RDT&E BUDGET ITEM JUSTIFICATION SHEET (R-2 Exhibit)								DATE June 2001		
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 2000	FY2001	FY2002	FY2003	FY2004	FY2005	FY2006	FY2007	Cost To Complete	Total Cost
Total Program Element (PE) Cost	124.272	166.769	140.080	140.000	156.000	169.000	169.000	169.000	Continuing	Continuing
Biological Warfare Defense Program BW-01	124.272	166.769	140.080	140.000	156.000	169.000	169.000	169.000	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.

(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).

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(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 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) Mission effectiveness requires rapid, correct medical responses to biological weapon threats or attacks. This project will provide comprehensive protocols to protect or treat combatants by using current and emerging biological countermeasures. It will provide accelerated situational awareness for biological warfare events by detecting exposure to agents through an analysis of casualty electronic theater medical records and will locate and determine the most effective logistical support for providing appropriate treatment and pathogen-specific resources required to mitigate effects of the attack.

(U) DARPA is working with a number of governmental organizations to exploit recent advances in high throughput genetic sequencers to obtain complete genetic information on a number of important pathogens and their non-pathogenic nearest neighbors. This will allow 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

(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

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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. 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 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.

(U) DARPA sponsored a one-year investigation in FY 2000 of a technology that uses a new material (aerogel) for the collection of agents of biological origin. Aerogel is a term used to describe very low-density, highly porous, polymeric materials that provide a highly efficient, lightweight collection medium for airborne particles. DARPA is also sponsoring a proof-of-principle program in FYs 2000 and 2001 evaluating the potential of delivery immune system enhancement via inhalation for defense against BW threats.

(U) The DNA Chip Technology Research program is a one-year effort to investigate 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 will also explore non-traditional approaches to desalination.

(U) Lastly, an additional $13 million was appropriated for BW counter terrorism response in FY 2001. This activity fell outside the scope of DARPA's charter and was therefore reprogrammed (IR 1415) to the DoD Chemical and Biological Defense Program (PE 0602384BP) in January 2001 for continuation of their efforts initiated in FY 2000.

(U) Program Accomplishments and Plans:

(U) FY 2000 Accomplishments:

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- Anti-Virals/Immunizations. ($ 16.999 Million)
  - Identified broad-spectrum strategies with potential for immunomodulatory activity against multiple pathogens.
  - Developed technologies for rapid design and development of new vaccines against novel pathogens.
  - Demonstrated (in-vitro) candidate anti-viral, small molecule therapeutics for selected targets.
  - Demonstrated (in-vivo) the efficacy of anti-viral peptides derived from hematopoietic stem cells.

- Anti-Bacterials/Anti-Toxins. ($ 17.065 Million)
  - Developed (in-vitro) broad spectrum, superantigenic, anti-toxin antagonists and vaccines.
  - Validated the efficacy (in-vivo) of antagonists to toxin receptors, toxin catalytic sites, and cellular platforms for toxin destruction.
  - Demonstrated (in-vivo) the efficacy of a broad-spectrum bacterial antagonist.
  - Used gene-shuffling techniques to generate molecules screened for superantigenic properties.

- Multi-Purpose. ($ 15.972 Million)
  - Explored concepts for therapeutics against bioregulators and other mid-spectrum agents.
  - Identified primary harmful immune responses to biological warfare (BW) agents.
  - Explored concepts for optimizing human immune response to BW agents.
  - Demonstrated in laboratory animal models the ability of modified stem cells to prevent disease.
  - Identified monomeric and dimeric DNA and RNA binding molecules as novel countermeasures against multiple pathogens.
  - Identified polyvalent inhibitors for inhibiting pathogens on the surface of target cells in-vivo.

- External Protection. ($ 17.137 Million)
  - Developed decoy molecules that prevent the adhesion of multiple pathogenic toxins or viruses in-vivo.
  - Demonstrated (in-vivo) a non-specific surfactant agent to neutralize biological threat agents.
  - Demonstrated initial performance of a prototype device for the purification of water contaminated with BW agent simulants.
  - Explored high throughput methods for the purification of contaminated air.
  - Demonstrated effectiveness of specific personnel protective toxin and pathogen neutralization strategies against virulent biological agents.

