RDT&E BUDGET ITEM JUSTIFICATION SHEET (R-2 Exhibit)								DATE February 2002	
APPROPRIATION/BUDGET ACTIVITY RDT&E, Defense-wide BA2 Applied Research				R-1 ITEM NOMENCLATURE Biological Warfare Defense PE 0602383E, R-1 #16					
COST *(In Millions)*	FY 2001	FY2002	FY2003	FY2004	FY2005	FY2006	FY2007	Cost To Complete	Total Cost
Total Program Element (PE) Cost	146.216	146.680	133.000	142.000	140.000	140.000	140.000	Continuing	Continuing
Biological Warfare Defense Program BW-01	146.216	146.680	133.000	142.000	140.000	140.000	140.000	Continuing	Continuing

(U) Mission Description:

(U) DARPA's Biological Warfare Defense project is budgeted in the Applied Research Budget Activity because its focus is on the underlying technologies associated with pathogen detection and remediation. This project funds programs supporting revolutionary new approaches to biological warfare (BW) defense and does not duplicate efforts of other government organizations.

(U) Efforts to counter the BW threat include developing barriers to block entry of pathogens into the human body (including unique methods for rapid air and water purification), countermeasures to stop pathogen and chemical consequence and to modulate host immune response, medical diagnostics for the most virulent pathogens and their molecular mechanisms, biological and chemically-specific sensors, advanced decontamination and neutralization techniques, consequence management tools, and integrated defensive systems. Program development strategies include collaborations with pharmaceutical, biotechnology, government, and academic centers of excellence.

(U) Pathogen countermeasures (e.g., Anti-Virals/Immunizations, Anti-Bacterials/Anti-Toxins, Multi-Purpose, and External Protection) under development include: (1) multi-agent therapeutics against known, specific agents and (2) therapeutics against virulence pathways shared by broad classes of pathogens. Specific approaches include developing a new class of antibiotics targeted to enzymes essential to bacterial pathogen survival, identification of virulence mechanisms shared by pathogens, development of therapeutics targeting these mechanisms, efficacy testing in cell cultures and animals, and advanced non-toxic decontamination strategies. The development of an artificial immune system through 3- dimensional tissue engineering will provide rapid, in vitro assessments of novel countermeasures against unique DoD threat agents.

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(U) In the early stages, many illnesses caused by BW agents have flu-like symptoms and are indistinguishable from non-BW related diseases. Early diagnosis is key to providing effective therapy. The advanced diagnostics efforts will develop the capability to detect the presence of infection by biological threat agents, differentiate them from other pathogens (including those of non-BW origin), and identify the pathogen even in the absence of recognizable clinical signs and symptoms (i.e., while the pathogen numbers are still low).

(U) The ability to rapidly detect biological warfare agents on the battlefield with a low false-alarm rate is a crucial requirement. To address this need, the program is creating more efficient and effective miniature sampling technologies that concentrate contaminated air and enhance the ability to capture biological warfare agents. The program is developing a new range of antibodies and "designer small molecules" to bind specific agents (to replace the lower affinity antibodies currently used). A biosensor based on universal probes is being developed for detecting known and possibly bio-engineered pathogens, as an environmental sensor and a diagnostic tool. The use of fluids as a requirement for biological agent detection is also being eliminated and replaced by a miniaturized time-of-flight mass spectrometer. Development of a bacterial biochip to identify genus and species without multiplying the DNA by the polymerase chain reaction (PCR) is also under development, thereby potentially saving over half the time required for identification. Additional efforts are focusing on standoff biological/chemical sensors, as well as the construction of molecular, cellular, and multicellular sensors for the rapid detection of biological threats. These cellular and tissue-based sensors have the ability to respond to both known and unknown threats, determine live vs. inactivated threat status, and report functional consequences of exposure (mechanisms of action). The use of organisms such as insects is also being explored as information collectors for environmental biological or chemical threats. A variety of applications for these sensors are being explored including protection of buildings from a biowarfare agent attack as well as novel surveillance systems for non-battlefield environments.

