Exhibit R-2, RDT&E Budget Item Justification: PB 2014 Defense Advanced Research Projects Agency	DATE: April 2013
APPROPRIATION/BUDGET ACTIVITY 0400: *Research, Development, Test & Evaluation, Defense-Wide* BA 2: *Applied Research*	R-1 ITEM NOMENCLATURE PE 0602115E: *BIOMEDICAL TECHNOLOGY*

COST ($ in Millions)	All Prior Years	FY 2012	FY 2013#	FY 2014 Base	FY 2014 OCO ##	FY 2014 Total	FY 2015	FY 2016	FY 2017	FY 2018	Cost To Complete	Total Cost
Total Program Element	-	95.661	110.900	114.790	-	114.790	123.742	129.603	133.309	133.000	Continuing	Continuing
BT-01: *BIOMEDICAL TECHNOLOGY*	-	95.661	110.900	114.790	-	114.790	123.742	129.603	133.309	133.000	Continuing	Continuing

FY 2013 Program is from the FY 2013 President's Budget, submitted February 2012

The FY 2014 OCO Request will be submitted at a later date

A. Mission Description and Budget Item Justification

This Program Element is budgeted in the applied research budget activity because it focuses on medical related technology, information, processes, materials, systems, and devices encompassing a broad spectrum of DoD challenges. Biowarfare defense includes the capability to predict and deflect pathogen evolution of natural and engineered emerging threats and therapeutics that increase survivability within days of receipt of an unknown pathogen. Continued understanding of infection biomarkers will lead to developing a detection device that can be self-administered and provide a faster ability to diagnose and prevent widespread infection in-theater. Other battlefield technologies includes a soldier-portable hemostatic wound treatment system, capability to manufacture field-relevant pharmaceuticals in theater, and a rapid after-action review of field events as a diagnostic tool for improving the delivery of medical care and medical personnel protection. Improved medical imaging will be approached through new physical properties of cellular metabolic activities. New neural interface technologies will reliably extract information from the nervous system to enable control of the best robotic prosthetic-limb technology. To allow medical practitioners the capability to visualize and comprehend the complex relationships across patient data in the electronic medical record systems, technologies will be developed to assimilate and analyze the large amount of data and provide tools to make better informed decisions for patient care. In the area of medical training, new simulation-based tools will rapidly teach increased competency in an open and scalable architecture to be used by all levels of medical personnel for basic and advanced training. Advanced information-based techniques will be developed to supplement warfighter healthcare and the diagnosis of post-traumatic stress disorder (PTSD) and mild traumatic brain injury (mTBI). This project will also pursue the applied research efforts for dialysis-like therapeutics.

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B. Program Change Summary ($ in Millions)	FY 2012	FY 2013	FY 2014 Base	FY 2014 OCO	FY 2014 Total
Previous President's Budget	95.000	110.900	97.069	-	97.069
Current President's Budget	95.661	110.900	114.790	-	114.790
Total Adjustments	0.661	0.000	17.721	-	17.721
• Congressional General Reductions	0.000	0.000			
• Congressional Directed Reductions	0.000	0.000			
• Congressional Rescissions	0.000	0.000			
• Congressional Adds	0.000	0.000			
• Congressional Directed Transfers	0.000	0.000			
• Reprogrammings	3.250	0.000			
• SBIR/STTR Transfer	-2.589	0.000			
• TotalOtherAdjustments	-	-	17.721	-	17.721

Change Summary Explanation

FY 2012: Increase reflects an internal below threshold reprogramming offset by the SBIR/STTR transfer.

FY 2014: Increase reflects planned expansion of the Dialysis-like Therapeutics and ADEPT programs.

C. Accomplishments/Planned Programs ($ in Millions)	FY 2012	FY 2013	FY 2014
Title: Pathogen Defeat	19.000	15.000	14.617

Description: Pathogens are well known for the high rate of mutation that enables them to escape drug therapies and primary or secondary immune responses. The Pathogen Defeat thrust area will provide capabilities to predict and deflect future threats. Pathogen Defeat focuses not on the threats that are already known but rather on the threats of newly emerging pathogens and future mutations, allowing pre-emptive preparation of vaccine and therapy countermeasures.