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- Advanced Diagnostics. ($ 15.092 Million)
  - Continued identification and development of probes to be used in diagnosis systems and began testing of probe panels in the laboratory.
  - Developed sample preparation techniques to optimize speed, accuracy, and reliability of diagnosis.
  - Identified promising strategies for rapid detection based on bodily responses or other biomarkers (including cytokines) to provide early indication of infection or exposure including non-invasive early detection of disease [e.g., nitric oxide in exhaled breath].
  - Determined feasibility of engineering red blood cells to detect and signal pathogen presence in the body.
  - Determined feasibility of rapid single molecule DNA sequencing for accelerated patient diagnosis.
  - Explored concepts for diagnosing patients for bio-regulator and other mid-spectrum agent attack.

- Sensors. ($ 21.507 Million)
  - Continued building and characterizing first-generation prototype of live agent biochip sensor.
  - Completed development of air sampling technology for airborne biological material.
  - Continued development of effective and rapid chip-reading capability with enhanced sensitivity.
  - Continued the development of unique signatures for bio-agents in mass spectrometry identification.
  - Continued the development of biosensor technology for next-generation (bioengineered) threat agents.
  - Developed methods for identifying bioregulator-based BW agents.
  - Explored options (e.g., training, genetic engineering, etc.) for the use of invertebrates in the detection of BW agents and associated chemicals.
  - Constructed cell and tissue engineered configurations to enhance optical or electrical signal output from the sensor.
  - Investigated optimal system designs for deployment of a single cell and tissue-based biosensor, which incorporated environmental sampling, microfluidics, and automated detection.
  - Evaluated cell and tissue based informatics from temporal and spatial signals in cell and tissue-based sensors.
  - Explored shelf-stabilization strategies for cells and tissues.
  - Began development and optimization of bio-agent sensors and other technologies for use in building protection.
  - Evaluated the capability to predict flow of airborne bio-agents in and around buildings (fate and transport).
  - Began the development of neutralization and decontamination techniques appropriate to buildings.

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- Genetic Sequencing of Biological Warfare Agents. ($ 4.000 Million)
  - Developed inventory of DoD-relevant BW agent pathogens requiring sequencing.
  - Determined best methods for rapidly sequencing biological warfare pathogens and related species and strains.
  - Began development of database mining techniques to find new targets for sensors, diagnostics, and therapeutics.
  - Initiated sequence analysis of four BW threat agents – *Rickettsia typhi, Coxiella burnetti, Burkholderia mallei, and Brucella suis* – and orthopox virus variants.

- Consequence Management. ($ 10.000 Million)
  - Developed distributed BW consequence management smart checklists for automatic pull and push of required information.
  - Continued development of Enhanced Consequence Management Planning and Support System (ENCOMPASS) software toolkit.
  - Developed automated playbook/checklists for BW attacks and incorporated Incident Command System capabilities.
  - Demonstrated use of ENCOMPASS for OCONUS air base force protection against a BW attack.
  - Demonstrated use of playbooks and automated checklists for training BW incident responders.
  - Integrated Consequence Assessment Tool Set (CATS) with Electronic Watchboard using the ENCOMPASS architecture.

- Asymmetrical Protocols for Biological Warfare Defense. ($ 3.500 Million)
  - Developed recommendation regarding whether cytokines are promising for further inhalational formulation development.

- Aerogel. ($ 3.000 Million)
  - Investigated capture efficiency as a function of aerogel porosity.
  - Continued the development of aerogel coatings with greater flexibility and adherence to mass spectrometer tape.
  - Developed tape manufacturing technology.
  - Tested collection efficiencies of a number of different aerogel compositions.

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(U) FY 2001 Plans:

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

- Anti-Bacterials/Anti-Toxins. ($ 20.730 Million)
  - Demonstrate surface expression of specific enzyme molecules for the rapid inactivation of various pathogens.
  - Demonstrate (in-vivo) the efficacy of a broad-spectrum bacterial pathogen antagonist.
  - Validate (in-vivo) broad spectrum, superantigenic, anti-toxin antagonists and vaccines.
  - Demonstrate (in-vivo) efficacy of broad spectrum, superantigenic, antitoxin antagonists and vaccines.