(U) DARPA is developing technologies for integrated defensive systems to be employed in military buildings to protect inhabitants and to enhance the capability to decontaminate exposed surfaces. The approach is to modify and augment the infrastructure of buildings to allow them in real-time to sense and defeat an attack by bio or chem agents. The program has three goals: to protect the human inhabitants from the effects of the agents; to restore the building to function quickly after the attack; and to preserve forensic evidence for treatment of victims, if necessary, and for attribution. The DARPA focus is on the challenging problem of protection from internal releases of agent, where active and timely control of airflow is required to prevent a building's HVAC system from spreading the agent throughout the building. To enable such building-protection systems, DARPA is pursuing low-pressure-drop filters, advanced decontamination and neutralization techniques, and fate and transport models to predict agent location and lethality. In addition, DARPA is investigating the systems-level issues of integrating and optimizing such active systems, as well as portal-barrier technologies to prevent the introduction of agents into facilities. These efforts will use full-scale test facilities to determine the effectiveness of protection components and to experiment with various strategies and architectures for protection. These experiments will be

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followed by systems design and optimization, initially targeted at the most proliferated threats and then progressing to more challenging future threats. This effort will culminate with a full-scale demonstration of a complete building protection system at a military installation and will leave behind a software tool for the design and optimization of building-protection systems for other military buildings.

(U) The Biological Warfare Agent (BWA) Surveillance Techniques program will develop and demonstrate effective and efficient BWA surveillance systems for urban environments, such as military bases and transportation centers, to detect a covert aerosol release of a BWA and to determine the approximate release location *before the onset of symptoms in humans*. The program will investigate the key architecture trades, including: the appropriate mix of stationary and mobile assets (collectors/samplers and identification sensors); the value of distributed sampling and identification (sensing) versus distributed sampling with centralized identification; the role of layered sensing, such as continuous wide-area surveillance followed by focused/targeted collects for confirmation; the importance of spatial and temporal resolution in enabling backtracking to determine release time and release location; and specialized collection and identification requirements in different environments. These trades will be carried out by modeling covert releases and then analyzing the ability of various architectures (1) to detect the release quickly and (2) to geo-locate the source. System cost and complexity will also be evaluated, and baseline background data will be collected. After the evaluation of candidate architectures, the program will develop a system design; develop the components (samplers, sensors, networking, and algorithms) as required; build and integrate the surveillance system; and demonstrate overall system performance.

(U) Mission effectiveness requires rapid, correct medical responses to biological weapon threats or attacks. This project has provided comprehensive protocols to protect or treat combatants by using current and emerging biological countermeasures. It provided accelerated situational awareness for biological warfare events by detecting exposure to agents through an analysis of casualty electronic theater medical records and located and determined the most effective logistical support for providing appropriate treatment and pathogen-specific resources required to mitigate effects of the attack. The last year of funding for this effort was FY 2001.

(U) DARPA worked with a number of governmental organizations to exploit recent advances in high throughput genetic sequencing to obtain complete genetic information on a number of important pathogens and their non-pathogenic nearest neighbors. This allowed development of an inventory of genes and proteins that distinguish pathogens from non-pathogens and to identify pathogenic markers in any guise. This information will be used to provide superior molecular targets and enable new generations of detectors, diagnostics, and therapeutics. Funding completed for this program in FY 2001.

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(U) The DNA Chip Technology Research program investigated the value of a new concept of "data mining" using the repetitive sequence-based polymerase chain reaction (PCR) patterns from a large data of biowarfare agents and the feasibility of using this approach on high-density microchips.

(U) DARPA also explored non-traditional approaches to desalination and evaluated the potential of delivering immune system enhancement via inhalation for defense against BW threats.

