materials and processing conditions for reactive fibers/membranes. Improve durability and overall cost effectiveness of scaled up electrospun self detoxifying membranes, N-halamine treated textiles, and materials containing reactive nanoparticles. Downselect reactive particles and processing approach for fibers/membranes. Select materials from DTO and related projects (DARPA SBIR, congressional program) for the development of prototype garments. Measure chemical/aerosol breakthrough of candidate fabrics. Measure durability and effectiveness of candidate fabrics from all sources. Conduct toxicology and live agent testing of manufactured fabrics. Optimize/downselect fabric design from agent and durability testing. • 1700 Individual Protection, Masks - Develop advanced mask system prototypes using enhanced technologies to the maximum extent possible. Continue optimization of candidate sorbent media structures by testing of the properties of the media and modification of that media to improve performance. Continue optimization of candidate lens materials through the evaluation of chemical and physical properties and the modification of that material to enhance performance. Develop at least three technology concepts by integrating best option technologies and conduct both laboratory and human factors evaluations. Establish and validate bio-aerosol protection factor assessment test procedures, and conduct human PF study with polydisperse inert aerosols. <p>Total 7928</p>		
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	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
Decontamination	5884	3150	3400

FY 2003 Accomplishments:

- 2100 Decontamination, Oxidative Decontamination Formulation (DTO CB44) - Conducted contact hazard and off gas testing on coupons and initiated material compatibility testing for the peroxy carbonate decontamination solution. Optimized formulations using the peracid approach and conducted live agent testing. Integrated other oxidative approaches into the DTO. Developed concepts for delivery of multi-component liquid and solid decontaminants.
- 1400 Decontamination, Sensitive Equipment - Completed feasibility studies for interior decontamination technology solutions for JSSSED using plasma technology approaches. Developed a man portable approach for the cleaning of small sensitive surfaces based upon reactive sorbents in solvent suspensions.
- 1520 Decontamination, Solution Chemistry - Completed evaluation of multi-enzyme decontamination system for G, V and H class agents.
- 864 Decontamination, Solid Phase Chemistry - Completed evaluation of novel solid and sorbent decontamination applications using nanoscale metal oxides, zeolites and solid phase reduction/oxidation couples.

Total 5884

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BUDGET ACTIVITY RDT&E DEFENSE-WIDE/ BA2 - Applied Research	PE NUMBER AND TITLE 0602384BP CHEMICAL/BIOLOGICAL DEFENSE (APPLIED RESEARCH)	PROJECT CB2
FY 2004 Planned Program:		
<ul style="list-style-type: none"> • 1905 Decontamination - Oxidative Formulation (DTO CB44) - Initiate chamber testing over operational temperature range, finish material compatibility testing and formulate peroxy carbonate and peracid candidates into a dry powder and/or concentrated liquid. Finalize formulation of newly added oxidative approaches and conduct material compatibility and agent testing. • 720 Decontamination, Sensitive Equipment - Complete evaluation of man portable approaches for the cleaning of small sensitive surfaces for use in the interior of vehicles and aircraft. • 525 Decontamination, Solid Phase Chemistry - Initiate evaluation of oxidatively enhanced nanoparticles as reactive sorbents for both chemical and biological agent decontamination. 		
Total 3150		
FY 2005 Planned Program:		
<ul style="list-style-type: none"> • 800 Decontamination, Solid Phase Chemistry - Assess new materials being investigated under basic research programs for potential use and transition as reactive and sacrificial coatings. Evaluate oxidatively enhanced reactive nanoparticles and initiate testing of novel nanocrystalline zeolites. • 300 Decontamination, Sensitive Equipment - Assess immature technologies as identified in market surveys and the analysis of alternatives for potential JSSED product improvements. • 2300 Decontamination - Oxidative Formulation (DTO CB44) - Complete chamber testing over operational temperature range, finish material compatibility testing, and formulate new oxidative approaches into a dry powder and/or concentrated liquid. 		
Total 3400		
<div style="display: flex; justify-content: space-between;"> Project CB2/Line No: 015 Page 20 of 64 Pages Exhibit R-2a (PE 0602384BP) </div>		

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	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
Supporting Science and Technology	17651	21937	27366

FY 2003 Accomplishments:

- 2790 Aerosol Technology - Fabricated and tested novel high efficiency aerosol inlet brassboard. Designed and fabricated first breadboards of novel aerosol collectors and concentrators for low temperature, low power, and full particle size range operation. Initiated computational fluid dynamics (CFD) studies to assess and improve performance of various aerosol collector and concentrator devices of military interest. Characterized performance of a variety of novel design and developmental aerosol collectors in aerosol chambers and wind tunnels. Developed novel aerosol generation device for high air speed testing. Initiated construction of enhanced lidar aerosol test cell. Fabricated and tested automated ink jet aerosol generator.