- Multi-Purpose. ($ 21.833 Million)
  - Develop therapeutic strategies against bioregulators and other mid-spectrum agents.
  - Demonstrate synthetic polymer complements for pathogenic antigens and virulence factors.
  - Develop therapeutic strategies for minimizing harmful immune responses to biological warfare agents.
  - Demonstrate (in-vitro) the efficacy of monomeric and dimeric DNA and RNA binding molecules as novel countermeasures against multiple pathogens.
  - Validate polyvalent inhibitors for blocking pathogens on the surface of target cells in-vivo.
  - Identify superantigens for broad protection against biological warfare agents with minimal side effects.
  - Validate (in-vivo) the efficacy of subcellular pathogen response imaging for rapid detection.
  - Validate technologies broadly applicable to enhance cellular therapeutics (delivery platforms) and virulence modulation (intracellular and inflammatory cascades).

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- External Protection. ($ 18.000 Million)
  - Develop a novel architectural approach for the manufacture of materials that are effective in blocking pathogens and limiting disease.
  - Demonstrate a non-aqueous advanced decontamination method.
  - Demonstrate a water purification system effective against a range of biological agents (including toxins and bioregulators).
  - Test initial performance of advanced sorbent materials for the purification of air contaminated with CW and BW agent simulants for individual protection.
  - Build and test a prototype air purification system for collective protection for a group of soldiers.
  - Begin testing of prototype protective system against non-virulent biological warfare agents, bio-toxins and regulators.

- Advanced Diagnostics. ($ 17.600 Million)
  - Test probe panels in relevant sample types including strategies for rapidly generating new/novel probes.
  - Demonstrate that sample collection and/or preparation techniques do not introduce artifacts.
  - Test, 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.
  - Develop the capability to diagnose exposure to bio-regulator and mid-spectrum agents.
  - Demonstrate, in the laboratory, the feasibility of engineering red blood cells to detect and signal pathogen presence in the body.
  - Evaluate the feasibility of additional strategies (e.g., exhaled breath) for direct identification or detection of infection without direct sample collection.
  - Demonstrate the ability to perform accelerated patient diagnosis using a rapid single molecule DNA sequencing technique in a model system.

- Sensors. ($ 24.056 Million)
  - Complete development and testing of first-generation prototype biochip sensor.
  - Continue the development of effective and rapid chip-reading capability with enhanced sensitivity and low false alarm rate.
  - Continue the development of advanced alternative technologies for live vs. dead bio-agent identification using peptides and other molecules.
  - Develop hierarchical biochip sensors.
  - Design and test techniques to replace antibody-based detection, such as short peptides, aptamers and lectins.

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APPROPRIATION/BUDGET ACTIVITY RDT&E, Defense-wide BA2 Applied Research	R-1 ITEM NOMENCLATURE Biological Warfare Defense PE 0602383E

- Design and test novel reporting/transduction techniques such as ion channels.
- Design and synthesize short peptide binding molecules for use in the detection of biological warfare agents.
- Evaluate and develop ion channel sensor systems for use in the detection of biological warfare agents.
- Evaluate methods for removing micro-encapsulation of disguised pathogens and/or sensing through the micro-encapsulation.
- Develop technologies required for next-generation miniature biological detectors including the use of microelectromechanical systems (MEMS), microfluidics, and mesoscopic-sized components.
- Evaluate false positive and false negative rates for systems of detectors using biomolecular cells or tissues.
- Exploit and/or mimic the olfactory sensors of biological systems for use in the detection of biological warfare agents.
- Demonstrate enhanced signal output from engineered cells and tissue based sensors and integrate information from these sensors with user interfaces for predictive responses.
- Engineer a deployable prototype cell and tissue sensor for field-testing.
- Evaluate sample collection technologies for cell and tissue sensors.
- Develop biosensor models and robust characterization protocols.
- Evaluate new resonant modes for biosensors.
- Investigate standoff techniques for trigger and identification.
- Develop concepts for sensors capable of detecting biological warfare agent production in underground facilities.
- Investigate critical design parameters for advanced biologically based BW sensor.
- Demonstrate use of organisms to collect chemical and biological warfare agents in the field.
- Develop and validate comprehensive performance model for time-of-flight (TOF) mass spectrometer detection of aerosolized live agents against clutter.
- Evaluate time-of-flight (TOF) mass spectrometer performance for counter-proliferation scenarios.
- Initiate the development, modeling, and validation of integrated sensor systems designed to meet detailed threat specifications.
- Evaluate novel concepts for warning systems, including stationary or mobile-networked surveillance systems.
- Explore a novel concept for universal BW probes as a possible foundation for a new sensor suitable for forensics, biomedical surveillance and environmental sensing and estimate performance against bacteria.
- Explore BW agent spectral signatures as a possible foundation for point, point-to-point and standoff BW sensors.
- Explore the use of social insects as BW agent collectors.

