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RDT&E BUDGET ITEM JUSTIFICATION SHEET (R-2 Exhibit)						DATE February 2008	
APPROPRIATION/BUDGET ACTIVITY RDT&E, Defense-wide BA2 Applied Research			R-1 ITEM NOMENCLATURE Biological Warfare Defense PE 0602383E, Project BW-01				
COST (In Millions)	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Total Program Element (PE) Cost	99.926	72.101	66.291	55.398	50.936	42.021	42.020
Biological Warfare Defense Program BW-01	99.926	72.101	66.291	55.398	50.936	42.021	42.020

(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, prevention, treatment and remediation. This project funds programs supporting revolutionary new approaches to biological warfare (BW) defense and is synergistic with efforts of other government organizations.

(U) Efforts to counter the BW threat include countermeasures to stop pathophysiologic consequences of biological or chemical attack, host immune response enhancers, medical diagnostics for the most virulent pathogens and their molecular mechanisms, tactical and strategic biological and chemical sensors, advanced decontamination and neutralization techniques, and integrated defensive systems. This program also includes development of a unique set of platform technologies that will dramatically decrease the timeline from military threat detection to countermeasure availability.

(U) Program Accomplishments/Planned Programs:

	FY 2007	FY 2008	FY 2009
Unconventional Therapeutics	35.000	26.235	26.470

(U) This thrust is developing unique and unconventional approaches to ensure that soldiers are protected against a wide variety of naturally occurring, indigenous or engineered threats. Past successes in this effort have come from developing therapeutics that are designed to work against broad classes of pathogens. This has led to several significant transitions, a separate thrust in Anthrax countermeasures, and most recently a program at Defense Threat Reduction Agency (DTRA) that directly capitalizes on previous DARPA investments. Work in this area has also uncovered new approaches to therapeutics that, rather than attacking specific pathogens, enhance innate human immune mechanisms against broad

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classes of pathogens. Not only will these approaches be more effective against known pathogens, they also promise to offer substantial protection against unknown pathogens including engineered pathogens and emerging pathogens from third-world environments.

(U) A current emphasis is on the discovery and development of technologies that will allow a rapid response (within weeks) to unanticipated threats, whether they are naturally encountered emerging diseases or agents from intentional attack. This thrust has a goal of radically transforming the protein design process by researching and developing new mathematical and biochemical approaches to the in silico design of proteins with specific functions. This program is also developing an interactive and functional in vitro human immune system using tissue engineering. This “immune system” will be able to test the efficacy of vaccines against threat agents that, at the present time, can only be tested in animal models, thus significantly decreasing the time needed and increasing the probability of success for biological warfare vaccine development. An additional focus is the development of entirely new technologies that will allow the rapid, cost-effective manufacture of complex therapeutic proteins such as monoclonal antibodies and vaccine antigens; these technologies will reduce the time for biologics manufacture from years (or even decades) to only a few weeks.

(U) Program Plans:

FY 2007 Accomplishments:

- Demonstrated that artificial human immune system simulates the actual human immune response to both viral and bacterial vaccines.
- Demonstrated in vitro antibody class switching in human lymphocytes exposed to a vaccine.
- Demonstrated primary antibody, recall antibody and naïve responses to a variety of vaccines of relevance to military force protection.
- Demonstrated that engineered organic nanoparticles elicit an immune response (antibody response, B-cell activation).
- Selected approaches to achieve accelerated manufacturing goals.
- Demonstrated single chain antibody synthesis in fungal and bacterial bio-industrial systems.
- Developed transfection methodologies for high throughput modification of plants.
- Optimized viral system to introduce vaccine/antibody coding sequences into shrimp.
- Developed approaches to ensure sufficient post-transcriptional processing in bacterial and fungal systems.
- Initiated a study to determine potential structure of antibodies.

FY 2008 Plans:

- Demonstrate a manufacturing rate for a 40µg vaccine ≥ 1 dose / (L * wks) and 400mg mAB ≥ 0.025 doses/(L * wks).