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<p>FY 2003 Accomplishments (Cont):</p> <ul style="list-style-type: none"> • 3955 Threat Agents and Simulants - Interfaced with intelligence community to determine synthesis targets. Continued to fill data gaps relative to physical properties of conventional and novel chemical threat agents. Continued to develop quantum chemical methods to discover novel synthesis routes for chemicals of interest. Interfaced with intelligence community to focus investigations of biological agents and stimulants of concern. Novel preparations of spores from stimulants, non-pathogenic and pathogenic anthrax were implemented. Size of multiple bacillus species was measured. Determined the fluorescence spectrum of seven different bacillus spores. Initiated TEM analysis of Yersinia species. Evaluated sporocidal activity of three military decontaminants on non-pathogenic and pathogenic anthrax on two surfaces of military interest. Initiated integration of data produced in this project with ASK Biological Database. Measured size distributions of several Bacillus species. Developed design for modifying Eh outer membrane protein using molecular genetic techniques. Demonstrated that antigens giving rise to bands in Western blot analysis are also present in cell wall preps from E. coli. Identified two cross-reaching proteins (E. coli and Eh) by N-terminal sequencing as outer membrane proteins. Identified additional CB stimulant and agent data requirements and data. ASK v2.1 reviewed for accuracy and software updated. ASK v2.0 User's Manual and help files were completed. Continued outreach program to maintain awareness of activities at other sites. Continued efforts to identify biosimulant needs of the RDT&E user community. Identified monoclonal antibodies for six antigenic targets against a 12-mer peptide library expressed in E. coli. • 5067 Low Level Operational Toxicology Studies - Completed inhalation data sets to define longer time, lower level operational effects for sarin (GB) in swine and a second generation agent (GF) in rats. Developed a valid marker (dosimetric) for nerve agent exposure suitable for predicting agent effects across species to refine operational human health risk assessment. 		
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<p>FY 2003 Accomplishments (Cont):</p> <ul style="list-style-type: none"> • 1516 Predictive Modeling - Agent Fate (DTO CB42) - Fielded Phase I Chemical Hazard Estimation Methodology and Risk Assessment Tool. (CHEMRAT). Constructed two tools for simulating and assessing the evaporation of toxic liquids from contaminated surfaces. Developed a surface evaporation assessment tool to evaluate methodologies and compare with actual agent test results. Completed a VLSTRACK sensitivity analysis. Completed a surface evaporation database, which includes 26,115 field trials and data for coated surfaces and other military materials. • 924 Methodology Development - Agent Fate (DTO CB42) - Determined VX fate (reaction kinetics) on/within concrete by nuclear magnetic resonance (NMR) methods. Developed methodology for varying humidity and temperature by NMR with simulants. Optimized and validated the head space solid phase micro extraction (HS-SPME) method for analyzing chemical warfare agents on surfaces. Completed HS-SPME measurements of VX on concrete, asphalt, and soil at multiple temperatures. • 1246 Lab-Scale Wind Tunnel Studies - Agent Fate (DTO CB42) - Focused technical efforts on building and validating lab wind tunnels for agent surface evaporation testing. Three levels/scales of laboratory apparatus have been characterized and proven out for agent fate testing. Measured surface evaporation of HD on glass in field and lab scale testing. Characterized properties affecting surface evaporation, i.e., spread factors, porosity, etc. • 1554 Large-Scale Wind Tunnel Studies - Agent Fate (DTO CB42) - Developed Agent Wind Tunnel Test Matrix for three agents (GD, HD, and VX) plus thickened variants, four substrates (asphalt, concrete, grass, sand), and three levels of temperature, relative humidity, wind speed, and droplet size. Defined statistically optimized test schedule of 62 experiments for each agent/surface combination. Validated mid scale lab wind tunnel for agent surface evaporation testing in Czech Republic and correlated with work in U.S. 		
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<p>FY 2003 Accomplishments (Cont):</p> <ul style="list-style-type: none"> 599 Environmental Fate of Agents - Conducted Phase 2 of the literature survey and analysis effort. A matrix of planned number of tests versus agent and substrate for laboratory, wind tunnel, and open-air scales was completed. Techniques for formulation and dispersal of thickened agent was established and documented. The surface evaporation database was completed to include data found by the literature search. Laboratory studies, wind tunnel tests, and field trials for live agents was performed and documented. Data addressed rates of evaporation, ad/absorption, desorption, decay, and droplet spread; chemical adsorption effects on equilibrium; and contact transfer as a function of time. A baseline improved surface evaporation inhalation and contact hazard module was developed. CHEMRAT used the baseline model and new threat scenarios. <p>Total 17651</p> <p>FY 2004 Planned Program:</p> <ul style="list-style-type: none"> 2859 Aerosol Technology - Experimentally and by CFD analysis, initiate investigations of inlets to facilitate aerosol collection in high air speed conditions. Continue experimental and CFD studies of microHEPA, electrostatic collector, mini-slit and other low power aerosol collection devices. Fabricate and test breadboard aerosol collector capable of low temperature operation. Characterize and evaluate emerging collectors and collection technology. Develop new aerosol generation and analysis techniques including methodology development to generate suitable chemical simulant aerosol challenges. Complete enhanced lidar aerosol test cell to support stand-off detection tests. Continue development of new methodology for quantifying biological aerosols captured in collector/concentrator characterization experiments. 		
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<p>FY 2004 Planned Program (Cont):</p> <ul style="list-style-type: none"> • 2756 Threat Agents and Simulants - Continue efforts to determine and validate new synthesis targets. Discontinue quantum chemistry research due to funding reductions. Continue to fill data gaps relative to classical and novel threat agents, toxic industrial chemicals, and CWA simulants. Complete investigations of physical and decontamination properties of B. anthracis. Investigate physical properties and decontamination properties of E. herbicola and baculovirus. Continue update of classified ASK databases and provide to CBIAC when completed. Continue effort to identify and validate non-pathogenic antigen mimics. Complete methodology development for assessing inhalation toxicity of non-traditional agents. • 5600 Low Level Operational Toxicology Studies (DTO CB51) - Complete initial inhalation studies for the nerve agents GF and VX. Deliver a refined operational human health risk assessment for those agents suitable for integration into Operational Risk Management processes used by commanders in military settings. Evaluate the utility of diverse non-human data for extrapolation to human conditions based on a common dosimetric. • 1690 Predictive Modeling - Agent Fate (DTO CB42) - Develop evaporation and liquid contact models and integrate into the Joint Effects Model (JEM). Expand surface evaporation database to include all agent/simulant data from large area surfaces and continually add data generated from the Agent Fate program. Expand the features and accuracy of CHEMRAT by including current data from the Agent Fate program to support Operation Iraqi Freedom and future military operations. Calibrate VLSTRACK by adjusting parameters relevant to secondary evaporation to provide better vapor hazard and liquid persistence estimates. Enhance SRFSIM and SURFIT assessment tools by including secondary evaporation methodology from the Hazard Prediction Assessment Capability model (HPAC). Perform sensitivity analysis of HPAC 4.0.3 secondary evaporation methodology. 		
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FY 2004 Planned Program (Cont):

- 1060 Methodology Development - Agent Fate (DTO CB42) - Determine degradation products of agents on surfaces of interest such as concrete. Using HS-SPME, measure and correlate VX, GD, and HD on Czech concrete vs. NIST standard concrete. Using HS-SPME, measure VX, GD, and HD on asphalt, soil and metal/glass at three humidity levels and compare single vs. multiple droplets surface contamination. Initiate HS-SPME measurements of NTAs. Initiate soil methodology development and determine sorption and fate of GD on dry sand and its response to simulated rainfall. Determine the fate of RVX, NTA, and HD on concrete by NMR and add GD if schedule allows.
- 2255 Lab-Scale Wind Tunnel Studies - Agent Fate (DTO CB42) - Measure surface evaporation of HD and GD on asphalt in lab wind tunnels. Measure surface evaporation of HD and VX on concrete in lab wind tunnels. Initiate investigations of VX and NTAs on asphalt.
- 2075 Large-Scale Wind Tunnel Studies - Agent Fate (DTO CB42) - Initiate surface evaporation of thickened GD, VX, and HD on concrete and asphalt. Complete fabrication and certification of large scale wind tunnel in the UK. Field Testing Methodology will be reviewed to prepare for resumption of outdoor testing in FY05. Continue wind tunnel testing of HD, GD, and VX on asphalt, sand, and vegetation.

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FY 2004 Planned Program (Cont):

- 1642 Threat Agents - Continue to synthesize small quantities for defensive RDT&E, toxicologically screen, and characterize identified new threat materials and fill identified data gaps for established chemical and biological threat agents. Continue to characterize fundamental properties of *Y. pestis*. Continue characterization of fundamental properties of a viral family and initiate characterization on a second viral family selected by biodefense priorities. Complete validation studies on simulant BG spores and continue improvement of *Erwinia herbicola* antigenicity, exploration of novel "peptide-based" bio simulants, and research on a new viral simulant. Continue development of an agent simulant knowledge base technical information system with emphasis on completion of environmental database and initiate the collection and quality assessment of classified and incapacitating agent data. Load bioinformatics database with fundamental non-medical properties.
- 2000 Biological Agent Fate - Initiate an accelerated all-source compilation and analysis of existing literature data that addresses the persistence (viability) of biological warfare agents released into the operational environment. Conduct a state of current research expert workshop in conjunction with NATO/allied investigators to document research efforts in the fate of biological agents. Deliver a documented assessment of identified data gaps and produce a targeted Defense Technology Objective (DTO) research program.

