

UNCLASSIFIED

RDT&E BUDGET ITEM JUSTIFICATION SHEET (R-2 Exhibit)

DATE
FEBRUARY 2000

BUDGET ACTIVITY
3 - Advanced Technology Development

PE NUMBER AND TITLE
0603384BP CHEMICAL/BIOLOGICAL DEFENSE (ADVANCED DEVELOPMENT)

COST (In Thousands)	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	FY 2004	FY 2005	Cost to	Total Cost
	Actual	Estimate	Estimate	Estimate	Estimate	Estimate	Estimate	Complete	
Total Program Element (PE) Cost	59186	56911	46594	53283	62722	83190	80934	Continuing	Continuing
CB3 CHEMICAL BIOLOGICAL DEFENSE (Adv Tech Dev)	21406	20223	6036	7693	10463	12890	14156	Continuing	Continuing
CP3 COUNTERPROLIFERATION SUPPORT (Adv Tech Dev)	7098	10434	10213	11416	7321	7663	13345	Continuing	Continuing
TB3 MEDICAL BIOLOGICAL DEFENSE (Adv Tech Dev)	14079	16809	19980	23063	33154	50328	40819	Continuing	Continuing
TC3 MEDICAL CHEMICAL DEFENSE (Adv Tech Dev)	16603	9445	10365	11111	11784	12309	12614	Continuing	Continuing

A. Mission Description and Budget Item Justification: This program element (PE) demonstrates technologies that enhance the ability of U.S. forces to deter, defend against, and survive chemical and biological (CB) warfare. This PE funds advanced technology development for Joint Service and Service-specific requirements in both medical and non-medical CB defense areas. The medical program aims to produce drugs, vaccines, and medical devices as countermeasures for CB threat agents. Specific areas of medical investigation include: prophylaxis, pretreatment, antidotes and therapeutics, personnel and patient decontamination, and medical management of casualties. In the non-medical area, the focus is on demonstrations of CB defense technologies, including biological detection, chemical detection, and decontamination. These demonstrations, conducted in an operational environment with active user and developer participation, integrate diverse technologies to improve DoD Chemical/Biological Warfare (CBW) defense and deterrence. These demonstrations are leveraged by the Counterproliferation Support Program and include remote Biological Detection. Work conducted under this PE transitions to and provides risk reduction for Demonstration/Validation (PE 0603884BP) and Engineering/Manufacturing Development (PE 0604384BP) activities. The work in this PE is consistent with the Joint Service NBC Defense Research, Development, and Acquisition (RDA) Plan. This PE also provides for the conduct of advanced technology development in the areas of real-time sensing, accelerated BW operational awareness, and the restoration of operations following a BW/CW attack. This program is dedicated to conducting proof-of-principle field demonstrations and tests of system-specific technologies to meet specific military needs.

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B. <u>Program Change Summary:</u>	<u>FY 1999</u>	<u>FY 2000</u>	<u>FY 2001</u>
Previous President's Budget (FY 2000/FY 2001)	52212	40910	44881
Appropriated Value	51610	57110	
Adjustment to Appropriated Value			
a. Congressional General Reductions			
b. SBIR/STTR	-858		
c. Omnibus or Other Above Threshold Reductions	6517	-115	
d. Below Threshold Reprogramming	1917	73	
e. Rescissions		-157	
Adjustments to Budget Years Since FY 2000/2001 PRES BUD			1713
Current Budget Submit (FY2001/PRES BUD)	59186	56911	46594

Change Summary Explanation:

Funding: FY99 - SBIR (-858). FY99 - Above Threshold - CB3 (6338) Funding transferred from USMC to the Chem Bio Defense Program for the Small Unit Biological Detector (SUB-D) and the Chemical Biological Individual Sampler (CBIS). FY99 - Below Threshold - CB3 (2421) for Joint Service Fixed Site Decon research; CB3, TB3, TC3, CP3 (-423) for revised economic assumptions; CB3, TC3, TB3, CP3 (-504) for higher priority programs; TB3 (602) for increased medical biological research. FY00 - Congressional Adjustments - TB3 (1500) for medical biological counterterrorism response program. FY00 - Reprogrammings from USMC to Chemical Biological Defense Program IAW P.L. 103-160 - CB3 (13700) for chemical biological identification system (CBIS); for chemical management information system (CMIS); for small unit biological detector (SUB-D). FY00 - Reprogramming from U.S. Army to Chemical Biological Defense Program IAW P.L. 103-160 - CB3 (1000) for small fast chemical biological detector.

