| Exhibit R-2, RDT&E Budget Item Justification: PB 2022 Defense Advanced Research Projects Agency | Date: May 2021 |
|---|---|
| **Appropriation/Budget Activity**<br>0400: *Research, Development, Test & Evaluation, Defense-Wide* / BA 2: *Applied Research* | **R-1 Program Element (Number/Name)**<br>PE 0602115E / *BIOMEDICAL TECHNOLOGY* |

| COST ($ in Millions) | Prior Years | FY 2020 | FY 2021 | FY 2022 Base | FY 2022 OCO | FY 2022 Total | FY 2023 | FY 2024 | FY 2025 | FY 2026 | Cost To Complete | Total Cost |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Total Program Element | - | 131.017 | 107.568 | 108.698 | - | 108.698 | - | - | - | - | - | - |
| BT-01: *BIOMEDICAL TECHNOLOGY* | - | 131.017 | 107.568 | 108.698 | - | 108.698 | - | - | - | - | - | - |

**A. Mission Description and Budget Item Justification**

This Biomedical Technology Program Element focuses on applied research for medical related technology, information, processes, materials, systems, and devices. Successful battlefield medical and neural interface technologies developed within this Program Element address a broad range of DoD challenges to ensure warfighter readiness, including both resilience to infectious disease and neurotechnology for improved warfighter performance. To maintain warfighter health, battlefield medical technologies research in this project will investigate novel biothreat detection, injury, and therapeutic response. Example programs include the development of a platform for the identification of early infection biomarkers to diagnose and prevent widespread infection in-theater, new methods to rapidly develop medical countermeasures in response to an emerging biothreat, and in-theater manufacturing capabilities for field-relevant pharmaceuticals to reduce the logistical burden and infrastructure requirements. To improve warfighter performance, this project will develop new neural architectures and data processing algorithms to interface the nervous system with multiple devices, facilitating human machine interaction. Additionally, advanced evidence-based techniques will be developed to supplement warfighter healthcare, including the development of shelf stable blood products, and treatment of spinal cord injury. This Program Element also supports innovation and robust transition planning in the technology cycle by working with entrepreneurs to increase the likelihood that DARPA funded technologies take root in the U.S. and provide new capabilities for national defense. This Program Element includes FY 2020 CARES Act funding in the amount of $52.0 million to prevent, diagnose, and treat COVID-19.

| B. Program Change Summary ($ in Millions) | FY 2020 | FY 2021 | FY 2022 Base | FY 2022 OCO | FY 2022 Total |
|---|---|---|---|---|---|
| Previous President's Budget | 92.771 | 107.568 | 110.953 | - | 110.953 |
| Current President's Budget | 131.017 | 107.568 | 108.698 | - | 108.698 |
| Total Adjustments | 38.246 | 0.000 | -2.255 | - | -2.255 |
| • Congressional General Reductions | 0.000 | 0.000 | | | |
| • Congressional Directed Reductions | 0.000 | 0.000 | | | |
| • Congressional Rescissions | 0.000 | 0.000 | | | |
| • Congressional Adds | 52.000 | 0.000 | | | |
| • Congressional Directed Transfers | 0.000 | 0.000 | | | |
| • Reprogrammings | -2.691 | 0.000 | | | |
| • SBIR/STTR Transfer | -11.063 | 0.000 | | | |
| • TotalOtherAdjustments | - | - | -2.255 | - | -2.255 |

**Change Summary Explanation**

FY 2020: Increase reflects COVID response CARES Act add offset by reprogrammings and SBIR/STTR transfer.