Total 21937

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<p>FY 2005 Planned Program:</p> <ul style="list-style-type: none"> • 3040 Threat Agents and Simulants - Continue and expand efforts to determine and validate new synthesis targets. Continue to fill data gaps relative to classical and novel threat agents, toxic industrial chemicals, and CWA simulants. Investigate physical properties and decontamination properties of <i>B. mallei</i> and baculovirus. Complete effort to identify and validate non-pathogenic antigen mimics. • 1670 Threat Agents - Continue to synthesize small quantities for defensive RDT&E, toxicologically screen, and characterize identified new threat materials and fill identified data gaps for established chemical and biological threat agents. Continue to characterize fundamental properties of <i>Y. pestis</i> and initiate work on <i>B. mallei</i>. Complete characterization of fundamental properties of a viral family and continue characterization of a second viral family selected by biodefense priorities. Complete improvement of <i>Erwinia herbicola</i> antigenicity, and continue exploration of novel "peptide-based" bio simulants and research on a new viral simulant. Continue upgrading the data in the agent/simulant knowledge base technical information system and initiate the collection and quality assessment of toxicology data. • 2119 Aerosol Technology - Continue investigations of approaches to advanced inlets for aerosol collection in high air speed conditions. Continue experimental and CFD studies of microHEPA, electrostatic collector, impeller, mini-slit, and other low power aerosol collection devices. Continue characterization of emerging collectors and collection technology. Upgrade existing chambers and wind tunnels. Continue evaluations of new and prototype chemical detectors using chemical simulant aerosols. Initiate CFD modeling for the windbreak approach of sampling omnidirectionally from high speed flows. 		
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<p>FY 2005 Planned Program (Cont):</p> <ul style="list-style-type: none"> • 1668 Biological Agent Fate - Initiate a targeted Defense Technology Objective (DTO) research program that corrects deficiencies in the understanding of the persistence (viability) of biological warfare agents intentionally released into operational environments. Multiple media, such as food and water deliveries, as well as concerns for interior surfaces as identified by the DoD Joint Requirements Office will be included in this effort. • 1324 Methodology Development - Agent Fate (DTO CB42) - Determine degradation products of agents on surfaces of interest such as concrete. Examine the fate of VX, GD and NTA on asphalt by NMR. Examine the fate of V analogs, NTAs and thickened agents on surfaces under different temperature and humidity conditions by HS-SPME. Determine sorption and fate of VX on sand and clay soil. Determine sorption and fate of GD and VX on assembled test soil. • 3180 Predictive Modeling - Agent Fate (DTO CB42) - Evaluate Agent Fate secondary evaporation model versus the VLSTRACK module and evaluate each with agent field trials to determine accuracy of downwind vapor predictions. Tune model/module and integrate into JEM. Transition effort to JEM Program Office. Continue to work the scaling of agent vapor concentrations from laboratory to outdoor test conditions. Continue CHEMRAT update with new agent fate test data. Continue to update secondary evaporation model with new agent fate test data and incorporate into JEM. • 4490 Lab-Scale Tunnel Studies - Agent Fate (DTO CB42) - Initiate surface residual agent testing to determine contact hazard. Complete surface evaporation tests of VX and NTAs on asphalt. Measure surface evaporation of thickened HD, GD and VX on asphalt and concrete. 		
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FY 2005 Planned Program (Cont):

- 4375 Large-Scale Wind Tunnel Studies - Agent Fate (DTO CB42) - Develop methodology to correlate lab scale to large scale and outdoor test results. Design and conduct validation tests of surface evaporation model for agents on concrete.
- 5500 Low Level Operational Toxicology Studies - Complete cross-validation studies, based on a validated dosimetric, for exposure route comparison that refine operational human health risk assessments for exposure to the nerve agents. Extend the useful range of prediction out in time for inhalation exposures to GF expected in various military response settings. Initiate VX studies that extend time-effect predictive capability.

Total 27366

	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
Information Technology Systems	6313	7010	8000

FY 2003 Accomplishments:

- 1216 Planning, Training and Analysis - Demonstrated HLA application of hazard models. Conducted statistical analysis of results of agent toxicity load variation in several hazard prediction models for fixed site application.

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FY 2003 Accomplishments (Cont):

- 1682 Environment (DTO CB55) - Improved next-generation model (MESO) to include wet biological modifications, improved accuracy over rough terrain, and further improvements to boundary layer atmospheric physics. Evaluated performance of computational fluid dynamics model (CBW-CFX) on ships and fixed land structures and identify areas for improvement. Demonstrated performance of coupled weather/CBW dispersion model. Evaluated performance of hazard evolution codes updated by agent environmental effects data.
- 674 Chemical and Biological Warfare Effects on Operations (DTO CB43) - Completed initial operational capability of Aerial Port of Debarkation (APOD) module. Conducted independent validation and verification (V&V) of fighter base module. Initiated development and testing of Sea Port of Debarkation (SPOD) module.
- 1424 Simulation Based Acquisition - Initiated testing of prototyping models against highest priority CBD objects. Developed and demonstrated a breadboard virtual prototype system.
- 1317 Battle Management - Expanded studies to address data fusion approaches for multiple sensors. Assessed value added at system-level (multiple networked CB sensors and non-CB sensors) through modeling and demonstration. Initiated examination of methods to improve real-time, network-aided decision making, and visualization of network responses.

Total 6313

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FY 2004 Planned Program:

- 2110 Battle Management - Initiate efforts to optimize data fusion and decision-making across networks and to provide visualization of network sensor responses under the auspices of Joint Warning and Reporting Network (JWARN) program requirements in concert with the C4ISR architecture.
- 1890 Planning, Training and Analysis - Test and finalize APOD and SPOD representation. Define Contamination Avoidance for Seaports of Debarkation (CASPOD) data requirements. Populate SPOD representation. Support Joint Operational Effects Federation (JOEF) Block I demonstration. Perform independent validation and verification on core model.
- 1800 Chemical and Biological Hazard Environment Prediction (DTO CB55) - Transition advanced predictive capabilities (MESO) to JEM Block II program. Further enhance the complex terrain and flow around structures modeling capability to address effects of vegetation and surface scavenging. Investigate availability of high altitude disbursement model in support of JEM Block II.
- 1210 Simulation Based Acquisition - Develop support tools for future acquisition decisions that would emerge from a study of CBDP requirements. Identify user base from within the CBDP. Begin prototype tool design efforts.

Total 7010

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FY 2005 Planned Program:

- 1500 Chemical and Biological Hazard Environment Prediction (DTO CB55) - Enhance the complex terrain and flow around structures modeling capability to address variable surface characterization and solar effects on agent evaporation. Perform code optimization and validation of the complex terrain and flow around structures tools.
- 1000 Simulation Based Acquisition - Complete tool design and begin prototype construction and testing. Use iterative user-focused design techniques to enhance tool usability and acceptance.
- 3250 Battle Management - Continue efforts to optimize data fusion and decision-making across networks and to provide visualization of network sensor responses within the current and planned C4ISR architecture.
- 2250 Chemical and Biological Warfare Effects on Operations (DTO CB43) - Test and finalize toward JOEF Block II transition. Develop Marine Expeditionary Force HQ, depot, and railhead modules. Perform internal V&V. Prepare for external V&V by PM.

Total 8000

	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
Applied Research	7704	26011	0

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<p>FY 2003 Accomplishments:</p> <ul style="list-style-type: none"> • 2889 Countermeasures to Biological and Chemical Threats - Continued studies of combinative toxicity of biological toxin mixtures. Continued study into mechanisms of cell death. Successfully performed initial tests of selenium based antibiotic and anti-viral compounds. Continued with successful development of non-woven materials for use in decontamination suits. Continued modeling of biological dispersion in buildings and cities. Continued studies of natural mechanisms of ricin breakdown. Continued development of an ultraviolet visible based miniature diode detector for chemical and biological agents. • 3851 Air Purification Collective and Individual Protection - Developed and evaluated filter material formulations for efficacy against biological threat agents. • 964 Air Contaminant Monitoring System - Employed novel networking technologies to link environmental air quality monitoring sensors to determine feasibility to detect, track and respond to an intentional chemical warfare agent release in an urban and suburban setting. <p>Total 7704</p> <p>FY 2004 Planned Program:</p> <ul style="list-style-type: none"> • 990 Automated Lipid Phase Detection of Toxic Compounds - Automated lipid phase detection of toxic compounds program is being baselined. • 2078 Bioinformatics - Continue creating tailored approaches to extract and rapidly analyze biological data to enhance the study of chemical and biological threat agent effects. 		
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<p>FY 2004 Planned Program (Cont):</p> <ul style="list-style-type: none"> • 1385 Bioinformatics Network - Create linkages which interactively approach the extraction of rapid analysis of biological data. • 1039 Bioinformatics Equipment - Explore technologies for bioinformatics equipment. • 990 Early Warning and Detection Program - Explore technologies for early warning and detection. • 5439 LSH-SAW Biosensor - Investigate acoustic wave technology for biosensors. • 2374 Detection of Chemical, Biological and Pollutant Agents in Water - Continue technology development to detect CB and pollutant agents in potable water sources. • 990 Air Containment Monitoring System - Continue development of systems for contained air monitoring for chemical agents. • 990 Atmospheric Plasma for Bio Defense Decon - Investigate technologies for atmospheric plasma for biological defense decontamination. • 1236 Rapid Decontamination System for Nerve Agents - Explore technologies for rapid decontamination system for nerve agents. • 990 Remote Optical Sensing Program - Explore technologies for remote optical sensing. • 3462 Consortium for Countermeasures for Biological Threats - Develop multiple technologies and implementations to counter the threat of attack using biological threat agents against civilian and military populations. • 2078 Center for Information Assurance Security - Investigate technologies for information assurance security. • 983 GMU Center for Bio Defense - George Mason University Center for biological defense program being baselined. 		
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FY 2004 Planned Program (Cont):

