Exhibit R-2, RDT&E Budget Item Justification: PB 2012 Defense Advanced Research Projects Agency	DATE: February 2011
APPROPRIATION/BUDGET ACTIVITY 0400: *Research, Development, Test & Evaluation, Defense-Wide* BA 1: *Basic Research*	**R-1 ITEM NOMENCLATURE** PE 0601117E: *BASIC OPERATIONAL MEDICAL SCIENCE*

COST ($ in Millions)	FY 2010	FY 2011	FY 2012 Base	FY 2012 OCO	FY 2012 Total	FY 2013	FY 2014	FY 2015	FY 2016	Cost To Complete	Total Cost
Total Program Element	-	-	37.870	-	37.870	44.676	53.500	52.500	55.500	Continuing	Continuing
MED-01: *BASIC OPERATIONAL MEDICAL SCIENCE*	-	-	37.870	-	37.870	44.676	53.500	52.500	55.500	Continuing	Continuing

A. Mission Description and Budget Item Justification

The Basic Operational Medical Science Program Element is budgeted in the Basic Research Activity because it will explore and develop basic research in medical-related information and technology leading to fundamental discoveries, tools, and applications critical to solving DoD challenges. Programs in this project address the Department's identified medical gaps in taking care of the warfighter such as blast-induced traumatic brain injury. Efforts will draw upon the information, computational modeling and physical sciences to discover properties of biological systems that cross multiple scales of biological architecture and function, from the molecular and genetic level through cellular, tissue, organ, and whole organism levels. This project will establish a fundamental understanding of brain function, short-term memory and the mechanism(s) of injury induced by exposure to blast. Basic research that aims at new methods and medical devices includes the ability to perform in-theater, continuous analysis of a warfighter's health as a preventative measure to mitigate widespread disease and development of biomaterials that allow long-term interfaces with neural tissue, electronics that provide sound attenuation and processes to remove harmful bacteria and their toxins in blood to prevent sepsis.

B. Program Change Summary ($ in Millions)

	FY 2010	FY 2011	FY 2012 Base	FY 2012 OCO	FY 2012 Total
Previous President's Budget	-	-	-	-	-
Current President's Budget	-	-	37.870	-	37.870
Total Adjustments	-	-	37.870	-	37.870
• Congressional General Reductions		-			
• Congressional Directed Reductions		-			
• Congressional Rescissions	-	-			
• Congressional Adds		-			
• Congressional Directed Transfers		-			
• Reprogrammings	-	-			
• SBIR/STTR Transfer	-	-			
• TotalOtherAdjustments	-	-	37.870	-	37.870

Change Summary Explanation

FY 2012: Increase reflects establishment of a new PE for basic medical sciences.

C. Accomplishments/Planned Programs ($ in Millions)

	FY 2010	FY 2011	FY 2012
Title: Preventing Violent Explosive Neurologic Trauma (PREVENT)	-	-	2.900

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C. Accomplishments/Planned Programs ($ in Millions)	FY 2010	FY 2011	FY 2012
Description: The Preventing Violent Explosive Neurologic Trauma (PREVENT) program seeks to understand the causes of blast-induced traumatic brain injury (TBI), an injury that while previously described in the warfighter population, has been referred to as a potential "hidden epidemic" in the current conflict. PREVENT will use a variety of modeling techniques based on in-theater conditions to assess potential TBI caused by blast in the absence of penetrating injury or concussion. Research will create a model that can be directly correlated to the epidemiology and etiology of injury seen in returning warfighters, and attempt to determine the physical and physiological underpinnings and causes of the injury. Mitigation and treatment strategies will be formulated based on our new knowledge of blast-induced brain injury with the eventual goal of reducing injury severity across the forces by over fifty percent, improving recovery time, and preventing future injuries. This program continues efforts previously funded in PE 0601101E, Project BLS-01. ***FY 2012 Plans:*** - Continue longitudinal study on warfighters pre- and post-deployment in order to relate specific in-theater blast exposure to evidence and rates of blast TBI. - Validate diagnostic devices and criteria in large animal models. - Transition and support studies of therapeutic strategies to military medical community.			
Title: Human Assisted Neural Devices* ***Description:*** *Previously funded in PE 0601101E, Project BLS-01 The Human Assisted Neural Devices program will develop the scientific foundation for understanding the language of the brain for application to a variety of emerging DoD challenges, including improving performance on the battlefield and returning active duty military to their units after injury. This will require an understanding of neuroscience, significant computational efforts, and new material design and implementation. Key advances expected from this research include determining the nature and means through which short-term memory is encoded, and discovering the mechanisms and dynamics underlying neural computation and reorganization. These advances will enable memory restoration through the use of devices programmed to bridge gaps in the injured brain. Further, modeling of the brain progresses to an unprecedented level with this novel approach. ***FY 2012 Plans:*** - Assess consistency of primate to retain long-term memory encoding following simulated injury through use of neural codes. - Determine potential for improvements in training and skill retention through the use of neural stimulation during task acquisition in primates. - Identify homogeneity of neural codes involving long-term memory between primates conducting differing long-term memory tasks.	-	-	14.970