Schedule:

Technical:

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BUDGET ACTIVITY 3 - Advanced Technology Development	PE NUMBER AND TITLE 0603384BP CHEMICAL/BIOLOGICAL DEFENSE (ADVANCED DEVELOPMENT)	PROJECT CB3
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COST (In Thousands)	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	FY 2004	FY 2005	Cost to Complete	Total Cost
	Actual	Estimate	Estimate	Estimate	Estimate	Estimate	Estimate		
CB3 CHEMICAL BIOLOGICAL DEFENSE (Adv Tech Dev)	21406	20223	6036	7693	10463	12890	14156	Continuing	Continuing

A. Mission Description and Budget Item Justification:

Project CB3 CHEMICAL BIOLOGICAL DEFENSE (Adv Tech Dev): This project demonstrates technology advancements for Joint Service application in the areas of: agent detection and identification, decontamination, and individual/collective protection which will speed maturing of advanced technologies to reduce risk in system-oriented Demonstration and Validation. This project funds the Integrated Biodetection Advanced Technology Demonstration (ATD). This ATD will fabricate, demonstrate and integrate advanced point and standoff biodetection technologies. This project is the only DoD program demonstrating new technologies to counter biological warfare threats and improving current developmental biodetection systems. This program also funds the Small Unit Biological Detector (SUBD) in support of consequence management against terrorist-initiated NBC incidents by demonstrating and developing state-of-the-art sensor technology.

This project funds the Joint Service Fixed Site Decontamination (JSFXD) Program, the Joint Service Warning and Identification LIDAR (Light Detection And Ranging) Detector (JSWILD) Program, the Joint Service Sensitive Equipment Decontamination (JSSED) Program, the Joint Chemical/Biological Agent Water Monitor (JCBAWM), and the Chemical/Biological Individual Sampler (CBIS).

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PROJECT

3 - Advanced Technology Development**0603384BP CHEMICAL/BIOLOGICAL DEFENSE
(ADVANCED DEVELOPMENT)****CB3****FY 1999 Accomplishments:**

- 2421 JSFXSD - Initiated characterization studies of mature technologies. Initiated biological efficacy and compatibility study. Conducted live agent decontamination testing.
- 5716 Bio ATD - Completed development, miniaturization of third-generation ultraviolet fluorescence particle sensor (reduced size to < 1 cu ft). Completed development, demonstration of first automated DNA diagnostic. Demonstrated soldier operability in Battle Lab Warfighter Experiment June 99.
- 3208 JSWILD - Continued fabrication of brassboard system and initiated planning for demonstration of system.
- 669 JS Large Area Decon - Completed front-end analysis of technologies to address multiple decontamination scenarios which include: skin and personal equipment decontamination, equipment decontamination in the field, equipment decontamination at fixed facilities, key areas at fixed facilities, sensitive equipment decontamination, and decontamination of interior spaces containing sensitive items, surfaces, and cargo. Identified and prioritized technologies for each functional area. Completed a master plan incorporating newly identified leads which will drive the Science and Technology (S&T) area for the coming developmental cycle and will be used to support the JSFXD Program.
- 1554 MONOPAK and Residual Life Initiatives - Prepared a fully permeable single layer (shell and liner) "monopak" chemically protective material for transition to the next joint protective ensemble program. A Chemical Protective Combat Uniform (CPCU) was constructed using the latest Army/Navy closure concepts for a comprehensive durability (7 day) field trial. Under the Residual Life Initiative (RLI), developed several promising concepts to address the condition of chemically protective uniforms. All material and concept item performance will be fully characterized as part of the transition support package.
- 1500 Biocide Ensembles (ATD) - Continued development of advanced biocide CBW protection material and application for personal protection and casualty care.
- 3413 SUBD - Continued development of the detector for continuous air monitoring of biological agents.
- 2925 CBIS - Continued development of a pager style dosimeter that can be worn by individual personnel and is capable of monitoring low level CB agent exposure (CBIS a.k.a. ChemBio Dosimeter).