- 987 Long Range Biometric Target ID System - Explore technologies for a long range biometric target identification system.

Total 26011

	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
SBIR/STTR	0	1388	0

FY 2004 Planned Program:

- 1388 SBIR - Small Business Innovative Research

Total 1388

C. Other Program Funding Summary:

	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>	<u>FY 2006</u>	<u>FY 2007</u>	<u>FY 2008</u>	<u>FY 2009</u>	<u>To Compl</u>	<u>Total Cost</u>
CB3 CHEMICAL BIOLOGICAL DEFENSE (ATD)	46712	93505	40527	25836	30838	31309	31957	Cont	Cont
CP3 COUNTERPROLIFERATION SUPPORT (ATD)	10815	4208	5257	4563	4114	3194	3259	Cont	Cont

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COST (In Thousands)	FY 2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	Cost to	Total Cost
	Actual	Estimate	Estimate	Estimate	Estimate	Estimate	Estimate	Complete	
TB2 MEDICAL BIOLOGICAL DEFENSE (APPLIED RESEARCH)	47183	47747	22622	15371	15658	16431	13113	Continuing	Continuing

A. Mission Description and Budget Item Justification:

Project TB2 MEDICAL BIOLOGICAL DEFENSE (APPLIED RESEARCH): This project funds applied research on the development of vaccines, therapeutic drugs, and diagnostic capabilities to provide an effective medical defense against validated biological threat agents including bacteria, toxins, and viruses. Innovative biotechnological approaches and advances will be incorporated to obtain medical systems designed to rapidly identify, diagnose, prevent, and treat disease due to exposure to biological threat agents. Categories for this project include Defense Technology Objectives (DTO); science and technology programs in medical biological defense (diagnostic technology, bacterial therapeutics, toxin therapeutics, viral therapeutics, bacterial vaccines, toxin vaccines, and viral vaccines); and directed research efforts, including the Chemical and Biological Defense Initiative (CBDI) fund.

B. Accomplishments/Planned Program

	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
Therapeutics	24867	15571	10984

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FY 2003 Accomplishments:

- 1622 Therapeutics, Bacterial - Evaluated novel antibiotics and other therapeutics in established in vitro assays and animal models. Established a database of therapeutic profiles for various species of bacterial threat agents.
- 7269 Therapeutics, Toxin - Continued high-throughput assessment of candidate therapeutic inhibitors for botulinum neurotoxin. Completed testing and development of cell-free assay for assessment of candidate therapeutic inhibitors of staphylococcal enterotoxin (SE). Selected lead candidate inhibitors based upon results in cell-free and cell-based assays and prepared toxin-inhibitor crystals for x-ray diffraction analysis. Evaluated the outcome of structural stabilization and optimization studies on lead inhibitors of botulinum and SE.
- 1319 Therapeutics, Viral - Continued assessing the potential for immunotherapy against Ebola virus in non-human primate models. Initiated characterization of sixteen monoclonal antibodies to identify other protective epitopes on Ebola virus glycoprotein (GP). Identified pharmacological compounds provided by industry that disrupt filovirus growth in cell culture. Assessed therapeutic action of compounds in mouse and higher animal models of filovirus infection. Continued research for development of a variola animal model at the Centers for Disease Control and Prevention (CDC).
- 1438 Therapeutics, Medical Countermeasures - Accelerated research to define criteria for successful therapeutics against toxins and viruses to obtain diverse compounds such as inhibitors, channel-blockers, natural product extracts, and peptides that show promise as potential therapeutics against botulinum neurotoxins, staphylococcal enterotoxin, ricin toxin, and viruses. Continued characterizing and refining the smallpox higher animal model for use in determining the effectiveness of post-exposure therapies.

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FY 2003 Accomplishments (Cont):

- 2875 Therapeutics, Genetically Engineered Threat Medical Countermeasures - Accelerated research efforts directed toward compiling and prioritizing function-based structural elements that constitute known toxins and virulence factors of biological threat agents. Continued developing integrated databases of protein domains or three-dimensional structural elements identified as virulence factors in biological threat organisms.
- 964 Therapeutics, Monoclonal Antibody Based Technology - Continued research toward development of a proprietary heteropolymer (HP) system as a potential therapeutic for acute anthrax intoxication. Conducted in vivo assessment of the HP system in a transgenic mouse strain expressing the human CR-1 receptor on red blood cells. Performed in vivo assessments comparing the therapeutic capability of monoclonal antibody 14B7, which has high affinity for anthrax toxin, alone and within the HP system.
- 2300 Therapeutics, Viral, Therapy for Smallpox and Other Pathogenic Orthopox Viruses (DTO CB54) - Determined the optimum dose of cidofovir in the appropriate non-human primate model using both the lethal pulmonary and lesional infection models with monkeypox. Characterized disease pathogenesis in both animal models. Performed studies to establish the therapeutic window in the variola model developed with the CDC.
- 1495 Therapeutics (CBDI), Bacterial, The National Center for Biodefense - Developed prophylaxes and treatments to test the effectiveness of a combination of lethal toxin inhibitors/blockers and antibiotics in reducing the mortality rate of anthrax infection. Tested the effectiveness of protease inhibitors in treating late-stage anthrax infection. Determined the role of Toll Like Receptors (TLRs) as targets for specific and broad-spectrum protection by developing and testing TLR antibodies and soluble receptors.

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FY 2003 Accomplishments (Cont):

- 2495 Therapeutics (CBDI), Bacterial, Heteropolymer Technologies for Anthrax Immunity - Developed an immunotherapeutic for the post-exposure treatment of inhalational anthrax in conjunction with antibiotics. This immunotherapeutic is a bispecific immunoconjugate heteropolymer (HP) biopharmaceutical agent targeting the protective antigen (PA) component of anthrax toxin. The two antibodies, anti-PA and anti-CR1, will be humanized.
- 1595 Therapeutics (CBDI), Bacterial, Oral Anthrax Antibiotic - Used combinatorial chemistry and rational drug design to synthesize additional antibacterial agents. Screened these agents for pharmacological activity. Optimized inhibitors to provide acceptable in vivo biological activity and other characteristics critical for drug development. Optimized lead compound synthesis for commercial production. Completed in vivo safety pharmacology and toxicology studies required for first-time-in-man and proof-of-principle biowarfare organisms.
- 1495 Therapeutics (CBDI), Bacterial, Rapid Antibody-Based Countermeasures - Analyzed convalescent sera samples from survivors of the Fall 2001 anthrax attacks in the USA, supplied by U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID), using a proteomics platform to identify key antigens that are recognized by the human immune system during an anthrax infection. Performed proteomics analysis for a fully virulent Yersinia pestis strain, the etiologic agent for plague, grown in animals to identify secreted or membrane proteins that can serve as targets for the development of vaccines or diagnostic and therapeutic antibodies. Optimized an existing diagnostic/therapeutic antibody using proprietary technologies.