(U) Program Accomplishments and Plans:

(U) FY 2001 Accomplishments:

- Anti-Virals/Immunizations. ($20.300 Million)
  - Tested and validated (in-vivo) a method of mucosal immunization based upon high level expression of pathogen antigens and epithelial transport molecules in edible transgenic plant products.
  - Tested and validated (in-vivo) the protective efficacy of vaccines and antibodies produced by plant cells against pathogens.
  - Demonstrated efficacy of the rapid and efficient delivery of pathogen antigens via new genetic vaccine vectors.
  - Demonstrated (in-vivo) the rapid design and development of new vaccines (or therapeutics) against unidentified or unknown pathogens.
  - Demonstrated broad-spectrum strategies with potential for immunomodulatory activity against multiple pathogens.

- Anti-Bacterials/Anti-Toxins. ($20.647 Million)
  - Demonstrated surface expression of specific enzyme molecules for the rapid inactivation of various pathogens.
  - Demonstrated (in-vivo) the efficacy of a broad-spectrum bacterial pathogen antagonist.
  - Validated (in-vivo) broad spectrum, superantigenic, anti-toxin antagonists and vaccines.
  - Demonstrated (in-vivo) efficacy of broad spectrum, superantigenic, antitoxin antagonists and vaccines.

- Multi-Purpose. ($21.833 Million)
  - Developed therapeutic strategies against bioregulators and other mid-spectrum agents.

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- Demonstrated synthetic polymer complements for pathogenic antigens and virulence factors.
- Developed therapeutic strategies for minimizing harmful immune responses to biological warfare agents.
- Demonstrated (in-vitro) the efficacy of monomeric and dimeric DNA and RNA binding molecules as novel countermeasures against multiple pathogens.
- Validated polyvalent inhibitors for blocking pathogens on the surface of target cells in-vivo.
- Identified superantigen antagonist for broad protection against biological warfare agents with minimal side effects.
- Validated (in-vivo) the efficacy of subcellular pathogen response imaging for rapid detection.
- Validated technologies broadly applicable to enhance cellular therapeutics (delivery platforms) and virulence modulation (intracellular and inflammatory cascades).

- External Protection. ($10.600 Million)
  - Developed a novel architectural approach for the manufacture of materials that are effective in blocking pathogens and limiting disease.
  - Demonstrated a non-aqueous advanced decontamination method.
  - Demonstrated a water purification system effective against a range of biological agents (including toxins and bioregulators).
  - Tested initial performance of advanced sorbent materials for the purification of air contaminated with CW and BW agent simulants for individual protection.
  - Built and tested a prototype air purification system for collective protection for a group of soldiers.
  - Began testing a prototype protective system against non-virulent biological warfare agents, bio-toxins and regulators.

- Advanced Diagnostics. ($12.681 Million)
  - Tested probe panels in relevant sample types including strategies for rapidly generating new/novel probes.
  - Demonstrated that sample collection and/or preparation techniques do not introduce artifacts.
  - Tested, in model systems, one or more of the most promising candidate strategies for rapid detection based on bodily responses or other biomarkers to provide early indication of infection or exposure.
  - Developed the capability to diagnose exposure to bio-regulator and mid-spectrum agents.
  - Demonstrated, in the laboratory, the feasibility of engineering red blood cells to detect and signal pathogen presence in the body.

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- Evaluated the feasibility of additional strategies (e.g., exhaled breath) for direct identification or detection of infection without direct sample collection.
- Demonstrated the ability to perform accelerated patient diagnosis using a rapid single molecule DNA sequencing technique in a model system.