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C. Accomplishments/Planned Programs ($ in Millions)	FY 2010	FY 2011	FY 2012
- Determine whether networks of neurons can be differentially activated through optogenetic stimulation. - Investigate how connectivity effects the rate at which information is transmitted between areas of the brain. - Evaluate the ability of functional Magnetic Resonance Imaging to accurately predict underlying behavior of groups of neurons through hemodynamic modeling. - Study the ability of primates to navigate virtual environments through the use of neural signals. - Determine if primates can evaluate and make use of information provided solely through a neural interface.			
Title: Autonomous Diagnostics to Enable Prevention and Therapeutics (ADEPT)* *Description:* *Previously funded in Synthetic Biology in PE 0601101E, Project TRS-01 The overarching goal of the Autonomous Diagnostics to Enable Prevention and Therapeutics (ADEPT) program is to create an ability to rapidly respond to a disease or threat and improve individual readiness and total force health protection. Service members in deployed settings have limited access to health care. The ability to perform continuous monitoring of physiological status to automatically and autonomously report a warning of a detrimental change and enable immediate diagnostic or therapeutic action would expand healthcare capabilities to these service members. Additionally, in vivo production of a vaccine would potentially eliminate the time to manufacture a vaccine ex vivo. This basic research effort will develop in vivo nucleic-acid circuits to control cellular machinery for diagnostic or vaccine applications and include research to: optimize orthogonality and modularity of genetic control elements; identify methods to increase sensitivity and specificity; and demonstrate methods to control cellular machinery in response to changes in physiological status. An additional strategic thrust is to develop methodologies for measuring health-specific biomarkers from a collected biospecimen to enable diagnostics at the point-of-need, in-garrison or deployed. This basic research effort will: develop new molecular methods for isolating and detecting health-associated biomarkers for application at the point-of-need or resource limited clinical facilities (point-of -care); develop new chemical and material methods for optimizing the analytical utility of minimal sample volumes; and, develop capabilities to archive and distribute biospecimens in a stable dried format without tubes, collection vials, or additional reagents. This program also has applied research efforts budgeted in PE 0602115E, Project BT-01. *FY 2012 Plans:* - Initiate development of modular and orthogonal nucleic acid-based elements for application within a detect-and-respond circuit. - Demonstrate controlled expression in mammalian cells of synthetic circuit in response to biomarkers associated with health status. - Develop oligonucleotide synthetic construct capable of utilizing cellular control elements to enhance potency, control dosing, and achieve effectiveness.	-	-	15.000

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C. Accomplishments/Planned Programs ($ in Millions)	FY 2010	FY 2011	FY 2012
- Develop novel materials and molecular approaches to enable deployable diagnostics. - Develop novel materials and approaches for stabilizing reagents and biospecimens at room temperature.			
Title: Dialysis-Like Therapeutics *Description:* Sepsis, a bacterial infection of the blood stream, is a significant cause of injury and death among combat-injured soldiers. The key goal of this program is to run the blood volume (approximately five liters) through an external machine (akin to a dialysis system) and literally scrub out harmful bacteria and their toxins. The proposed approach is low-shear/low-resistance fluidic structures to connect cellular and biomolecular purification techniques for blood purification. Initial basic research will develop novel low-shear, low-resistance fluidic structures that enable rapid, large volume blood filtration. Additional research will develop novel intrinsic separation techniques that selectively remove bacteria, toxins and host cells from complex fluids, as well as new methods for continuous sensing of these components. Finally, research into predictive control techniques for directing patient health will close the sense, scrub, and control loop. The applied research portion of the program is budgeted in PE 0602115E, Project BT-01. *FY 2012 Plans:* - Develop "label-free" intrinsic separation technologies that remove pathogens of different classes, toxins, and activated cells from complex fluids. - Design high flow, low shear microfluidics to transport wound fluid and blood without cellular activation. - Design pathogen sensors for continuous use in complex biological fluids. - Establish mathematical models to classify and predict patient state over relevant time scales.	-	-	5.000
Accomplishments/Planned Programs Subtotals	-	-	37.870

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.