Total 24867

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FY 2004 Planned Program:

- 559 Therapeutics, Bacterial - Perform additional in vivo studies on efficacy of selected antimicrobial compounds against various bacterial threat agents in small animal models. Initiate studies of selected Food and Drug Administration (FDA)-licensed antibiotics to support consideration for changing label indications against biological warfare (BW) threat agents.
- 1456 Therapeutics, Toxin - Initiate testing of lead inhibitors of SE using in vivo model systems for assessment of therapeutic efficacy. Standardize in vivo model systems for assessment of therapeutic efficacy and surrogate endpoints of human clinical efficacy.
- 596 Therapeutics, Viral - Develop fluorescent-based methods for high-throughput screening for antiviral efficacy and cellular toxicity. Continue research to identify pharmacological compounds provided by industry that may intervene in filovirus-induced shock. Continue the assessment of the therapeutic action of compounds in mouse models of filovirus infection. Complete research for development of a variola animal model at CDC.
- 2500 Therapeutics, Viral, Therapy for Smallpox and Other Pathogenic Orthopox Viruses (DTO CB54) - Continue preclinical virology studies (including animal efficacy studies) required for a supplemental New Drug Application for cidofovir and provide technical data and support to the drug license holder. Compare the variola animal model to the monkeypox animal model and human monkeypox to qualify models to be proposed under the FDA animal efficacy rule. Initiate development of an oral prodrug of cidofovir.

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FY 2004 Planned Program (Cont):

- 3900 Therapeutics, Toxin, Therapeutic Strategies for Botulinum Neurotoxins (DTO CB59) - Investigate recombinant human antibodies as passive immunotherapeutics. Synthesize structural analogs of active-site inhibitors identified by high-throughput screening. Identify candidate botulinum neurotoxin (BoNT) receptor antagonists as therapeutic candidates. Establish a central database and compound repository.
- 1900 Therapeutics, Viral, Therapeutic Strategies for Treating Filovirus (Marburg and Ebola Viruses) Infection (DTO CB63) - Develop assays methodologies and drug formulations or prodrugs for analysis. Evaluate monoclonal antibodies to viral specific proteins for their ability to neutralize virus. Identify critical host-cell proteins integral to viral replication, viral budding, or viral entry. Generate Ebola virus VP40 and GP mutant constructs as well as a tetra cysteine-fusion of VP40 in mammalian and bacterial expression vectors.
- 971 Therapeutics, Heteropolymer Monoclonal Antibody-Based Technology - Produce and purify milligram quantities of H25 antibody for a 4-liter scale spinner production. Determine functional and biophysical properties of the purified antibody. Confirm the utility and acceptability of the antibody produced from the cell lines for further product development. Develop analytical transfer methods and assays for monoclonal antibodies (MAbs) and heteropolymers (HPs) and conduct animal studies.
- 971 Therapeutics, Bacterial, Heteropolymer Technologies for Anthrax Immunity - Evaluate protective efficacy in rabbits exposed to lethal doses of aerosolized anthrax using the proprietary anthrax antibody, ETI-204. Assess the level of bacteremia in treated versus untreated animals.

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FY 2004 Planned Program (Cont):

- 2718 Therapeutics, Bacterial, Rapid Antibody-Based Biological Countermeasures - Develop diagnostic and therapeutic antibodies against anthrax and identify new targets associated with anthrax and plague pathology. Identify additional targets associated with anthrax and plague virulence and screen for novel antibodies to detect and protect against related bioweapons. Discover novel, validated protein targets. Develop diagnostic antibodies optimized for affinity and selectivity to biowarfare agents. Create a collection of human therapeutic antibodies for passive immunity protection against bioweapons and more effective treatment against pathogens and toxins.

Total 15571

FY 2005 Planned Program:

- 1498 Therapeutics, Bacterial - Perform therapeutic efficacy studies in non-human primate models. Continue studies on selected FDA-licensed antimicrobial compounds to support consideration for changing label indications for use against BW threat agents.
- 2962 Therapeutics, Toxin - Develop surrogate endpoints of human clinical efficacy for SE therapeutics.
- 624 Therapeutics, Viral - Assess therapeutic action of pharmacological compounds provided by industry in mouse and non-human primate models of filovirus infection.
- 2400 Therapeutics, Therapy for Smallpox and Other Pathogenic Orthopox Viruses (DTO CB54) - Complete preclinical virology studies (including animal efficacy studies) required for a supplemental New Drug Application for intravenous (IV) cidofovir. Continue evaluation of oral prodrug of cidofovir to determine its feasibility as a replacement for intravenous (IV) cidofovir.

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FY 2005 Planned Program (Cont):

- 2500 Therapeutics, Toxin, Therapeutic Strategies for Botulinum Neurotoxins (DTO CB59) - Test combinations of human monoclonal antibodies against multiple BoNT serotypes in cell-based systems. Expand proof-of-concept for BoNT target rescue and replacement in cholinergic neurons.
- 1000 Therapeutics, Viral, Therapeutic Strategies for Treating Filovirus (Marburg and Ebola Viruses) Infection (DTO CB63) - Generate mutant Marburg virus proteins and evaluate their ability to interact with other Marburg virus proteins. Develop information on characteristics distinguishing protective and nonprotective monoclonal antibodies.

Total 10984

	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
Diagnostics	6705	4068	4236

FY 2003 Accomplishments:

- 6705 Diagnostic Technologies - Applied new diagnostic approaches to the early recognition of infection, adapting the technologies to current and future comprehensive integrated diagnostic systems. Applied new technological approaches for diagnosis of potential biological warfare threat agents in laboratory and field studies using relevant clinical samples. Applied new technological approaches for concentrating and processing clinical samples to support rapid biological agent identification. Applied research reagents and associated assays for the detection of appropriate biological markers using relevant clinical samples.

Total 6705

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<p>FY 2004 Planned Program:</p> <ul style="list-style-type: none"> • 2468 Diagnostic Technologies - Continue to apply new diagnostic approaches directed toward early recognition of infection, selecting technologies that can be adapted to current and future comprehensive integrated diagnostic systems. Continue laboratory and field studies using relevant clinical samples to apply new technological approaches for diagnosis of potential biological warfare threat agents. Continue to apply new technological approaches for concentrating and processing clinical samples to support rapid agent identification and to apply research reagents and associated assays for the detection of appropriate biological markers using relevant clinical samples. • 1600 Diagnostic Technologies, Methodology to Facilitate Development of Biological Warfare Threat Agent Detection and Medical Diagnostic Systems (DTO CB56) - Develop laboratory-based test and evaluation standards for comparing similar diagnostic/detection assays and reagents. Elevate assays, previously handed off to advanced development, to consistent test and evaluation standards and prepare technical data packages for these assays/reagents. <p>Total 4068</p> <p>FY 2005 Planned Program:</p> <ul style="list-style-type: none"> • 2636 Diagnostic Technologies - Continue applying new diagnostic approaches to the early recognition of infections. Technologies will be adapted to current and future comprehensive integrated diagnostic systems. Continue applying new technological approaches for diagnosis of potential biological warfare threat agents in laboratory and field studies using clinical samples. Apply new technological approaches for processing clinical samples and apply research reagents and associated assays for the detection of appropriate biological markers using relevant clinical samples. 		
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FY 2005 Planned Program (Cont):

- 1600 Diagnostic Technologies, Methodology to Facilitate Development of Biological Warfare Threat Agent Detection and Medical Diagnostic Systems (DTO CB56) - Continue to elevate previously transitioned assays to test and evaluation standards established during FY04.