FY 2012 Accomplishments:

- Developed platforms to investigate evolutionary pathways of a virus under selective pressures.
- Developed algorithms to predict effects of selective pressures on viral evolutionary pathways.
- Used algorithm to investigate virus mitigation and frequency globally to predict the timing and geographic location of reassortment events.
- Modeled processes to accurately predict the drift and shift of virus in pre-human, animal reservoirs.
- Began development of a system for anticipating evolution of clinical drug resistance through the use of an in vitro viral-cell bioreactor.
- Demonstrated novel sequencing technologies that reduce the error rate.
- Demonstrated viral replication in cells encapsulated in microdroplets in a cell-viral infection system.

FY 2013 Plans:

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C. Accomplishments/Planned Programs ($ in Millions)	FY 2012	FY 2013	FY 2014
- Develop a platform to reproducibly demonstrate the evolutionary pathway of a virus under multiple selective pressures. - Validate algorithms' abilities to predict viral evolution in the presence of one or multiple pressures. - Predict timing, location(s) and nature of genetic mutation(s) responsible for antiviral failure in an infected viral host (animal) model. - Predict number of viral generations necessary for the acquisition of antiviral resistance in an infected viral host (animal) model. - Predict location of genetic mutation(s) responsible for failure of a monoclonal antibody to neutralize a virus. - Correlate influenza vaccine failure in syngeneic/specific pathogen-free poultry with pathogen evolution in the natural ecologies of Asia. - Use in vitro evolution reactors to predict emergence of novel, variant influenza strains from within-reservoir species, and to predict emergence of dengue virus mutations in a region where dengue has recently appeared. - Demonstrate that the in vitro evolution platform accelerates evolution of drug resistance or immune escape. ***FY 2014 Plans:*** - Demonstrate that the in vitro bioreactor can be used to predict alteration in cell tropism or host range. - Validate viral evolution platforms and predictive platforms with a live fire test. - Transition predictive algorithms and in vitro evolution platforms to the Center for Disease Control (CDC) and other interested government agencies to increase preparedness for seasonal influenza as well as other emerging pathogens. - Transition predictive algorithms and in vitro evolution platforms to the pharmaceutical industry for prediction of emergence of drug-resistant strains of commercially relevant viruses.			
Title: Autonomous Diagnostics to Enable Prevention and Therapeutics (ADEPT) ***Description:*** The overarching goal of the Autonomous Diagnostics to Enable Prevention and Therapeutics (ADEPT) program is to increase our ability to rapidly respond to a disease or threat and improve individual readiness and total force health protection by providing centralized laboratory capabilities at non-tertiary care settings. ADEPT will focus on the development of Ribonucleic Acid (RNA)-based vaccines, potentially eliminating the time and labor required for traditional manufacture of a vaccine while at the same time improving efficacy. ADEPT will also focus on advanced development of key elements for simple-to-operate diagnostic devices. A companion basic research effort is budgeted in PE 0601117E, Project MED-01. ***FY 2012 Accomplishments:*** - Increased stability of RNA-based vaccines. - Demonstrated efficacy of RNA-based vaccines in a small animal model. - Demonstrated sample preparation methods designed for integration in disposable diagnostics that can be carried on-person, or in reusable diagnostics that can be used at the point-of-care.	11.169	15.000	29.852