Total 21406

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PROJECT

3 - Advanced Technology Development**0603384BP CHEMICAL/BIOLOGICAL DEFENSE
(ADVANCED DEVELOPMENT)****CB3****FY 2000 Planned Program:**

- 5075 JSWILD - Complete fabrication of brassboard system, initiated Analysis of Alternative for technology to meet requirements and complete planning for demonstration.
- 331 MONOPAK and Residual Life Initiatives - A candidate "monopak" material will transition to the initial Joint Protective Aircrew Ensemble (JPACE) program with final transition to the Joint Chemical Biological Ensemble. Four technical approaches to develop residual life indicators (RLI) for protective clothing are being pursued. One RLI contractor is building a commercial version.
- 4736 CBIS - Develop prototypes for laboratory and field testing. This ensures force medical protection by sampling and recording low levels of Chemical/Biological (CB) agents or Toxic Industrial Materials (TIMs) that a warfighter may be exposed to. This testing will provide information necessary for the collection of targeted CB agents and TIMs at concentrations less than or equal to the Mild Effects Dose (MED), which is defined as the ocular or nasal vapor exposure level at the onset of miosis.
- 4736 Consequence Management Information System (CMIS) - Initiate development of an integrated command and control tool for displaying information relating to all aspects of Weapons of Mass Destruction (WMD) incident response.
- 4052 SUBD - Complete Phase I and II and provide an engineering prototype of components that successfully demonstrates the concept of an automated man-portable system. These prototypes will be comprised of (1) a collector/concentrator that samples the air and concentrates biological aerosols into a fluid media suitable for analysis and (2) a bio-sensor that analyzes the collected samples and identifies the biological agent in 5 to 10 minutes by using immunoassay technology. Initiate Phase III (pre-manufacture prototype development) which will integrate, fabricate, and test an Engineering Prototype based on these components.
- 1000 Small Fast CB Detectors - Conduct warfighting experiment using a proof-of-principle version of the detection system to demonstrate operational application of the concept. Assess the military utility of using small-scale sensors to detect biological or chemical agents in near real-time and relay that information in a timely fashion to tactical elements.
- 293 SBIR/STTR.

Total 20223

FY 2001 Planned Program:

- 740 JSWILD - Demonstrate brassboard system and transition technology to Program Definition and Risk Reduction (PDRR).
- 1985 JCBAWM - Initiate planning for technology transition to PDRR.

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BUDGET ACTIVITY 3 - Advanced Technology Development	PE NUMBER AND TITLE 0603384BP CHEMICAL/BIOLOGICAL DEFENSE (ADVANCED DEVELOPMENT)	
PROJECT CB3		
FY 2001 Planned Program (Cont):		
<ul style="list-style-type: none"> • • 	<ul style="list-style-type: none"> 2313 JSSED - Conduct development of sensitive equipment/items decontamination technologies (Block-I) with emphasis on the advanced development of technologies for interior decontamination (Block-II/III). Support the Defense Systems Acquisition Management Program which provides acquisition and transition management for the JSSED program. 998 Detection Technologies - Initiate evaluation for the transition of technology from man-portable detectors to enhance Joint Chemical Agent Detector (JCAD) and potential to meet requirements for Joint Chemical Biological Universal Detector. 	
Total	6036	