- Sensors. ($25.800 Million)
  - Completed development and testing of first-generation prototype biochip sensor.
  - Continued the development of effective and rapid chip-reading capability with enhanced sensitivity and low false alarm rate.
  - Continued the development of advanced alternative technologies for live vs. dead bio-agent identification using peptides and other molecules.
  - Developed hierarchical biochip sensors.
  - Designed and tested techniques to replace antibody-based detection, such as short peptides, aptamers and lectins.
  - Designed and tested novel reporting/transduction techniques such as ion channels.
  - Designed and synthesized short peptide binding molecules for use in the detection of biological warfare agents.
  - Evaluated ion channel sensor systems for use in the detection of biological warfare agents.
  - Evaluated methods for removing micro-encapsulation of disguised pathogens and/or sensing through the micro-encapsulation.
  - Developed technologies required for next-generation miniature biological detectors including the use of microelectromechanical systems (MEMS), microfluidics, and mesoscopic-sized components.
  - Evaluated false positive and false negative rates for systems of detectors using biomolecular cells or tissues.
  - Exploited and/or mimicked the olfactory sensors of biological systems for use in the detection of biological warfare agents.
  - Demonstrated enhanced signal output from engineered cells and tissue based sensors and integrated information from these sensors with user interfaces for predictive responses.
  - Engineered a deployable prototype cell and tissue sensor for field-testing.
  - Evaluated sample collection technologies for cell and tissue sensors.
  - Evaluated methods of cell stabilization for possible application to cell based sensors.
  - Developed biosensor models and robust characterization protocols.
  - Evaluated new resonant modes for biosensors.
  - Investigated standoff techniques for trigger and identification.

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- Investigated critical design parameters for advanced biologically based BW sensors.
- Demonstrated use of organisms to collect chemical and biological warfare agents in the field.
- Developed and validated a comprehensive performance model for time-of-flight (TOF) mass spectrometer detection of aerosolized live agents against clutter.
- Evaluated time-of-flight (TOF) mass spectrometer performance for counter-proliferation scenarios.
- Initiated the development, modeling, and validation of integrated sensor systems designed to meet detailed threat specifications.
- Evaluated novel concepts for warning systems, including stationary or mobile-networked surveillance systems.
- Explored a novel concept (Triangulation ID for Genetic Evaluation of Biological Risks [TIGER] biosensor) for universal BW probes as a possible foundation for a new sensor suitable for forensics, biomedical surveillance and environmental sensing and estimated performance against bacteria.
- Explored the use of social insects as BW agent collectors.

- Bio/Chem Defensive Systems. ($13.105 Million)
  - Continued fate and transport model development in and around buildings and began experimental evaluation.
  - Continued to develop decontamination techniques appropriate for structures.
  - Evaluated novel low-pressure-drop, broadband filter technologies.
  - Developed neutralization technologies for aerosolized agents.
  - Conducted hazard assessment for protection of military buildings from bio-chem attack; assessed protection strategies.
  - Identified facilities, and identified/designed the facility modifications required, for full-scale testing and evaluation of building-protection systems.
  - Evaluated concepts for novel protection systems, such as portal barriers.

- Genetic Sequencing of Biological Warfare Agents. ($7.000 Million)
  - Completed the genomic sequencing of high-threat known and potential biowarfare agents.

- Consequence Management. ($6.000 Million)
  - Demonstrated Enhanced Consequence Management Planning and Support System (ENCOMPASS) management of multi-site BW incidents.

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- Demonstrated and fielded the use of ENCOMPASS for CONUS military force protection against BW attacks, i.e., Pacific Battlelab & Kernal Blitz Experiment.
- Transitioned ENCOMPASS components to Initial Detection Units of the Air Force and to PACCOM, JFCOM, and Wilford Hall Medical Center.
- Transitioned ENCOMPASS components into Joint Chiefs of Staff Operations Center.

- Asymmetrical Products for BWD. ($3.750 Million)
  - Explored use of cytokines as biological warfare therapeutics.

- Desalination Research. ($ 3.000 Million)
  - Evaluated non-traditional approaches to desalination.

- DNA Chip Technology Research. ($1.500 Million)
  - Demonstrated feasibility of repetitive sequence polymerase chain reaction (PCR) on microchips.
  - Demonstrated fingerprint profiling of anthrax strains.
  - Determined “electronic barcodes” to distinguish closely related strains.