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C. Accomplishments/Planned Programs ($ in Millions)	FY 2012	FY 2013	FY 2014
- Developed high sensitivity colorimetric and electrical detection approaches of advanced instrumentation approaches for autonomous diagnostics that will be deployed as either on-person devices, or used at the point-of-care. ***FY 2013 Plans:*** - Demonstrate increased humoral and cellular responses with RNA-based vaccines as compared to benchmark vaccines in vivo. - Demonstrate increased efficacy of RNA-based vaccines in vivo in small and large animal models. - Demonstrate quantitative performance metrics for device components (sample preparation/reagent delivery/detection components) to enable diagnostic device capabilities in the remote-clinic and low resourced settings. ***FY 2014 Plans:*** - Demonstrate quantitative performance metrics for integrated components developed to demonstrate capability toward a complete diagnostic device prototype. - Demonstrate ability to manipulate type of immune response induced by RNA-based vaccines. - Demonstrate ability to target delivery of RNA-based vaccines to specific cell types. - Develop novel methodologies to deliver nucleic acid constructs encoding one or hundreds of antibodies identified from immunized or convalescent patients. - Demonstrate immediate broad spectrum transient immune prophylaxis in host via delivery of nucleic acids that transiently produce multiple antibodies.			
Title: Tactical Biomedical Technologies	18.223	15.500	13.321
Description: The Tactical Biomedical Technologies thrust will develop new approaches to deliver life-saving medical care on the battlefield. Uncontrolled blood loss is the leading cause of preventable death for soldiers on the battlefield. While immediate control of hemorrhage is the most effective strategy for treating combat casualties and saving lives, currently no method other than surgical intervention can effectively treat intracavitary bleeding. A focus in this thrust is the co-development of a materials-based agent(s) and delivery mechanism capable of damaged tissue-targeted hemostasis and wound control. This system will effectively treat compressible and non-compressible wounds regardless of geometry or location. Additionally, rapid response to emerging biological threats on the battlefield is impacted by logistical delays of delivering the necessary therapeutics. Creating a "pharmacy on demand" will enable far-forward medical providers to manufacture and produce small molecule drugs and biologics in order to ensure that the therapeutics are available when they need them. Another effort will develop assessment tools to identify soldiers in real time who represent depression and suicide risk by identifying speech biomarkers. This project will also develop new algorithms, protocols, and methods to allow registration and comparison of disparate sources of data in biology (across species, experimental systems, hierarchies and populations). ***FY 2012 Accomplishments:*** - Demonstrated hemostasis agent stability consistent with operational requirements.			

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C. Accomplishments/Planned Programs ($ in Millions)	FY 2012	FY 2013	FY 2014
- Demonstrated hemostasis in less than four minutes on a non-compressible injury model. - Demonstrated that hemostatic material does not induce intracavitary fibrosis within 28 days when left at the wound site. - Designed scale-up for large-volume hemostasis agent synthesis. - Initiated discussions for wound stasis system FDA approval. - On laboratory scale, completely synthesized the following active pharmaceutical ingredients (APIs) in continuous flow: Diphenhydramine, Diazepam, Ibuprofen, and Lidocaine. - On laboratory scale, developed crystallization process for seven APIs (Diphenhydramine, Diazepam, Ibuprofen, Lidocaine, Atropine, Fluoxetine, and Doxycycline), and liquid formulations for six and injection/tablet formulation for the seventh API (Atropine). - Designed and developed benchtop modular reactor and spiral reactor. - Conducted mixing and heat transfer simulations for modular reactor design and heat transfer simulations for spiral reactor design. - Developed integrated liquid-liquid separation technique using porous diaphragm membrane as feedback-based back pressure regulator. - Modeled end-to-end process (continuous flow chemistry and downstream processing) for Lidocaine and Diazepam. - Developed methods to improve efficiency of transcranial photon energy deposition.			
FY 2013 Plans: - Demonstrate a combined hemostasis agent and delivery mechanism that achieves hemostasis in less than four minutes, and does not interfere with standards of care. - Finalize a plan for wound stasis system FDA approval. - Assess manufacturing costs and processes required for pilot-scale production. - On laboratory scale, synthesize in continuous flow all seven APIs. - Demonstrate continuous flow synthesis of all seven APIs using integrated manufacturing platform. - Design and test drug product crystallization and formulation for the seven APIs in integrated manufacturing platform. - Engage the FDA for input on process analytical technologies (PAT) and current good manufacturing practice (cGMP) for the seven APIs. - Develop breadboard prototype device for treatment of intracranial hemorrhage using laser energy through the skull and tissues. - In vivo demonstration of transcranial photocoagulation of intracranial vessels. - In vivo demonstration of photo-induced vasospasm in intracranial vessels. - Develop advanced techniques to extract and evaluate both lexical and prosodic features from speech data collected from individuals linked to suicide risk in previous studies, and begin developing predictive models for depression and suicide assessment using speech biomarkers.			
FY 2014 Plans:			