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BUDGET ACTIVITY 3 - Advanced Technology Development	PE NUMBER AND TITLE 0603384BP CHEMICAL/BIOLOGICAL DEFENSE (ADVANCED DEVELOPMENT)	PROJECT CP3
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COST (In Thousands)	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	FY 2004	FY 2005	Cost to	Total Cost
	Actual	Estimate	Estimate	Estimate	Estimate	Estimate	Estimate	Complete	
CP3 COUNTERPROLIFERATION SUPPORT (Adv Tech Dev)	7098	10434	10213	11416	7321	7663	13345	Continuing	Continuing

A. Mission Description and Budget Item Justification:

Project CP3 COUNTERPROLIFERATION SUPPORT (Adv Tech Dev): The mission of the Counterproliferation Program (CP) is to address shortfalls in the Department of Defense (DoD) deployed capability to defend against and counter the proliferation of weapons of mass destruction (WMD). By focusing on near term results, the CP accelerates delivery of new tools, equipment, and procedures to combat forces. Under the passive defense pillar, CP enhances the efforts of the Chemical and Biological Defense Program. This project funds a variety of programs to defend our forces against WMD, such as the Biological Detection (BIODET), Biological Non-Systems (BIO Non Sys) efforts, Critical Reagents Program (CRP), and Restoration Operations (RestOps).

FY 1999 Accomplishments:

- 600 BIODET - Transitioned advanced materials technologies developed for the Miniaturized Environmental Air Sampler and Concentrator for Biological Materials to the combined aerosol sampler and detector.
- 3060 BIODET - Continued advanced technologies development for high sensitivity biological/chemical agent detection using broadband, miniaturized mass spectrometer techniques.
- 985 BIODET - Continued development upconverting phosphor technology development for miniaturized flow cytometer biological agent detection prototype.
- 583 BIO Non Sys - Collected background aerosol particle data and liquid samples for identification of potential battlefield interferents at outside the continental United States (OCONUS) fixed sites.
- 1870 RestOps - Continued concept development for technology prototyping with supporting survivability and hazard analysis for restoration of operations.

Total 7098

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PE NUMBER AND TITLE

PROJECT

3 - Advanced Technology Development**0603384BP CHEMICAL/BIOLOGICAL DEFENSE
(ADVANCED DEVELOPMENT)****CP3****FY 2000 Planned Program:**

- 943 BIODET - Initiate development of biological identification system using nucleic acids to allow for a less expensive and broader biological detection capability.
- 492 BIODET - Transition of upconverting phosphor technology development for miniaturized flow cytometer biological agent detection prototype.
- 1426 BIODET - Complete first generation of Biological Time-of-Flight (BIOTOF) Mass Spectrometer for transition to field testing.
- 382 CRP - Develop reagents (antibodies and antigens) that are critical to the development, testing, and support of CP Biological Detection Systems.
- 1072 BIO Non Sys - Development, testing and evaluation of automated sample preparation technology for Polymerase Chain Reaction (PCR) devices.
- 2148 BIO Non Sys - Initiate development of non-specific detection, multiplexed assays and associated reagents.
- 1967 RestOps - Initiate development of next generation chemical/biological transport models (to include complex terrain and urban environment) and simulations for Commander in Chief (CINC) Logistics/Warfighting Planning Tools for use the RESTOPS ACTD.
- 1853 RestOps - Initiate development of novel universal chemical/biological decontaminants for use in the RESTOPS ACTD and fixed site decontamination programs.
- 151 SBIR/STTR.

Total 10434

FY 2001 Planned Program:

- 1730 BIODET - Produce nucleic primer libraries for testing and continue development of a biological detection capability using nucleic acids.
- 978 BIODET - Initiate development of new antibodies or their replacements using advanced molecular techniques to achieve faster and less expensive antibody production for use in biological detector assays.
- 386 CRP - Continue to develop reagents (antibodies and antigens) that are critical to the development, testing, and support of CP Biological Detection Systems.
- 2224 BIO Non Sys - Continue development of non-specific detection, multiplexed assays and associated reagents to provide increased identification capability within current hardware constraints.
- 1448 BIO Non Sys - Continue development, testing, and evaluation of automated sample preparation technology and protocols for Polymerase Chain Reaction (PCR) devices to improve identification specificity and sensitivity in future biological systems.
- 759 BIO Non Sys - Initiate development for next generation environmental air sampler to reduce size and improve detection capability.

