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Exhibit R-2, RDT&E Budget Item Justification: PB 2011 Defense Advanced Research Projects Agency **DATE:** February 2010

APPROPRIATION/BUDGET ACTIVITY			R-1 ITEM NOMENCLATURE								
0400: <i>Research, Development, Test & Evaluation, Defense-Wide</i> BA 2: <i>Applied Research</i>			PE 0602383E: <i>BIOLOGICAL WARFARE DEFENSE</i>								
COST (\$ in Millions)	FY 2009 Actual	FY 2010 Estimate	FY 2011 Base Estimate	FY 2011 OCO Estimate	FY 2011 Total Estimate	FY 2012 Estimate	FY 2013 Estimate	FY 2014 Estimate	FY 2015 Estimate	Cost To Complete	Total Cost
Total Program Element	163.993	40.418	32.692	0.000	32.692	30.250	30.222	30.682	30.651	Continuing	Continuing
BW-01: <i>BIOLOGICAL WARFARE DEFENSE</i>	163.993	40.418	32.692	0.000	32.692	30.250	30.222	30.682	30.651	Continuing	Continuing

A. Mission Description and Budget Item Justification

(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 pathophysiological 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.

B. Program Change Summary (\$ in Millions)

	FY 2009	FY 2010	FY 2011 Base	FY 2011 OCO	FY 2011 Total
Previous President's Budget	56.139	40.587	0.000	0.000	0.000
Current President's Budget	163.993	40.418	32.692	0.000	32.692
Total Adjustments	107.854	-0.169	32.692	0.000	32.692
• Congressional General Reductions		-0.169			
• Congressional Directed Reductions		0.000			
• Congressional Rescissions	-0.007	0.000			
• Congressional Adds		0.000			
• Congressional Directed Transfers		0.000			
• Reprogrammings	109.438	0.000			
• SBIR/STTR Transfer	-1.577	0.000			
• TotalOtherAdjustments	0.000	0.000	32.692	0.000	32.692

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Change Summary Explanation

FY 2009

Increase reflects the reprogramming of funds for the H1N1 vaccine development offset by Section 8042 rescission of the FY 2010 Appropriations Act, the SBIR/STTR transfer and internal below threshold reprogramming.

FY 2010

Decrease reflects the Section 8097 Economic Adjustment.

FY 2011

Not Applicable

C. Accomplishments/Planned Program (\$ in Millions)

	FY 2009	FY 2010	FY 2011 Base	FY 2011 OCO	FY 2011 Total
<p>Unconventional Therapeutics</p> <p>(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. Work in this area has also uncovered new approaches to therapeutics that, rather than attacking specific pathogens, enhance innate human immune mechanisms against broad classes of pathogens. Integral to these efforts is the development of methods that rapidly identify a broad spectrum 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 and emerging pathogens from third-world environments.</p> <p>(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 significantly decreases the time needed and increases the probability of success for biological warfare vaccine development. An additional focus</p>	116.486	13.338	12.000	0.000	12.000

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C. Accomplishments/Planned Program (\$ in Millions)