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C. Accomplishments/Planned Programs ($ in Millions)	FY 2012	FY 2013	FY 2014
- On laboratory scale, demonstrate continuous flow synthesis of an additional seven APIs (Diethylcarbamazine, Ciprofloxacin, Azithromycin, Benzylbenzoate, Methylrosanilium chloride, Ipratropium, and Neostigmine). - Demonstrate continuous flow synthesis of additional seven APIs in handheld manufacturing platform. - Engage the FDA for input on PAT and cGMP for handheld manufacturing platform. - Test prototype device for treatment of intracranial hemorrhage using laser energy through skull and tissues and engage with FDA on GMP.			
Title: Military Medical Imaging	7.144	6.400	2.000
Description: The Military Medical Imaging thrust will develop medical imaging capabilities to support military missions and operations. The emergence of advanced medical imaging includes newly recognized physical properties of biological tissue, or metabolic pathway, or physiological function in order to map it into an image of diagnostic utility and performance. This thrust will examine the capability for new, portable spectroscopic techniques that can provide information for military medical use (e.g., analysis of traumatic brain injury) that is superior to that provided by an MRI. This need is ever increasing as researchers and scientists seek to better understand anatomical, functional and cellular level interactions. This thrust will also address how to improve the delivery of medical care and medical personnel protection by building a simulated environment for rapid after-action review of field events generated from current military systems. Finally, this thrust will allow safe, non-invasive detection of microscopic and functional alterations within tissues and organs of a living organism at early stages of injury. The advanced development of these tools will provide a formidable arsenal of diagnostic tools for warfighter performance and care.			
FY 2012 Accomplishments: - Developed software to convert disparate data formats into a common language, enabling visual display and integration for processing queries. - Demonstrated ability to automatically detect, track, and analyze similar events and incidents in temporal and physical space. - Conducted experiments to investigate the use of orbital angular momentum (OAM) in Terahertz (THz) spectroscopy and verify the theory describing photon OAM - molecule interaction theory. - Initiated the design of high efficiency X-ray optics appropriate for broadband, bench top X-ray sources. - Began experimenting with arrays of OAM photon beams and modeled new signal detection approaches in order to increase the signal-to-noise ratio and to hyperpolarize a larger volume.			
FY 2013 Plans: - Demonstrate, using a model of skin and bone, that X-rays focused with OAM can yield image and chemical analysis superior to an MRI without the use of a large magnet to hyperpolarize the nuclei.			

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C. Accomplishments/Planned Programs ($ in Millions)	FY 2012	FY 2013	FY 2014
- Investigate options for broadband nuclear magnetic resonance detection for the simultaneous acquisition of multiple nuclear species. ***FY 2014 Plans:*** - Design a compact prototype device for performing novel MRI-like imaging and spectroscopy using quantum orbital resonance spectroscopy (QORS) in military medical environments. - Obtain neurochemical spectra using QORS technique.			
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 goal of this program is to develop a portable device capable of controlling relevant components in the blood volume on clinically relevant time scales. Reaching this goal is expected to require significant advances in sensing in complex biologic fluids, complex fluid manipulation, separation of components from these fluids, and mathematical descriptions capable of providing predictive control over the closed loop process. The envisioned device would save the lives of thousands of military patients each year by effectively treating sepsis and associated complications. Applied research under this program further develops and applies existing component technologies and then integrates these to create a complete blood purification system for use in the treatment of sepsis. Included in this effort will be development, integration and demonstration of non-fouling, continuous sensors for complex biological fluids; implementation of high-flow microfluidic structures that do not require the use of anticoagulation; application of intrinsic separation technologies that do not require pathogen specific molecular labels or binding chemistries; and refinement of predictive modeling and control (mathematical formalism) with sufficient fidelity to enable agile adaptive closed-loop therapy. The basic research part of this program is budgeted in PE 0601117E, Project MED-01. ***FY 2012 Accomplishments:*** - Evaluated existing sensing, microfluidic flow, and intrinsic separation component technologies for use in an integrated blood purification system and initiated research plan to achieve significant improvements in line with the overall program goals. - Initiated integration plan for component technologies developed in the basic research aspect of this program. - Identified a regulatory pathway leading to an approved integrated device. ***FY 2013 Plans:*** - Refine integration strategy, develop a bread-board system, and demonstrate bread-board system. - Develop appropriate animal models, confirm regulatory plan, and begin regulatory approval process for the integrated device. ***FY 2014 Plans:***	5.000	10.000	20.000