(U) FY 2002 Plans:

- Anti-Virals/Immunizations. ($18.500 Million)
  - Assess feasibility of modeling viral RNA-protein structural interactions as a strategy to identify new targets for antiviral agents.
  - Identify new target candidates for new classes of anti-viral agents.
  - Demonstrate broad-spectrum therapeutic strategies against viral agents on the validated threat list, including smallpox.
  - Determine the feasibility of using one or more animal systems as a means of developing data sufficient to provide regulatory guidance for the approval of newly developed anti-viral agents effective against verified BW viral threats.
  - Test and validate (in-vitro) candidate antiviral therapeutic(s) developed by combinatorial chemistry for viral infections emanating from validated threats.

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- Test at least one candidate immunogen for mucosal immunization based upon high-level expression of pathogen antigens and epithelial transport molecules in edible transgenic plant products.
- Assess feasibility of strategies to develop edible multiagent vaccines.
- Assess feasibility of virally derived cytokine inhibitors as therapeutics for hemorrhagic fever viruses or other threat agents.
- Develop protocols to enable validated therapeutic products to transition to appropriate Service partner (e.g., USAMRIID).
- Develop strategies for Investigational New Drug (IND) enabling studies.
- Establish and validate common data set testing program for evaluation of transition candidate in standard models.
- Develop novel adjuvants to enhance vaccination, including anthrax, effectiveness.
- Transition shuffled antigen program for enhanced vaccine development to USAMRIID.
- Transition plant-based vaccine production program to USAMRIID.

- Anti-Bacterials/Anti-Toxins. ($18.500 Million)
  - Assess feasibility of identifying appropriate targets for anti-bacterial drug development by creating animal models innately resistant to infection.
  - Explore new concepts for identifying critical targets of host damage by pathogen (e.g., by development and use of animal models with engineered resistance, gene expression profiles).
  - Demonstrate both targeted and broad-spectrum therapeutic strategies against bacterial agents (e.g., anthrax).
  - Determine the feasibility of using one or more animal systems as a means of developing data sufficient to provide regulatory guidance for the approval of newly developed anti-bacterial agents effective against verified BW bacterial threats.
  - Test and validate (in-vivo) high-throughput screening technologies for bacterial infections emanating from validated threats.
  - Develop protocols to enable validated therapeutic products to transition to appropriate Service partner (e.g., USAMRIID).
  - Transition RNA-based discovery technology for drug target identification to USAMRIID.
  - Establish and validate common data set in-vivo qualifying systems for testing broad-spectrum anti-bacterial drugs.
  - Establish drug lead optimization program to facilitate transition process.

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- Assess the opportunity to extend window of effective treatment for late stage BW infection.

- Multi-Purpose. ($22.900 Million)
  - Test one or more candidate therapeutic strategies against bioregulator and other mid-spectrum agents.
  - Test (in-vivo) prototype monomeric and dimeric DNA and RNA binding molecules as novel countermeasures against multiple pathogens.
  - Identify novel opportunities to engineer metabolic response to threat agents.
  - Identify mechanisms for protection against catastrophic BW-induced shock.
  - Determine the feasibility of using one or more animal systems as a means of developing data sufficient to provide regulatory guidance for the approval of newly developed therapeutic agents effective against verified BW threats.
  - Demonstrate efficacy of subcellular pathogen response imaging for rapid detection.
  - Develop protocols to enable validated therapeutic products to transition to appropriate Service partner (e.g., immunomodulators).
  - Develop strategies for Investigational New Drug (IND) enabling studies.
  - Develop novel, bactericidal technologies for rapid post exposure treatment.
  - Evaluate ethyl-nitroso-urea (ENU) forward mutagenesis technology to create mouse lines that are resistant to BW infections.
  - Begin development of 3-dimensional printing culture system, including novel bioscaffolds for controlled development of artificial immune system.