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- Demonstrate purity, structural fidelity, and functionality of biologics produced in a variety of manufacturing platforms (crustacean, fungal, prokaryote and plants).
- Predict historical failed vaccines using only the artificial human immune system.
- Complete transition of vaccine technology to government and commercial partners.
- Develop approaches for on-site battlefield synthesis of small molecule therapeutics, including antibiotics.
- Merge molecular imprinting with organic nanoparticles to generate functional viral replicates.
- Demonstrate fusogenic properties of antibodies.

FY 2009 Plans:

- Demonstrate biologics manufacture rates 10x improved from FY 2008, at the 30L scale.
- Demonstrate pathway to protein structure, function, purity, and cost to meet end of program milestones.
- Develop tools that will predict pathogen mutations before they occur and develop appropriate medical countermeasures in advance of the emergence of new threat agents.

	FY 2007	FY 2008	FY 2009
External Protection	6.000	1.500	5.000

(U) This program is developing and demonstrating a variety of technologies to protect soldiers from the hazards of chemical, biological and radiological attack and other hazards such as large unstable weapons stores. The program includes the autonomous detection and self-cleaning of surfaces contaminated by an attack, and the safe neutralization of hazardous materials.

(U) **Program Plans:**

FY 2007 Accomplishments:

- Demonstrated proof of concept for active textiles that can decontaminate biological agents including dormant spores.
- Demonstrated a novel polyurethane coating system with the ability to continuously decontaminate its surface when exposed to biological agents including spores. The coating system is 100% compatible with the military chemical agent resistant coatings (CARC) currently being used on military vehicles.

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- Demonstrated a polymeric resin compatible with cold-plasma deposition that can self-decontaminate when exposed to biological agents such as spores.

FY 2008 Plans:

- Optimize the active textile cells for improved gas generation efficiency and lifetime, sporacidal ability, and cell reliability.
- Develop additives (surface active biocides, nutrients, microspheres) into a spray coatable CARC resin to enhance biocidal effect at low humidity.
- Develop atmospheric pressure cold plasma deposition processes to deposit biocidal materials that are 100% compatible with semiconductor devices and capable of killing spores.

FY 2009 Plans:

- Scale-up production of active self-decontaminating textiles to produce large bolts of cloth for field testing.
- Demonstrate feasibility of producing large area textiles that can actively decontaminate a surface or structure subjected to biological agents on demand.
- Field test the optimized self-decontaminating polyurethane based CARC on military vehicles at Dugway Proving Grounds using BW simulants.
- Scale up the deposition processes to handle larger pieces of electronics.
- Demonstrate the efficacy and compatibility of the biocides and process by demonstrating coating of military tactical radios.
- Develop an integrated thermal model of a combatant under operational conditions including bioheat generation, internal convective (blood) and conductive (tissue) heat transfer, and coupling to ambient heat baths by radiation, conduction, evaporation, and convection.
- Develop fabrics and garment architectures that allow tuning of evaporative and convective heat transfer from the body behind a chemically impermeable external shell.

	FY 2007	FY 2008	FY 2009
Advanced Diagnostics	20.193	16.539	11.527

(U) In the early stages, many illnesses caused by biological warfare (BW) agents are either asymptomatic, or else have flu-like symptoms and are indistinguishable from non-BW related diseases. Early diagnosis is key to providing effective therapy. The advanced diagnostics program

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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). Novel approaches including the use of breath and advanced mathematical analysis will be examined.

(U) Program Plans:

FY 2007 Accomplishments:

- Demonstrated utility of devices to detect exhaled volatile organic compounds in breath.
- Demonstrated the capability to mechanically and reversibly alter the protein structure of an assay system so as to alter the sensitivity and specificity of analyte detection.
- Initiated clinical studies to identify pre-symptomatic indicators of impending illness.
- Developed platforms for rapid assessment of biological samples for pre-symptomatic indicators of illness.
- Completed initial evaluation of technologies to allow rapid, non-invasive and inexpensive assessment of radiation exposure in humans.