Total 4236

	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
Vaccines	15611	19438	7402

FY 2003 Accomplishments:

- 350 Vaccines, Bacterial, Medical Countermeasures for Brucella (DTO CB31) - Determined whether over-expression of vaccine antigens in candidate live vaccines increases protective efficacy. Continued to develop and validate in vitro systems in mice and non-human primates to reliably quantify the intensity of potentially protective immune responses in animals vaccinated with live and subunit vaccines.
- 200 Vaccines, Viral, Medical Countermeasures for Encephalitis Viruses (DTO CB24) - Completed studies on production of the live attenuated Venezuelan equine encephalitis (VEE) virus vaccine constructs, their genetic stability, and their transmission potential as live attenuated viruses in competent vector mosquitoes.

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FY 2003 Accomplishments (Cont):

- 628 Vaccines, Alternative Delivery Methods for Recombinant Protein Vaccines (DTO CB32) - Downselected formulations for intranasal, inhalational, and/or transdermal delivery of recombinant protein vaccines. Proposed commercial or proprietary devices for delivery of vaccines.
- 4583 Vaccines, Bacterial - Developed mutants in various agents for in vivo expressed genes to examine role in virulence. Characterized the mechanism(s) of vaccine resistance in selected strains of various agents. Determined mechanisms and correlates of protection with efficacious glanders vaccines. Completed evaluation of immunogenicity and efficacy of recombinant protective antigen (rPA) isoform species in the rabbit model; continued to develop reagent standards for use in an in vitro potency assay; and completed collection of immune serum for evaluation in non-human primates passive transfer study, all in support of rPA vaccine candidate entry into technology development. Completed development of anti-V antigen competitive enzyme-linked immunosorbent assay (ELISA) and cytotoxicity inhibition assays; completed determination of the range of protection of the vaccine candidate against other virulent strains of *Y. pestis* in animals; and completed studies in mice on alternate vaccine administration routes, dose, formulation and mucosal adjuvants, all in support of recombinant plague F1-V vaccine candidate entry into technology development.
- 3242 Vaccines, Viral - Assessed mechanism of immunity that protects against disease from filoviruses (Marburg and Ebola viruses) in vivo. Developed assays to measure markers to validate the efficacy of vaccine candidates in established model systems for filoviruses. Developed non-human primate models for western equine encephalitis virus (WEE).
- 1437 Vaccines - Evaluated additional vaccine candidates for delivery using the multiagent delivery platform. Developed virus constructs and obtained commercially produced humanized mouse monoclonal antibodies to evaluate protective immune responses. Investigated the potential of live vaccine candidate for bacterial threat agents.

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FY 2003 Accomplishments (Cont):

- 964 Vaccines, Needle-less Delivery Methods for Recombinant Protein Vaccines - Assessed novel, minimally invasive delivery technologies for the administration of protein subunit biodefense vaccine candidates, including rPA and recombinant staphylococcal enterotoxin B (rSEB) vaccines, and either rSEA vaccine or recombinant F1-V fusion protein plague vaccine.
- 2407 Vaccines, Organic Vaccine Production - Evaluate and determine the usefulness of methods/technologies to develop vaccines through alternative unconventional means.
- 1800 Vaccines, Toxin, Recombinant Ricin Vaccine (DTO CB46) - Completed efficacy studies in rodents on recombinant ricin toxin A-chain (rRTA) vaccine candidates and downselected to lead candidate and alternate. Performed scale up process development for lead rRTA vaccine candidate; conducted analytical test qualification for identity and stability studies of lead rRTA candidate; and developed a potency assay for rRTA vaccine candidates. Developed non-human primate model for testing lead vaccine candidate.

Total 15611

FY 2004 Planned Program:

- 3557 Vaccines, Bacterial - Complete the evaluation of potential subunit and live-attenuated glanders vaccine candidates in small animal models and prepare a technical data package summarizing the glanders vaccine research program. Perform preliminary studies toward development of an acellular brucella vaccine candidate. Continue to perform in vitro and in vivo studies to support advanced development of the rPA vaccine candidate.

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FY 2004 Planned Program (Cont):

- 1533 Vaccines, Toxin - Initiate studies on the ability of intact catalytic and translocation domains of botulinum neurotoxins (BoNT) to elicit protective immunity in animal models. Initiate studies to increase immunogenicity of recombinant BoNT heavy chain (Hc) subunit vaccine candidates by varying adjuvant and/or method of delivery. Continue developing in-process and release assays for recombinant BoNT Hc vaccine candidates. Qualify in vivo and in vitro concept model systems for assessment of recombinant ricin vaccine candidate efficacy and surrogate endpoints of human clinical efficacy.
- 473 Vaccines, Viral - Investigate the use of the oligonucleotide CpG as an adjuvant with live attenuated alphavirus vaccine candidates to determine their effect on immunity conferred by the vaccines.
- 500 Vaccines, Viral, Western and Eastern Equine Encephalitis (WEE/EEE) Vaccine Constructs for a Combined Equine Encephalitis Vaccine (DTO CB58) - Initiate applied research to define correlates of immunity that protect against disease from alphaviruses (EEE and WEE viruses). Develop DNA and replicon-based vaccine constructs/platforms as western and eastern equine encephalitis (WEE/EEE) vaccine candidates.
- 1100 Vaccines, Viral, Vaccine Technologies for Protection Against Filovirus (Marburg and Ebola Viruses) Exposure (DTO CB60) - Initiate development of animal models of aerosol infection with filoviruses. Initiate applied research to define correlates of immunity that protect against disease from filoviruses. Develop animal models for Ebola-Sudan virus. Conduct preliminary characterization of leading vaccine candidates.

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FY 2004 Planned Program (Cont):

- 1941 Vaccines, Needle-less Delivery Methods for Vaccines - Examine the potential for intradermal (ID) delivery to provide antigen dose-sparing benefits, faster seroconversion, and reduction or elimination of alum. Examine the safety and immunogenicity of the ID delivery of the anthrax rPA with or without alum adjuvant. Compare intramuscular (IM) injection with standard needles. Pursue further development of formulation technologies for rPA and rSEB providing improved shelf-life stability. Develop and test rapidly reconstituting rPA powders and systems for ID delivery in mouse challenge studies. Identify rapidly reconstituting formulations and delivery systems for the rSEB vaccine candidate.
- 8149 Vaccines, Viral, Multivalent Ebola, Marburg Filovirus Program - Develop a multivalent vaccine platform capable of inducing potent humoral and cellular immune responses against two strains of Ebola viruses (bivalent) and three strains of Marburg viruses (trivalent) for biodefense.
- 971 Vaccines, Bacterial, Oral Anthrax and Plague Vaccine - Develop an oral combination vaccine against anthrax and plague using proprietary technology for attenuated live bacterial vaccines. Support preclinical animal testing of vaccine constructs developed for the oral combination vaccine against anthrax and plague.
- 1214 Vaccines, Bacterial, Novel Pharmaceuticals for Anthrax - Develop the Helinz-treated vaccine platform, with application in both cancer and infectious disease, including those agents that pose threats to bioterrorism.