- External Protection. ($8.180 Million)
  - Test a prototype air purification system for collective protection for a group of soldiers.
  - Demonstrate several individual water purification systems that can treat any biological, chemical or natural contaminant.
  - Demonstrate efficacy of individual air purification carrier technologies to reduce the pressure drop by one half, increase chemical warfare effectiveness factors (50 percent) and provide inherent HEPA filtration.
  - Test and demonstrate gas mask filter technologies against a full array of live BW and CW agents.
  - Demonstrate superior sorbent materials to adsorb CW agents and toxic industrial vapors.

- Advanced Diagnostics. ($18.000 Million)
  - Evaluate hyperspectral strategies for early clinical diagnosis of infection and other medical issues that affect soldier persistence.

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- Validate strategies for rapidly generating new probe panels for relevant sample types.
- Validate, in model systems, lead candidate strategies for rapid detection based on bodily responses or other biomarkers for early indication of infection or exposure.
- Evaluate multiplexed pathogen detection in microliter sample sizes.
- Explore new methods for rapidly sequencing DNA.
- Evaluate non-contact surface electrode for potential clinical applications.

- Sensors. ($30.000 Million)
  - Develop front end sampling modules for cell and tissue based biosensors.
  - Demonstrate utility of cell and tissue based biosensors in operationally relevant scenarios.
  - Identify and quantify the naturally occurring volatile chemicals that plants emit in response to plant and human BW pathogens.
  - Characterize transcriptional responses of plants to plants and human pathogens.
  - Continue development and evaluation of antibody replacement or enhancement techniques.
  - Continue development and evaluation of novel reporting/transduction techniques.
  - Characterize performance of hierarchical biochip sensors.
  - Expand library of signatures for bio-agents in mass spectrometry identification.
  - Optimize time-of-flight (TOF) mass spectrometer detection of aerosol live agents against clutter.
  - Continue time-of-flight mass spectrometer counter-proliferation related work.
  - Develop conceptual designs and critical technologies for novel warning systems, such as networked surveillance systems.
  - Develop Triangulation ID for Genetic Evaluation of Biological Risks (TIGER) gold standard biosensor to support environmental evaluations and system performance model validation.
  - Complete initial optimization of TIGER probe set for bacterial and viral threat.
  - Initiate statistical characterization of clutter for TIGER probe sets.
  - Explore BW background spectral signatures and initiate standoff sensor study to exploit agent unique signatures.
  - Develop front end sampling modules for cell and tissue based biosensors.
  - Demonstrate utility of cell and tissue based biosensors in operationally relevant scenarios.
  - Demonstrate the utility of social insects as BW agent collectors.
  - Evaluate rapid throughput methods for spore formers mortality due to decontamination.

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- Bio/Chem Defensive Systems. ($24.000 Million)
  - Continue fate and transport modeling around buildings for use in design and optimization of building-protection systems.
  - Continue development of building-appropriate decontamination techniques.
  - Evaluate novel approaches to combined filtration/neutralization.
  - Complete preliminary prototypes of enabling filtration, neutralization, and decontamination technologies for evaluation at full-scale.
  - Modify and instrument test facilities for evaluating building-protection systems.
  - Install preliminary protection components and prototypes into test facility.
  - Begin preliminary systems-level evaluation of protection strategies.
  - Initiate development of critical technologies for novel protection systems, such as portal barriers. Evaluate technologies suited to mail/package screening.

- Center for Water Security. ($1.000 Million)
  - Identify unique water purification techniques tailored to provide safe, potable water to population centers.
  - Resolve fundamental technical issues associated with large-scale purification techniques.

- Asymmetrical Products for BWD. ($3.000 Million)
  - Continue to explore use of cytokines as biological warfare therapeutics.

- Desalination Research. ($2.600 Million)
  - Continue to evaluate non-traditional approaches to desalination.