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BUDGET ACTIVITY 3 - Advanced Technology Development	PE NUMBER AND TITLE 0603384BP CHEMICAL/BIOLOGICAL DEFENSE (ADVANCED DEVELOPMENT)	
PROJECT CP3		
FY 2001 Planned Program (Cont):		
<ul style="list-style-type: none"> • • 	<ul style="list-style-type: none"> 1344 RestOps - Continue development of next generation chemical/biological transport models (to include complex terrain and urban environment) and simulations for CINC Logistics/Warfighting Planning Tools for use in the RESTOPS ACTD and other fixed site applications. 1344 RestOps - Continue development of universal novel chemical/biological decontaminants for use in the RESTOPS ACTD and fixed site decontamination programs. 	
Total	10213	

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BUDGET ACTIVITY 3 - Advanced Technology Development	PE NUMBER AND TITLE 0603384BP CHEMICAL/BIOLOGICAL DEFENSE (ADVANCED DEVELOPMENT)	PROJECT TB3
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COST (In Thousands)	FY 1999 Actual	FY 2000 Estimate	FY 2001 Estimate	FY 2002 Estimate	FY 2003 Estimate	FY 2004 Estimate	FY 2005 Estimate	Cost to Complete	Total Cost
TB3 MEDICAL BIOLOGICAL DEFENSE (Adv Tech Dev)	14079	16809	19980	23063	33154	50328	40819	Continuing	Continuing

A. Mission Description and Budget Item Justification:

Project TB3 MEDICAL BIOLOGICAL DEFENSE (Adv Tech Dev): This project funds preclinical development (pre-MS I activities) of safe and effective prophylaxes and therapies (vaccines and drugs) for pre- and post-exposures to biological threat agents. This project also supports the advanced technology development of diagnostic devices to rapidly diagnose exposure to biological agents in clinical samples. A broad range of technologies involved in the targeting and delivery of prophylactic and therapeutic medical countermeasures is evaluated so that the most effective countermeasures are identified for transition to Advanced Development (post-MS I). Transitioning candidate vaccines, therapeutics and diagnostic systems to Advanced Development requires the development of scientific/regulatory data packages (preclinical safety, efficacy and toxicity, regulatory documentation on quality control systems) to support the MS I decision, the Food and Drug Administration's (FDA) Investigational New Drug (IND) process, and, in the case of vaccines, preparation of a Biological License Application (BLA) to obtain a licensed product.

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PE NUMBER AND TITLE

PROJECT

3 - Advanced Technology Development**0603384BP CHEMICAL/BIOLOGICAL DEFENSE
(ADVANCED DEVELOPMENT)****TB3****FY 1999 Accomplishments:**