Total 19438

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<p>FY 2005 Planned Program:</p> <ul style="list-style-type: none"> • 3661 Vaccines, Bacterial - Continue to perform laboratory research (demonstrate surrogate efficacy, design and validate in vitro correlates of protection, and stability studies) to support development of lead vaccine candidates against plague (F1-V fusion antigen vaccine) and anthrax (rPA vaccine). • 1634 Vaccines, Toxin - Continue studies on the ability of intact catalytic and translocation domains of botulinum neurotoxins (BoNT) to elicit protective immunity in animal models. Continue studies to increase immunogenicity of existing recombinant BoNT vaccine candidates via adjuvants and/or delivery methods. Complete developing in-process and release assays for recombinant BoNT vaccine candidates. Continue recombinant ricin vaccine candidate stability testing. Develop surrogate endpoints of clinical efficacy in non-human primates for the candidate ricin vaccine. Test novel adjuvants with lead ricin vaccine candidate in vivo. • 907 Vaccines, Viral - Continue research studies investigating the effect on immunogenicity by the use of the oligonucleotide CpG as an adjuvant with live attenuated alphavirus vaccine candidates. • 500 Vaccines, Viral, Western and Eastern Equine Encephalitis (WEE/EEE) Vaccine Constructs for a Combined Equine Encephalitis Vaccine (DTO CB58) - Continue to analyze mutants with various engineered attenuating mutations to determine their suitability for use as vaccine platforms. Initiate studies to establish an eastern equine encephalitis (EEE) virus non-human primate efficacy model. • 700 Vaccines, Viral, Vaccine Technologies for Protection Against Filovirus (Marburg and Ebola Viruses) Exposure (DTO CB60) - Incorporate iterative improvements in vaccine candidates as determined from characterization studies and concurrent testing. <p>Total 7402</p>		
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	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
Medical Biological Warfare Defense	0	7861	0

FY 2004 Planned Program:

- 3396 Medical Biological Warfare Defense, Global Pathogen Portal - Collect and collate genetic information about pathogens from the CDC and the National Institute of Allergy and Infectious Diseases "A", "B", and "C" lists of pathogens and their close relatives using a global pathogen portal bioinformatic software architecture.
- 2426 Medical Biological Warfare Defense, Vaccines and Therapeutics to Counter Biothreats - Conduct applied research to develop vaccines and therapeutics to counter BW threat agents.
- 2039 Medical Biological Warfare Defense, Advanced Emergency Medical Response - Conduct applied research toward development of advanced emergency medical response capabilities.

Total 7861

	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
SBIR/STTR	0	809	0

FY 2004 Planned Program:

- 809 SBIR - Small Business Innovative Research

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FY 2004 Planned Program (Cont):
Total 809

C. <u>Other Program Funding Summary:</u>	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>	<u>FY 2006</u>	<u>FY 2007</u>	<u>FY 2008</u>	<u>FY 2009</u>	<u>To Compl</u>	<u>Total Cost</u>
TB3 MEDICAL BIOLOGICAL DEFENSE (ATD)	34677	45944	55621	39416	39440	42499	38625	Cont	Cont

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COST (In Thousands)	FY 2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	Cost to	Total Cost
	Actual	Estimate	Estimate	Estimate	Estimate	Estimate	Estimate	Complete	
TC2 MEDICAL CHEMICAL DEFENSE (APPLIED RESEARCH)	18768	22143	18269	19936	20059	20354	21779	Continuing	Continuing

A. Mission Description and Budget Item Justification:

Project TC2 MEDICAL CHEMICAL DEFENSE (APPLIED RESEARCH): This project funds medical chemical defense applied research and emphasizes the prevention of chemical casualties through application of pharmaceuticals for prevention and treatment of the toxic effects of nerve, blister, respiratory, and blood agents. This project supports applied research of prophylaxes, pretreatments, antidotes, skin decontaminants, and therapeutic drug compounds that have the potential to counteract the lethal, physical, and behavioral toxicities of chemical agents. It also supports development of medical chemical defense materiel that ensures adequate patient care, field resuscitation, and patient management procedures. Categories for this project include Defense Technology Objectives (DTOs), science and technology program areas (Nerve Agent Defense, Vesicant Agent Defense and Chemical Warfare Agent (CWA) Defense), and directed research efforts (Low Level CWA Exposure, Non-Traditional Agents (NTAs), and Mustard Gas Antidote).

B. Accomplishments/Planned Program

	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
Nerve Agent Defense	6095	8964	9391

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FY 2003 Accomplishments:

- 665 Nerve Agent Defense, Nerve Agent Anticonvulsants - Developed experimental protocol to evaluate drugs, drug combinations and drug treatment protocols with potential to control nerve agent-induced seizures. Evaluated ability of midazolam and anticholinergics to terminate nerve agent-induced seizures in a non-human primate model.
- 3530 Nerve Agent Defense, Biological Scavenger - Developed physiological pharmacokinetic models of CWAs. Evaluated the safety and circulatory stability of recombinant bioscavengers. Determined specific carbohydrate structures of human serum butyrylcholinesterase as reference material for Good Laboratory Practices (GLP) and current Good Manufacturing Practices (cGMP) production. Generated serum carboxylesterase-deficient mice for use in testing efficacy of nerve agent bioscavengers.
- 900 Nerve Agent Defense, Neuroprotection - Developed and tested neuroprotectant drugs to protect against status epilepticus following nerve agent exposure. Assessed alternate non-human primates as models for nerve agent toxicity and medical countermeasures.
- 1000 Nerve Agent Defense, Improved Oxime (DTO CB48) - Initiated chemical assay development to detect candidate oxime(s) for use against traditional nerve agents and NTAs in biological fluids, stability studies, and studies to identify and characterize a surrogate marker for efficacy, drawing from an array of promising compounds already identified.

Total 6095

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FY 2004 Planned Program:

- 634 Nerve Agent Defense, Nerve Agent Anticonvulsants - Determine efficacy of midazolam and anticholinergic drug combinations against seizures and lethality caused by nerve agents. Determine minimal amount of atropine needed to sustain survival in non-human primates exposed to nerve agent.
- 3601 Nerve Agent Defense, Biological Scavenger - Determine pharmacokinetics of CWAs and the impact of pretreatment in guinea pigs. Determine x-ray crystallographic structure of catalytic scavengers. Continue pretreatment intervention studies of vectors to deliver bioscavenger genes. Characterize animal models to test efficacy of nerve agent bioscavengers. Test physiologic pharmacokinetic model of CWAs.
- 729 Nerve Agent Defense, Neuroprotection - Test Food and Drug Administration (FDA)-approved drugs shown to be neuroprotective in both anatomic and behavioral studies.
- 1000 Nerve Agent Defense, Improved Oxime (DTO CB48) - Continue assay development, stability studies, and studies to identify and characterize a surrogate marker for efficacy of candidate oxime(s) for use against traditional nerve agents and NTAs.
- 3000 Nerve Agent Defense, Non-Traditional Nerve Agent Medical Countermeasures (DTO CB57) - Determine the effects of NTAs on energy metabolism of cardiac cells and the effectiveness of decontamination on percutaneous NTAs. Conduct electrophysiological evaluation of cardiovascular, respiratory, muscular and cortical dysfunction.

Total 8964

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FY 2005 Planned Program:

- 600 Nerve Agent Defense, Nerve Agent Anticonvulsants - Define in vitro and in vivo models for study of improved nerve agent countermeasures.
- 3341 Nerve Agent Defense, Biological Scavenger - Complete development of transgenic animal models that can produce sufficient amounts of recombinant enzyme scavengers for clinical trials. Complete feasibility testing of vector/gene combinations to validate the concept of gene therapy for bioscavengers. Continue pretreatment intervention studies of vectors to deliver bioscavenger genes.
- 450 Nerve Agent Defense, Neuroprotection - Continue testing FDA-approved drugs shown to be neuroprotective in both anatomic and behavioral studies.
- 1000 Nerve Agent Defense, Improved Oxime (DTO CB48) - Complete assay development and stability studies. Complete the identification and characterization of a surrogate marker for efficacy of candidate oxime(s) for use against traditional nerve agents and NTAs.
- 4000 Nerve Agent Defense, Non-Traditional Nerve Agent Medical Countermeasures (DTO CB57) - Evaluate the effectiveness of anticonvulsants against seizures produced by NTAs, in vivo persistence of NTAs, and current medical countermeasures against NTAs. Conduct evaluation of respiratory dynamics and lung biochemistry.