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C. Accomplishments/Planned Programs ($ in Millions)	FY 2012	FY 2013	FY 2014
- Integrate continuous sensing, biocompatible high-flow fluid manipulation, intrinsic separation from complex fluid, and predictive modeling and control in a prototype device for the treatment of sepsis. - Use feedback from initial animal model testing to inform the development of a prototype device for additional safety and efficacy studies in a large animal model. - Continue regulatory approval process and initiate plan for investigational device exemption submission.			
Title: Warrior Web ***Description:*** Musculoskeletal injury and fatigue to the warfighter caused by dynamic events on the battlefield not only impacts immediate mission readiness, but also can have a deleterious effect on the warfighter throughout his/her life. The Warrior Web program will mitigate that impact by developing an adaptive, quasi-active, joint support sub-system that can be integrated into current soldier systems. Because this sub-system will be compliant and be transparent to the user, it will reduce the injuries sustained by warfighters while allowing them to maintain performance. Success in this program will require the integration of component technologies in areas such as regenerative kinetic energy harvesting to offset power/energy demands; human performance, system, and component modeling; novel materials and dynamic stiffness; actuation; controls and human interface; and power distribution/energy storage. The final suit is planned to weigh no more than 9kg and require no more than 100W of external power. Allowing the warfighter to perform their missions with reduced risk for injuries will have immediate effects on mission readiness, soldier survivability, mission performance and the long-term health of our veterans. This effort was previously funded in the Maintaining Combat Performance Thrust in PE 0602715E, Project MBT-02. ***FY 2013 Plans:*** - Complete injury assessment and component technology integration into open source biomechanical model. - Complete initial verification and validation of component technologies in military environments. - Conduct Preliminary Design Review to demonstrate that individual component technologies (e.g., energy, actuation) can be integrated to meet Warrior Web performance requirements. ***FY 2014 Plans:*** - Leverage open source biomechanical model to iterate design. - Complete component technology based on results of Preliminary Design Review. - Initiate design of full Warrior Web including integration into current solider system. - Conduct Critical Design Review of full Warrior Web solider system combination.	0.000	10.750	12.000
Title: Revolutionizing Prosthetics* ***Description:*** *Previously funded in PE 0602715E, Project MBT-02.	0.000	17.000	10.000