- 520 Bacterial Countermeasures - Showed that existing candidate vaccines were effective against selected emerging threat agents or genetically engineered microbes. Compared candidate surrogate markers of immunity to validate vaccine efficacy. Developed system for comparison of genomic sequence database of threat agents and their virulence factors.
- 1870 Bacterial Countermeasures - Compared protective efficacy of live attenuated vs. subunit vaccines (Brucella); initiated development of a surrogate marker ELISA using a monoclonal antibody to the plague F1 protein and initiated evaluation of immune serum derived from dose-response studies in mice; performed initial safety and efficacy studies for typhus and plague vaccine candidates.
- 3703 Toxin Countermeasures - Transitioned recombinant vaccines against botulinum neurotoxin stereotypes A, B, C, E and F to MS I; determined toxicity of drugs in animal models to evaluate use in therapeutic treatment of botulinum neurotoxin and Staphylococcal enterotoxin exposure.
- 1889 Toxin Countermeasures - Continued preclinical trials of ricin A subunit vaccine candidate for safety and efficacy and evaluated surrogate markers of protection; conducted preclinical safety and efficacy trials of ricin A chain in second animal species.
- 1008 Viral Countermeasures - Evaluated data to support eventual milestone transition of eastern equine encephalitis (EEE) virus and western equine encephalitis (WEE) virus vaccines; obtained MS I decision to transition VEE 1A/B infectious clone vaccine candidate to Phase 1; and constructed rapid assay and confirmation-level assay systems for the orthopox viruses to differentiate smallpox.
- 1969 Viral Countermeasures - Evaluated the safety and efficacy of Marburg and Ebola vaccine candidates in animal models; demonstrated for the first time a vaccine candidate that induces protection against Marburg virus.
- 2639 Diagnostics - Evaluated stability of immunological diagnostic reagents and potential endogenous interfering substances to circumvent interference interactions when tested on multiplexed diagnostic platforms; compared candidate diagnostic technologies for down-selection development of diagnostic devices and tests.
- 481 Bacterial/Viral Countermeasures - Began evaluation of multiple vaccine candidates in replicon and naked DNA simultaneous challenge models; constructed models for multivalent vaccines including use of viral (replicon)- or bacterial (Brucellae)-vectored vaccines or DNA vaccines; tested selected combinations of replicon vaccine constructs in animal models and demonstrated that this approach allowed successful immunization in animal models.

Total 14079

FY 2000 Planned Program:

- 1361 Bacterial Countermeasures - Assess the efficacy of new antibiotics against classical threat agents.

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PROJECT

3 - Advanced Technology Development**0603384BP CHEMICAL/BIOLOGICAL DEFENSE
(ADVANCED DEVELOPMENT)****TB3****FY 2000 Planned Program (Cont):**

- 1929 Toxin Countermeasures - Prepare (collect, analyze, validate, and organize) all scientific, technical and regulatory documentation in accordance with Food and Drug Administration (FDA) and DoD acquisition requirements to transition to Phase I (i.e., post-MS I) a ricin A subunit vaccine that will protect and reduce lung injury due to inhaled ricin.
- 567 Toxin Countermeasures - Finalize preparation of scientific, technical and regulatory documentation in accordance with FDA and DoD acquisition requirements (transition documentation) supporting the MS I transition of the recombinant multivalent vaccine candidate for botulinum neurotoxins.
- 2099 Toxin Countermeasures - Prepare (collect, analyze, validate, and organize) all scientific, technical and regulatory documentation in accordance with Food and Drug Administration (FDA) and DoD acquisition requirements to transition a Staphylococcal enterotoxin B (SEB) vaccine candidate to Phase I (i.e., post-MS I).
- 2269 Viral Countermeasures - Compare candidate filovirus vaccines in animal models for safety and efficacy against aerosolized filoviruses.
- 794 Viral Countermeasures - Transition to Phase I (i.e., post-MS I) a multivalent vaccine effective against Venezuelan equine encephalitis (VEE) types 1 A/B/C, 1E, and III.
- 284 Viral Countermeasures - Compare efficacy of candidate therapeutic countermeasures against aerosol challenge with orthopox viruses.
- 1133 Diagnostics - Validate PCR and immunologically-based diagnostic assays for a panel of classic, simulated, and potential BW threat agents.
- 1959 Diagnostics - Compare nucleic acid-based methodologies allowing for rapid identification of the genetic association/genetic distance between biological agents leading to the capability to rapidly determine the potential biological threat in the field.
- 1423 Diagnostics (Medical CB Counter Terrorism Response) - Develop and test technologies for biological agent identification; develop laboratory procedures specific for medical diagnosis/identification of chemical/biological (C/B) agent exposure; develop information/educational modules for collecting and processing samples; provide initial technical training for biological counterterrorism response on assays for transition to Rapid Assessment and Initial Detection (RAID) teams operational units of National Guard Mobile Analytical Laboratory System [MALS].
- 1725 Bacterial/Viral Countermeasures/Diagnostics - Continue to compare candidate technologies in applied research on diagnostic devices and tests. Continue advanced screening for efficacy of therapeutic interventions gleaned from genomic sequencing studies, as applied to known threat agents. Continue to develop candidate surrogate markers of immunity for validation as acceptable markers of vaccine efficacy. Compare novel therapies and vaccines developed against genetically engineered potential threats. Prepare preliminary safety and efficacy data for candidate medical countermeasures to emerging threat agents.
- 1022 Bacterial/Viral Countermeasures - Evaluate immunogenicity of a multi-agent vaccine and analyze the data for possible interference interactions between the combined components (i.e., whole organisms, antigens, DNA, viral vectors).
- 244 SBIR/STTR.