FY 2021: N/A

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FY 2022: Decrease reflects minor program repricing.

| C. Accomplishments/Planned Programs ($ in Millions) | FY 2020 | FY 2021 | FY 2022 |
|---|---|---|---|
| ***Title:*** Neural Signal Interfaces and Applications (NSIA) | 17.125 | 16.924 | 16.205 |
| ***Description:*** As part of their daily duties, many military personnel must handle large volumes of data and interact with complex systems. These tasks could be made less difficult with advanced neurotechnology platforms, but all such devices currently require invasive surgery to implement. The Neural Signal Interfaces and Applications (NSIA) program is developing non-invasive neurotechnologies able to interface with the nervous system with high resolution and precision without surgery. NSIA is utilizing recent advances to transduce neural signals through tissue. Resulting technologies will restore function in wounded warriors and facilitate standard human-machine interfaces for improved workload balance between man and machine.<br><br>***FY 2021 Plans:***<br>- Integrate initial neural read and write subcomponent's functionality into a bidirectional system design.<br>- Optimize neural transducer delivery plan.<br>- Develop algorithms for noninvasive interaction with neural tissue.<br>- Conduct initial testing of integrated record and stimulate capabilities in vivo.<br><br>***FY 2022 Plans:***<br>- Evaluate system ability to input multiple channels of information into a single volume of neural tissue.<br>- Quantify system latency when used in real time.<br>- Assess performance of read and write components on tissue of varying thickness.<br>- Conduct initial in vivo tests evaluating system use for controlling multiple outputs.<br><br>***FY 2021 to FY 2022 Increase/Decrease Statement:***<br>The FY 2022 decrease reflects minor program repricing. | | | |
| ***Title:*** Pandemic Prevention | 64.954 | 23.250 | 8.521 |
| ***Description:*** Military personnel are deployed all over the world for traditional operations that can involve exposure to endemic infectious disease, and are often specifically called upon in response to emerging or re-emerging disease outbreaks with pandemic potential (e.g., Ebola). In both instances, the DoD needs effective countermeasures to protect its deployed forces and maintain warfighter readiness. The Pandemic Prevention program is focusing on novel methods to accelerate countermeasure discovery, pre-clinical testing, and manufacturing. This program seeks to advance and integrate newly developed approaches including bioinformatics assessment of genetic sequencing and nucleic acid-based vaccines and to address technology bottlenecks associated with each stage of medical countermeasure development. Additional research will investigate new methods improving the manufacturability, distribution, and delivery of novel therapeutics. Pandemic Prevention will enable an integrated therapeutic development platform that leverages state-of-the-art technologies to prevent disease outbreaks. | | | |

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| C. Accomplishments/Planned Programs ($ in Millions) | FY 2020 | FY 2021 | FY 2022 |
|---|---|---|---|
| ***FY 2021 Plans:***<br>- Demonstrate the ability to manufacture clinical doses of gene-encoded antibody product at scale.<br>- Initiate a Phase I clinical safety study of a gene-encoded antibody.<br>- Conduct a demonstration of integrated technologies identifying, maturing, and delivering a gene-encoded antibody against a virus revealed just prior to demonstration.<br>- Investigate the potential for a link between antibody sequence and level of expression from a nucleic acid construct.<br>- Investigate novel approach to deliver DNA-encoded monoclonal antibodies without electroporation.<br>***FY 2022 Plans:***<br>- Complete clinical monitoring of patients in a Phase I clinical safety study.<br>- Investigate antibody medical countermeasure products that bind and neutralize more than one target.<br>- Integrate methodologies for mitigating viral mutant escape from candidate antibodies<br>***FY 2021 to FY 2022 Increase/Decrease Statement:***<br>The FY 2022 decrease reflects the conclusion of clinical study research and final evaluations of nucleic acid vectors. | | | |
| ***Title:*** Forensic Indicators of Threat Exposure (FITE) | 21.804 | 13.285 | 12.957 |
| ***Description:*** The Forensic Indicators of Threat Exposure (FITE) program is developing a field-deployable resource for indicators of an individual's exposure history to Weapons of Mass Destruction (WMD) and WMD precursors. FITE will investigate the ability to characterize epigenetic signatures in an individual's genome caused by specific exposures. The program will create the framework for modular technology capable of performing forensic or diagnostic analysis using epigenetic information to provide high specificity of the type of exposure and when it occurred. This novel capability could serve as a field-forward forensic tool for use by the DoD to assist in Chemical, Biological, Radiological, and Nuclear (CBRN) threat detection and response.<br>***FY 2021 Plans:***<br>- Perform pressure tests to assess the ability to distinguish viral from bacterial host-based epigenetic signatures in clinical samples.<br>- Generate host-based epigenetic signatures that reveal temporal resolution of exposure events from WMD or WMD precursor exposure events.<br>- Finalize selection of module components and complete system design for deployable platform prototype.<br>***FY 2022 Plans:***<br>- Perform pressure tests to assess the ability to identify time since exposure on collected samples.<br>- Expand human exposure signatures based on collected samples.<br>- Finalize bioinformatics algorithms for increased sensitivity and specificity of the epigenetic signatures. | | | |