Total 9391

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	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
Vesicant Agent Defense	6074	8155	4000

FY 2003 Accomplishments:

- 1367 Vesicant Agent Defense, Vesicant Medical Countermeasures - Evaluated antagonists of apoptosis and the blockade of sulfur mustard (HD)-induced toxicity.
- 1684 Vesicant Agent Defense, Cutaneous Therapeutics - Evaluated new FDA-approved drugs for treatment of HD-induced ocular injury. Optimized formulation for an ocular rinse that treats HD-induced ocular injury.
- 1000 Vesicant Agent Defense, Medical Countermeasures for Vesicant Agents II (DTO CB30) - Identified therapeutic window for administering compounds to mitigate the effects of HD exposure. Evaluated combination therapies for HD exposure in animal models.
- 2023 Vesicant Agent Defense, Mustard Gas Antidote - Explored the use of free and liposome-encapsulated antioxidants as a medical countermeasure to HD exposure.

Total 6074

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FY 2004 Planned Program:

- 1662 Vesicant Agent Defense, Vesicant Medical Countermeasures - Conduct screening of candidate antivesicant compounds. Develop in vitro and in vivo models to support efficacy studies of new antivesicant countermeasures.
- 2127 Vesicant Agent Defense, Cutaneous Therapeutics - Identify candidate treatment strategies and collate findings in concert with medical experts and relevant research teams. Define in vitro/in vivo models, establish pathophysiological endpoints, and define cellular and tissue consequences of exposure.
- 4366 Vesicant Agent Defense, Mustard Gas Antidote - Enhance the effectiveness of Signal Transduction Inhibition Methodology Antioxidant Liposomes (STIMAL), also known as the Redox Regulating Liposome (RRL), by further product development. Elucidate the pathophysiology of mustard agents in previously developed in vitro and in vivo models. Explore additional modalities such as pharmacogenomically-based drugs and complement blockade. Complete initial efficacy studies of STIMAL against HD. Conduct detailed studies on the inhalation of mustards (bis-2-CEES) to determine if oxidative stress is a significant part of the pathophysiology.

Total 8155

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FY 2005 Planned Program:

- 2000 Vesicant Agent Defense, Vesicant Medical Countermeasures - Define pharmacological categories for points of intervention in vesicant injury process. Screen potential antivesicant compounds.
- 2000 Vesicant Agent Defense, Cutaneous Therapeutics - Characterize pathophysiological endpoints and continue elucidation of pathophysiological schema. Develop in vitro biological tissue assays. Identify additional potential intervention strategies.

Total 4000

	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
Chemical Warfare Agent Defense	6599	4650	4878

FY 2003 Accomplishments:

- 659 Chemical Warfare Agent Defense, Cyanide Medical Countermeasures - Evaluated several classes of compounds that behave by different mechanisms of action, to include methemoglobin formers and sulfur donors, to pursue development of cyanide pretreatment.
- 703 Chemical Warfare Agent Defense, Inhalation Therapeutics - Evaluated treatments for HD-induced pulmonary injury.
- 492 Chemical Warfare Agent Defense, Medical Diagnostics - Continued development of analytical methods to measure biological matrices (e.g., blood, urine, tissue) following CWA exposure. Developed confirmatory diagnostic capabilities and rapid screening technology for field applications. Pursued development of an ocular device for self-examination of pupillary response to nerve agent exposure.

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<p>FY 2003 Accomplishments (Cont):</p> <ul style="list-style-type: none"> • 245 Chemical Warfare Agent Defense, Skin and Wound Decontamination - Evaluated the toxicity of percutaneously applied organophosphorus compounds and the effectiveness of skin decontamination methods. • 2000 Chemical Warfare Agent Defense, Low Level CWA Exposure: Effects and Countermeasures (DTO CB51) - Assessed short-term behavioral, physiological, and neuropathological effects of sarin (GB) nerve agent in rodents following low-dose exposures for varying durations and their potential impact on human operational readiness. • 2500 Chemical Warfare Agent Defense, Non-Traditional Agents (NTAs) - Evaluated cardiac toxicity following NTA exposure in cardiac muscle cells and animal models. Evaluated bioscavenger pretreatment as medical countermeasure against NTAs in guinea pigs. <p>Total 6599</p> <p>FY 2004 Planned Program:</p> <ul style="list-style-type: none"> • 496 Chemical Warfare Agent Defense, Cyanide Medical Countermeasures - Evaluate cyanide toxicity using an inhalation model. Investigate efficacy of sulfur donors and methemoglobin formers as cyanide pretreatment. • 731 Chemical Warfare Agent Defense, Inhalation Therapeutics - Screen clinically available drugs for potential efficacy against HD using the mouse model. 		
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<p>FY 2004 Planned Program (Cont):</p> <ul style="list-style-type: none"> • 486 Chemical Warfare Agent Defense, Medical Diagnostics - Initiate development of diagnostic applications for miniaturized mass spectrometer. Develop diagnostics that can be used to diagnose exposure via respiratory route. Refine analytical methods to measure scopolamine levels in blood and tissue. Investigate applicability of ocular device for self-examination of pupillary response. • 237 Chemical Warfare Agent Defense, Skin and Wound Decontamination - Pursue development of screening procedures for the evaluation of decontaminants using analytical techniques and animal models. Determine the extent that HD forms a reservoir in skin using pig and hairless guinea pig skin models. • 2700 Chemical Warfare Agent Defense, Low Level CWA Exposure: Effects and Countermeasures (DTO CB51) - Assess short-term behavioral, physiological, and neuropathological effects of VX nerve agent in rodents following low-dose exposures for varying durations and their potential impact on human operational readiness. Initiate studies on the effects of current prophylactic and therapeutic treatments on the maximum tolerated dose for repeated CWA exposures and on other indices of chemical agent toxicity. <p>Total 4650</p>		
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FY 2005 Planned Program:

- 500 Chemical Warfare Agent Defense, Cyanide Medical Countermeasures - Screen anti-cyanide compounds for efficacy.
- 500 Chemical Warfare Agent Defense, Inhalation Therapeutics - Test efficacious drugs in a modified inhalation therapy system.
- 500 Chemical Warfare Agent Defense, Medical Diagnostics - Continue development of diagnostic applications for miniaturized mass spectrometer.
- 678 Chemical Warfare Agent Defense, Skin and Wound Decontamination - Continue development of analytical and animal screening procedures for the evaluation of decontaminants and use them to screen for efficacy. Evaluate formulations designed to remove HD from reservoirs in the skin.
- 2700 Chemical Warfare Agent Defense, Low Level CWA Exposure: Effects and Countermeasures (DTO CB51) - Assess VX nerve agent and HD-induced changes in respiratory function produced by low-dose exposures of varying duration. Complete assessments of the short-term effects of VX nerve agent on higher order behavioral tasks in non-human primates following a range of low-dose exposures for varying durations to improve estimates of impact on human operational readiness. Complete assessments of the effects of current CWA treatments on toxicity at low doses of exposure.

Total 4878

	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>
SBIR/STTR	0	374	0

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FY 2004 Planned Program:

- 374 SBIR - Small Business Innovative Research

Total 374

C. <u>Other Program Funding Summary:</u>								<u>To Compl</u>	<u>Total Cost</u>
TC3 MEDICAL CHEMICAL DEFENSE (ATD)	<u>FY 2003</u>	<u>FY 2004</u>	<u>FY 2005</u>	<u>FY 2006</u>	<u>FY 2007</u>	<u>FY 2008</u>	<u>FY 2009</u>	Cont	Cont

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