	FY 2009	FY 2010	FY 2011 Base	FY 2011 OCO	FY 2011 Total
<p>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 weeks. Leveraging these current and previously proven technologies, such as the Modular IMMune in Vitro Construct (MIMIC) artificial human immune system device, a complementary rapid response to the H1N1 pandemic is being accelerated. This includes identifying the symptoms and progression, predicting and diagnosing exposed individuals, developing a safe and effective treatment, and demonstrating technologies for mass-producing low cost vaccines.</p> <p><i>FY 2009 Accomplishments:</i></p> <ul style="list-style-type: none"> - Expressed two DARPA-specified challenges to demonstrate flexibility of platform; one of which is in accordance with Food and Drug Administration (FDA) current good manufacturing processes (cGMP). - Demonstrated plant platform capability to produce millions of doses of DARPA-specified vaccines in twelve weeks with improved biochemistry metrics. - Demonstrated improved vaccine biochemistry metrics which include: protein solubility (greater than ninety-nine percent), fragmentation (less than 0.1 percent) and folding (greater than 99.9 percent). - Demonstrated reduced vaccine prototype production costs of less than one dollar per dose and/or monoclonal production of less than ten dollars per dose. - Determined common synthesis pathways for a set of pharmaceuticals frequently used and relevant to combat support hospital and far-forward care. - Researched controlled environment to monitor pathogen evolution in response to host specific interactions including vaccination. - Began developing a geometric, dynamic model to capture transportation flow and person-to-person interactions on local and global scales for informing potential upcoming pandemic hot spots. - Began overlaying sequencing and bio-informatics on the geometric model to capture biological dynamics, transmission, and viral evolution to identify virus mutation/reassortment possibilities that may require new vaccine countermeasures. 					

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C. Accomplishments/Planned Program (\$ in Millions)

	FY 2009	FY 2010	FY 2011 Base	FY 2011 OCO	FY 2011 Total
<ul style="list-style-type: none"> - Began developing pre-symptomatic biomarker model predictive of H1N1 disease progression in individuals. - Began validating pre-symptomatic biomarker models to high probabilities of detection and low probabilities of false alarm early on after contact with a pathogen. - Sequenced early H1N1 virus and introduced it into plant-based vaccine technology which resulted in protein expression within 21 days. - Expanded plant-based vaccine prototype manufacturing capacity to meet target capability of 10 million doses/month at a Current Good Manufacturing Practices (cGMP) facility. - Evaluated national H1N1 vaccine candidate prior to an FDA clinical trial using DARPA's Rapid Vaccine Assessment an in vitro artificial human immune system. - Demonstrated cross protection of (H1N1) vaccine against emerging H1N1 mutations. - Prepared pre-investigational new drug (pre-IND) package for submission to the FDA. <p><i>FY 2010 Plans:</i></p> <ul style="list-style-type: none"> - Complete demonstration of 100-fold increase in vaccine manufacturing rate for other non-egg-based platforms to show a manufacturing rate greater than or equal to 100 doses per liter times number of weeks. - Demonstrate dose efficacy for other non-egg-based vaccines using animal models and DARPA's Rapid Vaccine Assessment, an in vitro artificial immune system. - Document vaccine contaminants, system development, and quality control to facilitate pre-investigational new drug meetings with FDA. - Identify means to prevent initial infection and secondary transmission of any contagious agent from primary to secondary contact. - Develop approaches for slowing disease progression and sustain survival from highly lethal infections until either immunity is achieved or treatment is administered. - Develop techniques to provide temporary protection against a pathogen in which the host has no immunity against. 					

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C. Accomplishments/Planned Program (\$ in Millions)

	FY 2009	FY 2010	FY 2011 Base	FY 2011 OCO	FY 2011 Total
<ul style="list-style-type: none"> - Develop strategies that accelerate acquisition of effective persistent immunity before death from a lethal pathogen. <p><i>FY 2011 Base Plans:</i></p> <ul style="list-style-type: none"> - Develop innovative approaches to counter any known, unknown, naturally occurring or engineered pathogen. - Demonstrate that various technologies can increase the median lethal dose (LD50) of a given pathogen by 100-fold compared to the untreated control LD50 in order to prevent infection. - Demonstrate a 4-fold increase in survival time after a lethal dose (LD95) challenge of a given pathogen due to administered technology. - Demonstrate 95% survival against a first LD95 challenge of a given pathogen using a therapy developed within 7 days of receipt of a blinded pathogen, and deteriorating survival against subsequent challenge(s) with the initial LD95. - Demonstrate 95% survival after three LD95 challenges of a given pathogen spaced 1 week apart = 7 days post countermeasure. - Identify and confirm via animal studies one or more novel molecular approaches that disarms pathogens, thus allowing them to be eliminated by the host immune defenses. 					
<p>External Protection</p> <p>(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 will focus on the integrated thermal model of combatant in operational conditions and address the heat transfer coupling for better evaporative cooling.</p> <p><i>FY 2009 Accomplishments:</i></p> <ul style="list-style-type: none"> - Demonstrated biocidal efficacy of active textile cells on animal remains. - Field tested the optimized self-decontaminating polyurethane based chemical agent resistant coating (CARC) on military vehicles at Dugway Proving Grounds using biological warfare simulants. 	4.848	2.000	0.000	0.000	0.000