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(U) FY 2003 Plans:

- Anti-Virals/Immunizations. ($12.000 Million)
  - Down-select successful animal model system(s) and validate utility in the regulatory process for newly developed anti-viral agents against validated threat list agents.
  - Test initial viral targets identified by modeling viral RNA-protein interactions.
  - Demonstrate efficacy and validate (in-vivo) candidate antiviral therapeutic developed by combinatorial chemistry for viral infections emanating from validated threats.
  - Test candidate virally-derived cytokine inhibitor as a therapeutic for hemorrhagic fever viruses or other threat agents.
  - Evaluate (in-vivo) prototype multi-agent (two or more antigens) edible/mucosal vaccine.
  - Implement protocols to enable validated therapeutic products to transition to appropriate Service partner.
  - Implement strategies for Investigational New Drug (IND) and New Drug Application (NDA) enabling studies.
  - Develop in-vitro model system to evaluate potential of vaccine candidates.

- Anti-Bacterials/Anti-Toxins. ($12.000 Million)
  - Evaluate strategies for new therapeutics based on critical targets of host damage by pathogen (e.g., by development and use of animal models with engineered resistance, gene expression profiles).
  - Evaluate utility of animal models innately resistant to infection for identifying new therapeutic targets and host resistance factors.
  - Down-select successful animal model system(s) and validate utility in the regulatory process for newly developed anti-bacterial agents against validated threat list agents.
  - Demonstrate efficacy of high-throughput screening technologies in evaluating bacterial infections.
  - Develop strategies for new therapeutics based on host-pathogen signaling pathways and/or controlling pathogen gene expression.
  - Implement protocols to enable validated therapeutic products to transition to appropriate Service partner.
  - Implement strategies for Investigational New Drug (IND) and New Drug Application (NDA) enabling studies.
  - Develop treatment for late stage BW infections.

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- Multi-Purpose. ($15.000 Million)
  - Down-select successful animal model system(s) and validate utility in the regulatory process for newly developed therapeutic agents against validated threat list targets.
  - Demonstrate broadly applicable technologies to enhance cellular therapeutics and virulence modulation.
  - Evaluate (in-vivo) and validate monomeric and dimeric DNA and RNA binding molecules as novel countermeasures against multiple pathogens.
  - Identify and develop additional targets for subcellular pathogen imaging.
  - Implement protocols to enable validated therapeutic products to transition to appropriate Service partner.
  - Implement strategies for Investigational New Drug (IND) enabling studies.
  - Demonstrate novel approach in engineering metabolic responses to threat agents.
  - Develop methods for providing super normal protection from BW induced shock.
  - Engineer biological system with altered metabolic rate that demonstrates increased longevity and stability.
  - Optimize application of tissue engineering to DoD needs, including directed healing, tissue sculpting, and device development for two-dimensional and three-dimensional structures.
  - ID mutated genes that create BW resistance in mouse ethyl-nitroso-urea (ENU) models as potential targets for developing novel protective agents.
  - Develop bioreactive scaffolding for controlled release of differentiation factors in 3-dimensional tissue precursors.
  - Combine printing, scaffolding and differentiation to demonstrate in vitro organ constructs for immune system.

- External Protection. ($7.500 Million)
  - Demonstrate an air purification system suitable for both personal warfighter protection and collective protection for a group of soldiers.
  - Implement protocols to enable demonstrated protective products to transition to appropriate Service partners.

- Advanced Diagnostics. ($13.500 Million)
  - Demonstrate strategies for rapidly generating new probe panels for relevant sample types.
  - Demonstrate, in model systems, lead candidate strategies for rapid detection based on bodily responses or other biomarkers for early indication of infection or exposure.

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- Demonstrate multiplexed pathogen detection in microliter samples.
- Demonstrate new methods for rapid sequencing DNA.