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C. Accomplishments/Planned Programs ($ in Millions)	FY 2012	FY 2013	FY 2014
The goal of this thrust is to radically improve the state of the art for upper limb prosthetics, moving them from crude devices with minimal capabilities to fully integrated and functional limb replacements. Current prosthetic technology generally provides only gross motor functions, with very crude approaches to control. This makes it difficult for wounded soldiers to re-acquire full functionality and return to military service if so desired. The advances required to provide fully functional limb replacements will be achieved by an aggressive, milestone driven program combining the talents of scientists from diverse areas including: medicine, neuroscience, orthopedics, engineering, materials science, control and information theory, mathematics, power, manufacturing, rehabilitation, psychology and training. The results of this program will radically improve the ability of combat amputees to return to normal function. ***FY 2013 Plans:*** - Complete demonstration of neural control of arms with closed-loop feedback by spinal cord injured patients. - Demonstrate safety and stability of sensory feedback over multiple months to support use in human research participants. - Support design modifications of neural recording and stimulation devices to reduce patient burden and gain Food and Drug Administration (FDA) approval for commercialization. - Complete FDA requirements, additional human trials and testing, to gain commercial transition of non-invasively controlled prosthetic arm system. ***FY 2014 Plans:*** - Support pre-launch activities of non-invasively controlled prosthetic arm system. - Demonstrate brain control of bilateral prosthetic arms simultaneously. - Incorporate design updates in prosthetic arm systems to improve reliability and reduce cost. - Continue human spinal cord injured patient trials demonstrating longevity of cortical control.			
Title: Restoration of Brain Function Following Trauma	0.000	0.000	8.000
Description: The Restoration of Brain Function Following Trauma program will exploit recent advances in the understanding and modeling of brain activity and organization to develop approaches to treat traumatic brain injury (TBI). Critical to success will be the ability to detect and quantify structural and molecular changes produced in the human brain from explosive blast and correlate those changes with neurocognitive evaluation. This program will also develop technologies for monitoring and controlling the cells responsible for immune and regenerative responses in the human body. The ultimate goal is identification of efficacious therapeutics or other therapies that can halt progression of injury and/or reduce the severity or duration of TBI. This program is a follow-on to a basic research effort funded under Human Assisted Neural Devices in Program Element 0601117E, Project MED-01. ***FY 2014 Plans:***			

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C. Accomplishments/Planned Programs ($ in Millions)	FY 2012	FY 2013	FY 2014
- Develop a platform prototype computational model of neural activity that integrates neural activity of brain structures at numerous scales and across anatomically distributed regions. - Develop approaches to detect and model the structural and molecular changes produced in the human brain during explosive blast.			
Title: Translational Understanding of Blast Effects (TransBlast) ***Description:*** The TransBlast program is a prospective longitudinal study designed to rapidly advance understanding of blast-induced neurotrauma by closely coupling the biomechanical, medical, blast physics, and event measurement components into an integrated effort. The program will follow high-risk populations of service members to elucidate injury from both isolated and repeated events. Service members in the program are tested with a combination of imaging and neurocognitive functional exams prior to training, after training workup-but before deployment, and again after deployment. During training and deployed operations the service members wear blast dosimetry systems to document any exposures. All exposures are analyzed through detailed 3-dimensional reconstructions, combined with medical evaluations and testing records to determine the complex relationships between mechanical properties of blasts and the initiation of pathophysiologic responses. This effort builds on the successful deployment of the Blast Gauge measurement system in association with clinical indices of neurologic and psychiatric status to define a quantifiable relationship between timing and intensity of blast exposures and development and recovery of physiologic and clinic changes in an active duty population exposed to repetitive sub-clinical blast exposures and at an increased risk of involvement in clinically significant blast events. ***FY 2014 Plans:*** - Complete program protocols and gain Institutional Review Board approval. - Work with military units to complete population selections with emphasis on service members that are at high-risk for blast exposure based on: their military role, the unit in which they operate, their anticipated deployments, and their probable availability for 4 years. - Complete baseline testing of selected populations. Test regiment will be constructed to balance gaining structural and functional information on each service against the need to minimize impact on the training regiment. - Outfit all service members in the program with blast dosimetry system (Blast Gauge) to ensure that events in training and combat operations are recorded. - Complete training of all medical support teams in units and areas of operation on how to use Blast Gauges and recover data from them. - Deploy support personal at training locations and forward locations to match the training and deployed requirements of the service members.	0.000	0.000	5.000
Title: Detection and Computational Analysis of Psychological Signals (DCAPS) - Medical*	0.000	8.100	0.000