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| C. Accomplishments/Planned Programs ($ in Millions) | FY 2020 | FY 2021 | FY 2022 |
|---|---|---|---|
| - Build platform prototype and perform initial tests for module integration in field forward device.<br><br>***FY 2021 to FY 2022 Increase/Decrease Statement:***<br>The FY 2022 decrease reflects minor program repricing. | | | |
| ***Title:*** Improved Personnel Placement (IPP)<br><br>***Description:*** The Improved Personnel Placement (IPP) program aims to improve force lethality and overmatch by identifying and training candidates for specialized military positions in order to maximize performance and resilience, while minimizing attrition. IPP will study the relationships between genotype and phenotype to identify unique physical, cognitive, and behavioral traits associated with a broad spectrum of military specialties. The program will link these phenotypic traits to underlying biological expression circuits driving performance. This knowledge will help individualize training for specialized roles, while providing training cadres greater precision for identifying the correct candidates without bias. Measuring an individual's biological system will ensure that they achieve their maximum potential while facilitating readiness and resilience for the DoD.<br><br>***FY 2021 Plans:***<br>- Implement novel phenotypic detection assays in military cohorts.<br>- Validate the ability to create layered biological data for building gene expression circuits.<br>- Determine correlation of biomarkers across different biological samples (e.g., saliva, blood, urine, stool).<br>- Identify gene expression circuits linked to elite performance.<br><br>***FY 2022 Plans:***<br>- Refine the mathematical and computational tools used to perform in silico analysis of phenotypic and biological variables.<br>- Refine protocols to measure phenotypic traits and biological features.<br>- Validate phenotypes linked to high performance.<br>- Validate expression circuits related to detected phenotypes.<br><br>***FY 2021 to FY 2022 Increase/Decrease Statement:***<br>The FY 2022 decrease reflects the reduction of phenotypic and biological measurements based on the refinement of protocols that predict military performance. | 18.870 | 21.167 | 16.866 |
| ***Title:*** Deployable Medical Countermeasures for Warfighter Readiness<br><br>***Description:*** Maintaining robust protection and treatment against infectious disease threats during stabilization operations (e.g., Humanitarian and Disaster Relief [HADR]) can cause a drug discovery, manufacturing and supply chain burden. A major limitation of our current response to emerging biological and chemical threats is the lack of immediate availability of ideal medical countermeasures (MCMs) for rapid response. The Deployable Medical Countermeasures for Warfighter Readiness program aims to develop an on-demand deployable platform to manufacture nucleic acid drugs at scale, in short timeframes. The platform will be | - | 11.728 | 16.877 |