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- Bio/Chem Defensive Systems. ($ 10.000 Million)
  - Continue fate and transport model development in and around buildings and begin experimental evaluation.
  - Continue to develop decontamination techniques appropriate for structures.
  - Evaluate novel low-pressure-drop, broadband filter technologies.
  - Develop neutralization technologies for aerosolized agents.
  - Conduct hazard assessment for protection of military buildings from bio-chem attack; assess protection strategies.
  - Identify facilities, and identify/design the facility modifications required, for full-scale testing and evaluation of building-protection systems.
  - Evaluate concepts for novel protection systems, such as portal barriers.

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

- Consequence Management. ($ 6.000 Million)
  - Demonstrate Enhanced Consequence Management Planning and Support System (ENCOMPASS) management of multi-site BW incidents.
  - Demonstrate and field the use of ENCOMPASS for CONUS military force protection against BW attacks, i.e. Pacific Battlelab & Kernal Blitz Experiment.
  - Transition ENCOMPASS components to Initial Detection Units of the Air Force and to PACCOM, JFCOM, and Wilford Hall Medical Center.
  - Transition of ENCOMPASS components into Joint Chiefs of Staff Operations Center.

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

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

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

- Biological and Chemical Terrorism Response. ($ 13.000 Million)
  - This effort was reprogrammed to the DoD Chemical and Biological Defense Program in January 2001.

(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.
  - 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 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.

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- 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 common data set in-vivo qualifying systems for testing broad-spectrum anti-bacterial drugs.
  - Establish drug lead optimization program to facilitate transition process.

- 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 IND enabling studies.
  - Develop novel, bactericidal technologies for rapid post exposure treatment.

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- External Protection. ($ 8.180 Million)
  - Test a prototype air purification system for collective protection for a group of soldiers.
  - Demonstrate an individual water purification system 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.
  - 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.

- 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 hierarchial biochip sensors.
  - Extend standoff techniques for improved discrimination.
  - 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 TOF mass spectrometer counter-proliferation related work.

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- Complete first end-to-end performance characterization for complete sensor systems in real operational environments.
- Develop conceptual designs and critical technologies for novel warning systems, such as networked surveillance systems.
- Design and begin fabrication of universal probe biosensor suitable for forensics, biomedical surveillance, and environmental sensing.
- Evaluate universal probe biosensor against non-culturable organisms.
- Develop techniques for universal probes appropriate to viruses.
- Explore BW background spectral signatures and initiate standoff sensor development 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.

- 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.
  - Initiate systems design for building protection systems.
  - 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.
  - Develop critical technologies for novel protection systems, such as portal barriers.

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(U) **Program Change Summary:** (*In Millions*)

	FY2000	FY 2001	FY 2002
Previous President's Budget	131.705	162.064	160.180
Current Budget	124.272	166.769	140.080

(U) **Change Summary Explanation:**

FY 2000	Decrease reflects SBIR reprogramming and minor program repricing.
FY 2001	Increase reflects net effect of congressional program reduction; congressional adds for DNA Chip Technology Research, Bio & Chem Terrorism Response Training Program, Asymmetrical Protocols for BWD, and Desalination Research; the Section 8086 reduction; and the government-wide rescission.
FY 2002	Decrease reflects end of Consequence Management and Genetic Sequencing efforts in FY 2001.

(U) **Other Program Funding Summary Cost:**

- Not Applicable.

(U) **Schedule Profile:**

- Not Applicable.