FY 2008 Plans:

- Identify parameters that indicate presence of a viral infection before symptoms occur.
- Develop algorithms that can predict illness from rhinovirus prior to onset of symptoms.
- Develop medical countermeasures that alleviate radiation exposure in experimental models.
- Complete evaluation of volatile organic compounds in the breath of explosive handlers.
- Demonstrate Receiver Operating Curve (ROC) for detection of explosive handlers and bystanders.
- Demonstrate reversible mechanical alterations in protein structure that yield a 10-fold change in affinity to biological, chemical and environmental agents.
- Complete evaluation of non-invasive rapid biodosimeters that can be used to triage large populations in the event of a large radiological/nuclear event.

FY 2009 Plans:

- Refine predictive model of impending illness to increase the probability of detection and reduce probability of false alarms.
- Confirm predictive model of impending illness accuracy in large sample-size, warfighter relevant populations.
- Evaluate radiation technologies at Air Force Radiobiology Research Institute (AFRRI) in a live fire test to identify best biodosimeters.

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	FY 2007	FY 2008	FY 2009
Sensors	21.733	14.327	12.000

(U) The Sensors program goal is to develop a unique set of biological warfare (BW) sensors that will greatly improve sensitivity and response time to bacteria, viruses and/or toxins.

(U) The overall goal of DARPA's Handheld Isothermal Silver Standard Sensor (HISSS) program was to develop a sensor that is capable of detecting the entire biological warfare threat spectrum (bacteria, DNA viruses, RNA viruses and protein toxins) with the same "silver standard" specificity as current laboratory techniques, but in a fast, reliable, handheld unit. Today, this standard is achieved for DNA and RNA threats using polymerase chain reaction, which is slow because of the associated temperature cycling. For proteins, the standard is met using Enzyme Linked Immunosorbent Assay (ELISA), which requires skilled laboratory technicians to complete. The equipment required for these tests is bulky and difficult to use under field conditions. Under HISSS, DARPA was to develop fundamentally new ways to exploit previously developed identification mechanisms (DNA and RNA primers, protein antibodies) in an integrated, isothermal system that will allow a single, handheld sensor to detect the full range of BW threats.

(U) The Spectral Sensing of Bio-Aerosols (SSBA) program involved the active probing of bioaerosols with electromagnetic (EM) energy, which holds the promise of extremely fast, and potentially long-range, detection and identification of bio agents. Only a small portion of the EM spectrum is exploited in today's trigger sensors (e.g., optically based particle sizers, sometimes enhanced with fluorescence measurements). However, anecdotal evidence suggests that other portions of the spectrum may offer substantial improvement in trigger sensors, as well as potentially agent-specific discrimination capability. Various types of spectra in the visible, infrared, and ultraviolet (UV) wavelengths were measured for prototype systems development. Additional spectral information such as UV fluorescence lifetime and single particle mass spectroscopy was also evaluated. An aerosol testbed has been developed to provide calibrated exposures of threat agent simulants and complex clutter mixtures for sensor performance evaluation.

(U) The goal of the Femtosecond Adaptive Spectroscopy Techniques for Remote Agent Detection (FASTREAD) program is to provide a capability to detect biological agents at standoff distances. This goal will be accomplished by performing coherent nonlinear optical spectroscopy, laser pulse shaping techniques, and adaptive optics coupled to strategies that optimize the return signal from the agent under interrogation. By

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using short pulse lasers in conjunction with coherence effects, both the spectral and temporal information contained in the backscattered signal can be exploited, enabling identification of specific agents and providing a mechanism to adapt the system to new agents.

(U) The Hyperadsorptive Atmospheric Sampling Technology (HAST) program will develop systems that permit exhaustive, accurate, and economical collection of atmospheric trace constituents to support chemical mapping of urban and military environments. The system, which integrates three technical components, will demonstrate materials, packaging, and extraction technologies that sample atmospheric impurities whose concentration ranges from 20 parts per trillion to 200 parts per million by volume from 100 liter-atmospheres of gas in less than five minutes.