| C. Accomplishments/Planned Programs ($ in Millions) | FY 2020 | FY 2021 | FY 2022 |
|---|---|---|---|
| comprised of a fully contained system capable of selectively manufacturing relevant doses of current Good Manufacturing Process (cGMP) grade nucleic acid therapeutics at or near the point of care. This on-demand platform will enable countermeasures capable of combating novel threats, allowing a small force to prevent regional outbreaks from becoming global emergencies.<br><br>***FY 2021 Plans:***<br>- Initiate development of hardware and software to support production of nucleic acids in a laboratory setting.<br>- Demonstrate the ability to biochemically or chemically synthesize and purify initial nucleic acid constructs.<br>- Initiate studies to determine the efficacy of biochemically or chemically synthesized nucleic acids.<br>- Establish the ability to purify and analyze synthesized nucleic acids in a laboratory setting.<br>***FY 2022 Plans:***<br>- Determine the most effective methods for nucleic acid synthesis.<br>- Initiate stability studies for enzymes, intermediate nucleic acid products, and reaction components.<br>- Demonstrate automation of each of the modules for nucleic acid synthesis, purification, and formulation.<br>- Develop schematics for integration of modules for nucleic acid synthesis, purification, and analysis into an alpha prototype.<br>***FY 2021 to FY 2022 Increase/Decrease Statement:***<br>The FY2022 increase reflects the culmination of the program's second capability demonstration and beginning of end-to-end integration, prototype development, and FDA engagement. | | | |
| ***Title:*** Bridging the Gap after Spinal Cord Injury | - | 15.997 | 16.754 |
| ***Description:*** The Bridging the Gap after Spinal Cord Injury program will develop and integrate technologies to heal and restore function associated with spinal cord injuries. Building upon foundational work done under the Prosthetic Hand Proprioception & Touch Interfaces program, this program will significantly advance treatment technologies by developing implantable, adaptive devices to address different stages of spinal cord injury (acute, sub-acute, and chronic). For early phases of injury, this program will develop technologies for real-time biomarker tracking and delivery of therapies to stabilize or rebuild nerve connections at the injury site. For final phase of injury, the Bridging the Gap after Spinal Cord Injury program will develop and integrate a network of devices deployed across the body to effectively create a synthetic nervous system and "bridge the gap" of the spinal cord injury to restore function and sensory feedback. The Bridging the Gap after Spinal Cord Injury program will dramatically improve the quality of life for wounded warfighters and veterans suffering from spinal cord injuries.<br><br>***FY 2021 Plans:***<br>- Investigate approaches to design initial prototypes for multiple sensors that will monitor temperature, pressure, blood flow, etc., at the local state of the spinal cord injury.<br>- Initiate assessment of the prototype devices that will stabilize the injury site and restore function. | | | |

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| C. Accomplishments/Planned Programs ($ in Millions) | FY 2020 | FY 2021 | FY 2022 |
|---|---|---|---|
| - Establish preliminary design plans for system integration.<br>- Initiate the design of a software development kit that will facilitate system modularity.<br><br>***FY 2022 Plans:***<br>- Complete critical design review for implantable devices for spinal cord injury.<br>- Initiate experiments toward achieving regulatory approval for the system sub-components.<br>- Initiate test of system of systems for spinal cord injury stabilization and restoration of function.<br>- Verify Artificial Intelligence (AI) and machine learning algorithms for each sensor to monitor the spinal cord injury progression and intervene appropriately.<br><br>***FY 2021 to FY 2022 Increase/Decrease Statement:***<br>The FY 2022 increase reflects minor program repricing. | | | |
| ***Title:*** Distributed Access to Critical Biotherapeutics for Warfighters<br><br>***Description:*** The goal of the Distributed Access to Critical Biotherapeutics for Warfighters program is to ensure DoD access to critical medical countermeasures (MCMs) by establishing the foundational technologies needed for fully distributable, on-demand manufacturing of protein-based medical countermeasures. To achieve this, investments will be made in technologies that enable immediate synthesis of bioactive protein MCMs at large yields. This technology will allow the DoD to scale up and scale out MCM production on an immediate time scale, securing access to both protein and nucleic acid based MCMs without reliance on complex supply chains or slow development cycles.<br><br>***FY 2022 Plans:***<br>- Investigate novel biological platforms to produce MCMs.<br>- Investigate processes to ensure the quality of MCMs.<br>- Initiate development of technologies to increase the production yield of MCMs.<br>- Initiate development of hardware designs for high throughput testing and production of candidate MCMs.<br><br>***FY 2021 to FY 2022 Increase/Decrease Statement:***<br>The FY 2022 increase reflects program initiation. | - | - | 10.273 |
| ***Title:*** Next-Generation Combat Casualty Care<br><br>***Description:*** The Next-Generation Combat Casualty Care program will develop advances in critical efforts to preserve warfighter life and wellbeing in the battlefields of the future. This research will directly address a leading cause of potentially preventable battlefield casualties by investigating new approaches for developing whole blood substitutes for traumatic injury that can be deployed on the battlefield in far forward settings. Additional potential uses apply to disaster relief, mass casualty events, and | - | - | 10.245 |