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C. Accomplishments/Planned Programs ($ in Millions)	FY 2012	FY 2013	FY 2014
Description: *Funded in PE 0602304E, Project COG-03 in FY 2012 The Detection and Computational Analysis of Psychological Signals (DCAPS) program is developing automated information systems that identify group and individual trends indicative of post-traumatic stress disorder (PTSD) and traumatic brain injury (TBI) and anomaly detection algorithms that identify emerging physical and psychological crises. These will complement commercial offerings that have not focused on issues specific to the warfighter. DCAPS recognizes that security and privacy are critical to user acceptance and Health Insurance Portability and Accountability Act compliance and so incorporates strong authentication and other security mechanisms as needed to protect patient data. The program is also developing partnerships with key DoD organizations working in this area, including the Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury, the Defense Medical Research and Development Program, the Army Telemedicine & Advanced Technologies Research Center, and the National Center for TeleHealth and Technology. ***FY 2013 Plans:*** - Operationalize/harden system software and obtain approvals to conduct user trials. - Perform user trials of mobile psychological health and telehealth applications in coordination with transition partners. - Modify and optimize mobile psychological health and telehealth applications based on the results of user trials. - Obtain final certifications and accreditation and deliver technology to military health community transition partners.			
Title: Unconventional Therapeutics	7.359	3.000	0.000
Description: 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. This program will develop approaches to counter any natural or man-made pathogen within one week. This includes development of countermeasures that do not require prior knowledge of the pathogen and are broadly applicable to multiple unrelated bacterial and/or viral infectious agents. The integration of academic research programs with pharmaceutical development efforts will result in reducing the traditional drug development cycle timeframe. ***FY 2012 Accomplishments:*** - Demonstrated various technologies that can increase the median infectious dose of a given pathogen by 100-fold in an animal model compared to the untreated control in order to prevent infection. - Demonstrated a 4-fold increase in survival time after a lethal dose challenge of a given pathogen in an animal model due to administered technology. - Demonstrated 95% survival against a first lethal dose challenge of a given pathogen in an animal model using a therapy developed within 7 days of receipt of an unknown pathogen.			

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C. Accomplishments/Planned Programs ($ in Millions)	FY 2012	FY 2013	FY 2014
- Demonstrated 95% three week survival after three lethal dose challenges of a given pathogen in an animal model spaced 1 week apart. ***FY 2013 Plans:*** - Demonstrate 95% survival after three lethal dose challenges of an unknown pathogen in two-animal models. - Transition good laboratory practice approved technology to U.S. pharmaceutical company for clinical development.			
Title: Reliable Neural-Interface Technology (RE-NET) ***Description:*** Wounded warriors with amputated limbs cannot exploit recent advances in prosthetic-limb technology because the interfaces used to extract limb-control information are low-performance and unreliable. The goal of the Reliable Neural Technology (RE-NET) program is to develop the technology and systems needed to reliably extract motor-control information at the scale and rate necessary to control state-of-the-art high-performance prosthetic limbs. In support of this goal, the RE-NET program is developing methods to quantitatively assess and model the leading causes of neural interface degradation and failure. Through this focus on reliability, the RE-NET program will enable clinically relevant technology transitions in support of wounded warriors. ***FY 2012 Accomplishments:*** - Developed peripheral nerve recording interfaces and control algorithms that capture motor intent signals from the residual nerves in amputees, a relatively non-invasive surgical technique that directly acquires nervous system activity. - Developed a flexible clinical-grade electromyography-lead technology integrated with an implantable myoelectric sensor (IMES), a very small single-channel wireless telemetry system, ready for clinical translation toward use by DoD amputees. - Developed and preliminarily demonstrated a living peripheral-nerve interface (micro targeted muscle reinnervation [microTMR]), that forms a long-term and reliable connection between single motor fascicles from a peripheral nerve that are implanted into individual muscle fiber transplants. - Developed and preliminarily demonstrated high-channel-count flat interface nerve electrodes (FINE), which when placed around individual peripheral nerves, can be used to record motor-control information. - Developed and demonstrated new pattern-recognition algorithms that can process motor-control information extracted from targeted muscle reinnervation (TMR) patients, and for the first time, provide simultaneous control of two or more degrees of freedom in the prosthetic limbs used by existing DoD amputees with TMR. - Demonstrated the ability to stimulate sensory-nerve activity and record motor-nerve activity through electrodes placed in the spinal cord dorsal root ganglion and ventral root respectively. - Developed and demonstrated a high-precision upper-limb motion-capture system capable of simultaneously tracking 28 degrees of freedom in real time.	24.000	10.150	0.000