- Sensors. ($25.000 Million)
  - Develop genomics-based tools to engineer plant and other organism responses to pathogens and chemicals in ways that are observable at a distance.
  - Integrate and test molecular replacement components into sensor systems.
  - Develop networked biosensors and algorithms for their integration to reduce false alarms.
  - Optimize biochip sensor and software analysis.
  - Complete optimization of Triangulation ID for Genetic Evaluation of Biological Risks (TIGER) probe set for full threat spectrum against clutter.
  - Complete TIGER biosensor performance modeling and prototpe preliminary design (PDR).
  - Demonstrate cell and tissue sensors in air and water quality applications.
  - Evaluate metrics of performance for social insect BW agent collector systems in the field.
  - Begin exploring the possibility that microbe specific chemical agents can tag microbial aerosols and make them observable at a distance via spectrometry.
  - Continue development of new engineering tools for designing and enhancing biological regulatory circuits.

- Bio/Chem Defensive Systems. ($32.000 Million)
  - Complete development of building-appropriate filtration, neutralization, combined filtration/neutralization, and decontamination techniques, and produce prototypes for full-scale testing.
  - Evaluate prototype performance against live agents in appropriate testing facilities.
  - Based on FY02 experimentation, design and implement full-scale protection systems optimized for a subset of threats. Carry out full-scale testing of system performance.
  - Collect data in full-scale test facilities for validation of transport models.
  - Develop software models of component and system behavior.
  - Initiate integration of software-based planning tool to model threat and mitigation effectiveness for building protection.

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- Select military site for full-scale demonstration of building protection, and begin site characterization including chemical/biological background sampling.
- Perform threat assessment for demonstration site.
- Continue technology development and develop the design and infrastructure requirements for novel protection systems. Conduct feasibility experiments for mail/package screening.

- BW Surveillance Techniques. ($ 9.000 Million)
  - Conduct trade studies of various potential detection architectures in selected urbanized areas; estimate system performance.
  - Initiate technology development to optimize components for this application.
  - Initiate development of analytic methods to geo-locate source based on detector output, meteorology, etc.
  - Initiate extensive background characterization experiments.

- Stand-Off BWD Sensors. ($ 7.000 Million)
  - Conduct controlled measurements of aerosol signature (fluorescence lifetime, Raman scattering, laser induced breakdown spectroscopy, etc.).
  - Develop predictive models for use in evaluating stand-off sensor concepts.
  - Develop prototypes of advanced techniques such as Surface Enhanced Raman Spectroscopy and UV Resonant Enhanced Raman Spectroscopy.

(U) **Program Change Summary: (*In Millions*)**	**FY 2001**	**FY 2002**	**FY 2003**
FY02 Amended President's Budget	166.769	140.080	140.000
Current Budget	146.216	146.680	133.000

RDT&E BUDGET ITEM JUSTIFICATION SHEET (R-2 Exhibit)	DATE February 2002
APPROPRIATION/BUDGET ACTIVITY RDT&E, Defense-wide BA2 Applied Research	R-1 ITEM NOMENCLATURE Biological Warfare Defense PE 0602383E, R-1 #16

(U) Change Summary Explanation:

FY 2001 Decrease reflects the transfer of the Bio & Chem Terrorism Response Training Program to 0602384BP, the SBIR reprogramming and minor program realignments.

FY 2002 Increase reflects congressional adds for Asymmetrical Protocols for Biological Defense, the Center for Water Security and Hydrate Fractionation Desalination Technology.

FY 2003 Decrease reflects completion of initial development and transition of several anti-viral, multipurpose, and anti-bacterial/anti-toxin pharmaceuticals into pre-approved investigation studies to be conducted by the services, offset by additional sensor and surveillance program efforts.

(U) Other Program Funding Summary Cost:

	FY 2001	FY 2002	FY 2003
Title IX, BWD Post-Exposure Therapeutics	0.000	30.000	0.000
Defense Emergency Response Fund (DERF)	0.000	0.000	(30.000)

Title IX funds were added by Congress for the Biological Warfare Defense (BWD) post-exposure therapeutics program. This effort will take six BW therapeutics far enough into clinical trials to accelerate availability in case of military necessity. In FY 2003, $30 million is requested from the DERF to complete this effort.

(U) Schedule Profile:

- Not Applicable.