| C. Accomplishments/Planned Programs ($ in Millions) | FY 2020 | FY 2021 | FY 2022 |
|---|---|---|---|
| stabilization missions. Advances within this program will ensure that the U.S. remains able to care for servicemembers in peer and near-peer conflict by addressing gaps in combat casualty care.<br><br>***FY 2022 Plans:***<br>- Begin to develop in vitro models for rapid product prototyping, testing, and evaluation.<br>- Begin to investigate approaches for stabilizing the products to enable storage in field conditions.<br>- Begin to investigate key biological functions of a whole blood substitute for trauma settings.<br><br>***FY 2021 to FY 2022 Increase/Decrease Statement:***<br>The FY 2022 increase reflects program initiation. | | | |
| ***Title:*** Restoration of Auditory and Visual Function After Injury<br><br>***Description:*** The Restoration of Auditory and Visual Function After Injury program is developing neurotechnology to mitigate the effects of physical injury to the auditory and visual systems of military personnel. Research is also focusing on understanding various forms of sensing and actuation to improve outcomes and how biofeedback over time can alter human brain function. Technologies developed through this program will provide foundational neural interface technology for restoring lost capability, improving situational awareness, and enhancing cognitive and physical effectiveness.<br><br>***FY 2021 Plans:***<br>- Submit documentation for regulatory approval of preliminary device evaluation to minimize technical transition risk.<br>- Construct a sensory restoration testbed for the fully integrated input-output platform.<br>- Quantify improvements offered by large-scale (e.g., tens of thousands) recording capabilities.<br><br>***FY 2021 to FY 2022 Increase/Decrease Statement:***<br>The FY 2022 decrease reflects program completion. | 6.676 | 5.217 | - |
| ***Title:*** Prosthetic Hand Proprioception & Touch Interfaces (HAPTIX)<br><br>***Description:*** Wounded warriors often suffer from neural injury due to spinal cord injury or amputations. Military personnel with amputated limbs get limited benefit from recent advances in prosthetic-limb technology because the user interface for controlling the limb is low-performance and unreliable. Through investments in the DARPA Reliable Neural-Interface Technology (RE-NET) program, novel interface systems have been developed that overcome these issues and are designed to last for the lifetime of the patient. The goal of the Prosthetic Hand Proprioception & Touch Interfaces (HAPTIX) program was to create the first bi-directional (motor & sensory) peripheral nerve implant for controlling and sensing advanced prosthetic limb systems. With a strong focus on transition, the HAPTIX program created and transitioned clinically relevant technology in support of wounded warriors suffering | 1.588 | - | - |

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| C. Accomplishments/Planned Programs ($ in Millions) | FY 2020 | FY 2021 | FY 2022 |
|---|---|---|---|
| from single or multiple limb loss. Research in this area also addressed similar interface technologies with other nerve pathways such as the spinal cord. Technologies developed in this program transitioned to the Army. | | | |
| **Accomplishments/Planned Programs Subtotals** | 131.017 | 107.568 | 108.698 |

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

N/A

**Remarks**

**E. Acquisition Strategy**

N/A