(U) Program Plans:

– Handheld Isothermal Silver Standard Sensor (HISSS)

FY 2007 Accomplishments:

- Components were designed and fabricated including: 1) a handheld user interactive device; 2) a field-swappable cartridge interface module with onboard optical detection hardware; and 3) a disposable cartridge that incorporated sample preparation , stabilized lyophilized reagents, and optical windows for assay readout.
- Stabilized reagents were developed for fieldable cartridges.

– Spectral Sensing of Bio-Aerosols (SSBA)

FY 2007 Accomplishments:

- Completed fabrication of two prototype trigger bioaerosol sensors; one sensor exploits mass spectrometry for single particle identification and the other exploits multi-spectral fluorescence for simulant identification in bulk.
- Testbed demonstrated at least one week of continuous and autonomous aerosol challenges consisting of at least eighty types of complex environmental clutter backgrounds that represented seven outdoor/indoor locations used for sensor prototype testing.
- Characterized sensor prototype behavior in operational environments against four classes of bio-agent aerosol simulants.

– Femtosecond Adaptive Spectroscopy Techniques for Remote Agent Detection (FASTREAD)

FY 2007 Accomplishments:

- Demonstrated detection of dipicolonic acid (chemical associated with anthrax) by Coherent Antistokes Raman Spectroscopy (CARS) at a range of 200 meters using femtosecond lasers and a guide star.

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- Obtained in the laboratory the Coherent Antistokes Raman signature of a number of molecules and determined the Receiver Operating Curve (ROC) at a number of signal to number (S/N) and signal to curve (S/C) ratios.

FY 2008 Plans:

- Expand FASTREAD detection range using the CARS technique to 1 km.
- Lower FASTREAD false alarm rate by an order of magnitude at a fixed probability of detection of 0.99.

FY 2009 Plans:

- Expand FASTREAD detection range using the CARS technique to 3 km without using a guide star while detecting dipicolonic acid at 100 agent containing particles per liter of atmosphere while lowering the false alarm rate by an order of magnitude at a fixed probability of detection of 0.999.

- Hyperadsorptive Atmospheric Sampling Technology (HAST)

FY 2008 Plans:

- Demonstrate materials, packaging, and extraction technologies that sample atmospheric impurities.

FY 2009 Plans:

- Complete a light-weight trace element system for indexing for one hundred atmospheric samples as well as demonstrating GPS geolocation.

	FY 2007	FY 2008	FY 2009
Threat Agent Cloud Tactical Intercept Countermeasure (TACTIC)	10.000	10.000	8.430

(U) The Threat Agent Cloud Tactical Intercept and Countermeasures (TACTIC) program will develop and demonstrate the capability to 1) rapidly detect, classify and identify an airborne chemical warfare agent/biological warfare agent (CWA/BWA) battlefield threat at stand-off distances, and 2) use countermeasures to neutralize and/or precipitate the threat before it reaches the intended target. The TACTIC program will develop a prototype system having an integrated approach for the classification/identification (CI) and countermeasure (CM) of aerosolized CWA/BWA threat clouds. The TACTIC system prototype will be evaluated in controlled breeze tunnel testing environments with variations in range, concentration and wind speed. Upon successful completion of the preliminary design and critical design reviews, a prototype system will be built to demonstrate an effective CI and CM systems capability in open air tests. A memorandum of agreement (MOA) is in place with the Joint Program Executive Office for Chemical and Biological Defense (JPEO-CBD) for transitioning this capability to the Army.