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C. Accomplishments/Planned Program (\$ in Millions)

	FY 2009	FY 2010	FY 2011 Base	FY 2011 OCO	FY 2011 Total
<p><i>FY 2010 Plans:</i></p> <ul style="list-style-type: none"> - 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. - Investigate fabrics and garment architectures that allow tuning of evaporative and convective heat transfer from the body behind a chemically impermeable external shell. 					
<p>Advanced Diagnostics</p> <p>(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 developed 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 were also examined.</p> <p><i>FY 2009 Accomplishments:</i></p> <ul style="list-style-type: none"> - Refined predictive model of impending illness to increase the probability of detection and reduce probability of false alarms. - Confirmed predictive model of impending illness accuracy in large sample-size, warfighter relevant populations. - Evaluated potential diagnostic platforms for rapid identification of host molecular markers, which indicate viral infection prior to the onset of symptoms. - Developed proof of concept biosensors based on “best fit” of diagnostic platforms, predictive models, and host molecular marker studies. - Evaluated radiation technologies at the Armed Forces Radiobiology Research Institute (AFRRI) in a live fire test to identify best biodosimeters. 	8.593	0.000	0.000	0.000	0.000

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C. Accomplishments/Planned Program (\$ in Millions)

	FY 2009	FY 2010	FY 2011 Base	FY 2011 OCO	FY 2011 Total
<p>Hyperadsorptive Atmospheric Sampling Technology (HAST)*</p> <p>*Formerly Sensors.</p> <p>(U) The Hyperadsorptive Atmospheric Sampling Technology (HAST) program will enable exhaustive, accurate, and economical collection of atmospheric trace constituents to support chemical mapping of urban and military environments. The system will demonstrate materials, packaging, and extraction technologies that sample atmospheric impurities whose concentrations range from 10 parts per trillion to 100 parts per million by volume from 100 liter-atmospheres of gas in less than five minutes. New systems to provide rapid, comprehensive, and quantitative trace gas analysis without preconceived lists or libraries of target chemicals will also be developed. The analysis systems will integrate sophisticated separation and spectroscopic techniques with advanced quantum chemistry algorithms to enable library-free identification and ranking (by concentration) of all components present in complex gas mixtures. This capability will revolutionize our understanding of the environment through chemical mapping and reconnaissance. Reproducible analysis of atmospheric samples using sophisticated analytical technology will yield maps of baseline conditions, natural variability, and permit detections of nefarious anomalies involving production, movement, and storage of weapons.</p> <p><i>FY 2009 Accomplishments:</i></p> <ul style="list-style-type: none"> - Developed sampling technology based on carbide derived carbon, cyclodextrins, and metal-organic framework complexes. - Confirmed through independent testing that HAST capsules satisfied program requirements for 85% fidelity (ability to collect arbitrary compounds) and 85% accuracy (ability to correctly rank relative concentrations). - Extended dynamic range of time of flight mass spectrometry instruments. <p><i>FY 2010 Plans:</i></p> <ul style="list-style-type: none"> - Engineer portable prototype systems for autonomous collection on mobile and stationary platforms. - Integrate sample labeling with meteorological data, time, and geographic coordinates. 	28.974	25.080	20.692	0.000	20.692