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PROJECT

3 - Advanced Technology Development**0603384BP CHEMICAL/BIOLOGICAL DEFENSE
(ADVANCED DEVELOPMENT)****TB3****FY 2000 Planned Program (Cont):**

Total 16809

FY 2001 Planned Program:

- 1302 Viral Countermeasures - Assemble scientific data of safety, efficacy, and toxicity of candidate filovirus countermeasures (vaccines and therapeutics) in multiple animal model systems.
- 1148 Diagnostics - Prepare (collect, analyze, validate, and organize) all scientific, technical and regulatory documentation in accordance with Food and Drug Administration (FDA) and DoD acquisition requirements to transition to Advanced Development (post-MS I) a portable diagnostic device to identify threat agent nucleic acids.
- 2574 Diagnostics - Compare nucleic acid-based methodologies allowing rapid identification and genetic association/genetic distance of biological agents leading to the capability to rapidly determine the potential biological threat in the field.
- 2341 Generic Medical Countermeasures - Conduct advanced assessment of immunomodulators and other types of broad-spectrum compounds for safety and for efficacy against multiple biological threat agents.
- 1655 Generic Medical Countermeasures - Perform laboratory investigations to obtain data necessary for transition of DARPA-developed diagnostic and preventive therapeutic technologies to DoD applications: safety studies in animals, efficacy studies in animal models, definition of surrogate markers of efficacy, pharmacokinetic studies, formulation studies, assay development, and down selection of candidate compounds.
- 1424 Bacterial/Viral Countermeasures - Test efficacy of products (individually and combined) intended for use in a multi-agent vaccines.
- 2998 Bacterial/Viral Countermeasures - Evaluate candidate immunomodulation strategies using cytokines, chemokines, and cellular receptors as subcellular targets as sites of intervention in the pathogenic process.
- 1391 Bacterial Countermeasures - Evaluate previously identified virulence factors as vaccine candidates for Yersinia pestis; test selected immunomodulators in appropriate animal models, for protection against plague; validate correlates of immunity for protection against Bacillus anthracis; evaluate vaccine candidates and correlates of immunity for Burkholderia mallei.
- 544 Viral Countermeasures - Assemble scientific data from safety, efficacy, and toxicity studies of candidate therapeutic compounds to orthopox viruses in animal models.
- 2302 Bacterial/Viral Countermeasures/Diagnostics - Validate animal models defining agent pathogenesis and immunology. Complete comparison of candidate diagnostic technologies in applied research on diagnostic devices and tests. Complete development of surrogate markers of immunity for validation as acceptable markers of vaccine efficacy.

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PROJECT TB3		
FY 2001 Planned Program (Cont):		
<ul style="list-style-type: none"> • 	2301 Bacterial/Viral Countermeasures - Complete screening of therapeutic interventions gleaned from genomic sequencing studies, as applied to known threats and their virulence factors. Complete demonstration of usefulness of existing candidate medical countermeasures applied to emerging threat agents or genetically engineered microbes. Demonstrate animal models defining agent pathogenesis and immunology. Demonstrate promising generic medical countermeasures against threat agents for exploratory development studies in suitable model systems.	
Total	19980	

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BUDGET ACTIVITY 3 - Advanced Technology Development	PE NUMBER AND TITLE 0603384BP CHEMICAL/BIOLOGICAL DEFENSE (ADVANCED DEVELOPMENT)	PROJECT TC3
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COST (In Thousands)	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	FY 2004	FY 2005	Cost to	Total Cost
	Actual	Estimate	Estimate	Estimate	Estimate	Estimate	Estimate	Complete	
TC3 MEDICAL CHEMICAL DEFENSE (Adv Tech Dev)	16603	9445	10365	11111	11784	12309	12614	Continuing	Continuing