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C. Accomplishments/Planned Programs ($ in Millions)	FY 2012	FY 2013	FY 2014
- Developed sophisticated real-time classification algorithms designed to operate dexterous control of an upper limb neuroprosthetic using EEG and non-biological signals captured entirely from non-invasive, non-penetrating, sources without the surgical risks associated with neural implants. - Identified significant microprobe degradation following chronic invasive implantation into the cortex of the brain. ***FY 2013 Plans:*** - Demonstrate human amputee use of clinical-grade DARPA RE-NET-developed peripheral-interface technologies that capture motor-control intent from endogenous nerves and muscle tissue. - Complete safety and efficacy testing of a flexible clinical-grade electromyography-lead technology integrated with an implantable myoelectric sensor (IMES), is a very small single-channel wireless telemetry system. - Submit and receive investigational-device-exemption (IDE) approval from the Food and Drug Administration (FDA) for testing leaded IMES in human amputees. - Complete safety and efficacy testing of implanted thin-film longitudinal intrafascicular electrodes (tfLIFE) and micro-targeted-muscle-reinnervation (microTMR) interfaces and plan experiments to demonstrate the ability to control prosthetic limbs. - Complete and demonstrate an implantable, reliable, and biocompatible electronics package capable of amplifying and processing motor-control signals detected by high-channel-count flat interface nerve electrodes (FINE). Perform safety and efficacy testing of implanted high-channel-count FINE interfaces. Prepare FDA IDE application submission. - Demonstrate a small implantable RF-powered electronics package capable of amplifying, processing, and wirelessly transmitting electromyography-based motor-control signals, such as those involved with TMR and microTMR. - Demonstrate an EEG-based fully non-invasive, non-penetrating, neural-interface system capable of providing prosthetic limb control for unconstrained human users. - Develop and demonstrate real-time control of a 28 degree-of-freedom avatar using decoded neural activity from the motor cortex of the brain.			
Title: Preventing Violent Explosive Neurologic Trauma (PREVENT) ***Description:*** The Preventing Violent Explosive Neurologic Trauma (PREVENT) program illuminated 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 used 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 worked to create a model that can be directly correlated to the epidemiology and etiology of injury seen in returning warfighters, and attempted to determine the physical and physiological underpinnings and causes of the injury. Raw data was collected from in-theater blast gauges, along with medical and event reports to form a comprehensive analysis. As part of the mitigation and treatment strategy, candidate therapeutics were tested in order to alleviate inflammation from both acute and chronic injury. ***FY 2012 Accomplishments:***	3.766	0.000	0.000

Exhibit R-2, RDT&E Budget Item Justification: PB 2014 Defense Advanced Research Projects Agency	DATE: April 2013
APPROPRIATION/BUDGET ACTIVITY 0400: *Research, Development, Test & Evaluation, Defense-Wide* BA 2: *Applied Research*	**R-1 ITEM NOMENCLATURE** PE 0602115E: *BIOMEDICAL TECHNOLOGY*

C. Accomplishments/Planned Programs ($ in Millions)	FY 2012	FY 2013	FY 2014
- Continued study on blast-exposed warfighters using magnetic resonance spectroscopy (MRS) imaging post-deployment showed, for the first time, injury to the hippocampus, the part of the brain associated with learning and memory, and correlated with memory deficits. - Studied animal models to evaluate the impact of blast pressure on the brain, which showed structural neuropathological and molecular changes along with neurobehavioral changes, and confirmed that pure blast pressure can injure the brain. - Replicated some of the changes seen in the blast exposed warfighters in the animal model, such as injury to the hippocampus. - Developed potential therapeutic agents for treating blast TBI in warfighters.			
Accomplishments/Planned Programs Subtotals	95.661	110.900	114.790

D. Other Program Funding Summary ($ in Millions)

N/A

Remarks

E. Acquisition Strategy

N/A

F. Performance Metrics

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