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C. Accomplishments/Planned Program (\$ in Millions)

	FY 2009	FY 2010	FY 2011 Base	FY 2011 OCO	FY 2011 Total
<ul style="list-style-type: none"> - Extend accuracy and fidelity of HAST capsules to 95%. - Test prototype architecture using calibrated gas mixtures. - Engineer systems for 100 samples per shift (125 samples per hour). <p><i>FY 2011 Base Plans:</i></p> <ul style="list-style-type: none"> - Deliver and field test functional sampling technology prototypes for autonomous vehicle-borne operation. - Demonstrate adsorbent manufacturing technology and economical (<\$0.10/sample) collection. - Integrate sampling technologies with laboratory analytical systems. - Build and demonstrate prototype analytical systems that analyze 3,000 mixtures per day with up to 300 components ranging in concentration from 50 micromoles to 50 picomoles. - Design and validate a system to analyze up to 300,000 samples per day for less than \$0.10 per sample that fits in a standard shipping container. - Field test fully integrated system for chemical map generation. - Identify chemical composition of unknown materials for which library spectra are unavailable. 					
<p>Threat Agent Cloud Tactical Intercept Countermeasure (TACTIC)</p> <p>(U) The Threat Agent Cloud Tactical Intercept Countermeasure (TACTIC) program explored methodologies to proactively defend against biological warfare agent (BWA) and chemical warfare agent (CWA) attacks on fixed sites and mobile troops on the battlefield. The approach was to develop a standoff (kilometers), integrated system for rapid identification and neutralization of BWA/CWA threat clouds. As part of the overall system design, the program developed modeling and simulation (M&S) capabilities to model threat agent plume generation, transport and dispersion, as well as threat agent and counteragent interactions such as agglomeration/coagulation, and adsorption/absorption.</p> <p><i>FY 2009 Accomplishments:</i></p> <ul style="list-style-type: none"> - Completed preliminary design reviews (PDRs) for integrated systems development. - Completed independent Government testing of a neutralization solution. 	2.228	0.000	0.000	0.000	0.000

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C. Accomplishments/Planned Program (\$ in Millions)						
		FY 2009	FY 2010	FY 2011 Base	FY 2011 OCO	FY 2011 Total
<ul style="list-style-type: none"> - Began post-PDR software development effort to model BWA/CWA threat cloud transport and dispersion and interaction of threat agent and counteragent aerosol/vapor clouds on the battlefield and in urban areas. - Continued development of high-fidelity model to accurately simulate threat agent transport and dispersion, threat agent and counteragent interactions, and the effectiveness and limitations of various applied countermeasures under a variety of atmospheric conditions. - Delivered the M&S software and associated documentation to the Government. - Transitioned the M&S software capability to the Defense Threat Reduction Agency (DTRA). 						
<p>Mission-Adaptable Chemical Sensors (MACS)</p> <p>(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 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 focused on reduction of size and simplicity of function to achieve portability and simultaneous detection of a large number (hundreds) of species. The result of the program is a portable chemical sensor that achieved all the above goals. It is unique in that it achieves the highest sensitivity (ppt) with highest selectivity (virtually no false alarms in numerous tests of sample mixed gases).</p> <p><i>FY 2009 Accomplishments:</i></p> <ul style="list-style-type: none"> - Identified users and particularized the MACS sensor for their objectives. - Extended the spectral reference library of analytes to hundreds to suit the different applications. - Automated the sensor to identify the chemical analytes within a sample using computer lookup. - Reduced sample analysis time to less than one minute. 		2.864	0.000	0.000	0.000	0.000
Accomplishments/Planned Programs Subtotals		163.993	40.418	32.692	0.000	32.692

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D. Other Program Funding Summary (\$ in Millions)

N/A

E. Acquisition Strategy

N/A

F. Performance Metrics

Specific programmatic performance metrics are listed above in the program accomplishments and plans section.

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