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- (U) Program Plans:
- FY 2007 Accomplishments:
- Investigated technologies to defeat CWA/BWA cloud so as to eliminate the threat to unprotected war-fighters.
 - Investigated technologies for stand-off assays that rapidly identify CWA/BWA threat clouds.
- FY 2008 Plans:
- Develop models of CI/CM subsystem performance for open air tests.
 - Conduct trade studies between competing CI/CM subsystems.
 - Conduct in-house laboratory tests to validate performance of CI/CM subsystem components.
- FY 2009 Plans:
- Integrate optimal CI and CM components into a prototype system.
 - Test prototype system in scaled aerosol breeze tunnel test chamber.
 - Transition program to JPEO-CBD.

	FY 2007	FY 2008	FY 2009
Mission-Adaptable Chemical Sensors (MACS)	6.000	3.000	2.864

(U) At present, chemical sensors are unable to combine sensitivity (parts-per-trillion (ppt)) and selectivity (unambiguous identification of molecular species) with low false alarm rate. This effort will develop a sensor, based upon rotational spectroscopy of gases that will have superior capability in all categories; it will achieve the highest possible sensitivity (in ppt) for unambiguous detection of all chemical species. A preliminary blind test showed complete and unambiguous identification of an unknown sample containing several chemical species with a sampling time of one second and a false alarm probability below 0.001%. At present, the program has investigated the nature of the atmospheric background “clutter” at the parts per billion (ppb) level and below to enable the identification of target signatures at highest sensitivity. The program will focus on reduction of size and simplicity of function to achieve portability and simultaneous detection of a large number (hundreds) of species. The capabilities will far surpass all other current sensors.

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- (U) Program Plans:
FY 2007 Accomplishments:
- Completed subsystem designed for the sample acquisition, frequency management, and terahertz-generation modules, for subsequent integration within the MACS system.
 - Completed evaluation of basic circuitry, and began fabrication of subsystem components.
- FY 2008 Plans:
- Complete fabrication and integration of the modules.
 - Conduct testing and evaluate system performance.
 - Complete development of a portable sensor with 100 ppt sensitivity, false-alarm rate less than 0.1/day.
- FY 2009 Plans:
- Extend the number of analytes assayed into hundreds, with automatic identification using computer lookup.
 - Include fractionization of test within the sample acquisition module for improved sensitivity performance.
 - Build a compact, fully portable, highly sensitive sensor system.

	FY 2007	FY 2008	FY 2009
Detecting Emerging Classes of Explosives	1.000	0.000	0.000

- (U) This effort researched technologies for emerging classes of explosives.

- (U) Program Plans:
FY 2007 Accomplishments:
- Explored technologies for emerging classes of explosives.

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	FY 2007	FY 2008	FY 2009
Biomedical Engineering Initiative	0.000	0.500	0.000

- (U) Program Plans:
FY 2008 Plans:
– Develop biosensors to identify blood-borne biomarkers of tissue trauma that convey information concerning injury severity and prognosis.

(U) <u>Program Change Summary:</u> <i>(In Millions)</i>	<u>FY 2007</u>	<u>FY 2008</u>	<u>FY 2009</u>
Previous President's Budget	112.814	99.137	106.982
Current Budget	99.926	72.101	66.291
Total Adjustments	-12.888	-27.036	-40.691
 Congressional program reductions	 -10.000	 -27.536	
Congressional increases	0.000	0.500	
Reprogrammings	0.000		
SBIR/STTR transfer	-2.888		

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(U) **Change Summary Explanation:**

FY 2007	The decrease reflects the SBIR/STTR transfer and Section 8043 Rescission.
FY 2008	The decrease reflects a PE execution adjustment, the cancellation of the Spectral Sensing Bio-Aerosols program, and reductions for Section 8097 Contractor Efficiencies and Section 8104 Economic Assumptions, offset by a congressional add for Biomedical Engineering Initiative.
FY 2009	The decrease reflects draw down of BWD efforts as programs transition directly to elements of the DoD (i.e., the Army, DTRA) that have cognizance over Service BWD materials and systems, and reclassification of several sensor development programs to protect the technological attributes of the systems.

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

- Not Applicable.

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