A. Mission Description and Budget Item Justification:

Project TC3 MEDICAL CHEMICAL DEFENSE (Adv Tech Dev): This project supports the investigation of new medical countermeasures to include antidotes, pretreatment drugs, and topical skin protectants to protect U.S. forces against known and emerging chemical warfare (CW) threat agents. Capabilities are maintained for reformulation, formulation, and scale-up of candidate compounds using current good laboratory practices (GLP). Analytical stability studies and safety and efficacy screening, in addition to pre-clinical toxicology studies, are performed prior to full-scale development of promising pretreatment or treatment compounds.

FY 1999 Accomplishments:

- 1351 Pretreatments - Conducted dose-ranging studies and efficacy studies of candidate nerve agent scavengers.
- 1111 Pretreatments - Assessed the efficacy of and rank ordered 160 barrier creams for reactive topical skin protectants. This led to the down-selection of eight candidates, which will lead to Milestone 0 in FY00.
- 4382 Therapeutics - Assessed efficacy and safety of lead candidate antivesicants in vivo models in support of FY00 Milestone 0.
- 417 Therapeutics - Determined the efficacy of available off-the-shelf, FDA-approved ocular therapies against sulfur mustard (HD). Evaluated in an animal model selected available therapeutic interventions for inhalation exposure to HD, and continued testing of candidate therapies effective against the pulmonary consequences of HD exposure.
- 2123 Therapeutics - Initiated Milestone I technical data package for advanced anticonvulsant. Completed nonhuman primate pharmacokinetic/pharmacodynamic studies with advanced anticonvulsants, which determined the optimal blood levels effective against nerve agent seizures.
- 7219 Therapeutics - Evaluated a research proposal by Wright State University (WSU) to study health effects of low-level exposure to chemical warfare agents. Conducted an extramural and intramural review and provided comments to WSU. Funding is being released based on revised WSU proposals.

Total 16603

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3 - Advanced Technology Development**0603384BP CHEMICAL/BIOLOGICAL DEFENSE****TC3****(ADVANCED DEVELOPMENT)****FY 2000 Planned Program:**

- 5960 Therapeutics - Prepare supporting documentation for Milestone 0 technical data package for lead countermeasures for vesicant agents. Select lead candidate countermeasures from in vivo and in vitro screens performed at a contractor owned, contractor operated facility dedicated to the medical chemical defense research program. Acquire drugs/compounds in forms acceptable for advanced antivesicant testing.
- 546 Pretreatments and Therapeutics - Select lead compounds for safety and efficacy testing in nonhuman primates against novel threat agents.
- 1756 Pretreatments - Estimate the protection achievable by lead candidate scavengers in animal models.
- 523 Pretreatments - Initiate Phase 0 studies for efficacy and safety of best candidate reactive moieties for reactive topical skin protectants.
- 523 Therapeutics - Confirm the efficacy and safety of advanced anticonvulsant in two animal species, identify important potential interactions with other countermeasures, and transition candidates to Phase 1.
- 137 SBIR/STTR.

Total 9445

FY 2001 Planned Program:

- 1606 Diagnostics - Acquire, modify, and measure advanced development equipment or technologies for far-forward screening and confirmation of exposure to blister and nerve agents; conduct market investigations of existing commercial technologies and test suitability of these items.
- 4443 Pretreatments - Select best bioscavenger candidate(s) for nerve agents based on comparison of performance in decision tree network and other differentiating studies.
- 1796 Therapeutic - Select best countermeasure to novel threats based on comparison of performance in decision tree network and other differentiating studies.
- 2520 Therapeutics - Select best countermeasure to vesicants based on comparison of performance in decision tree network and other differentiating studies. Conduct safety and efficacy studies in higher animal species as part of concept exploration phase.

Total 10365