Exhibit R-2, RDT&E Budget Item Justification: PB 2023 Defense Advanced Research Projects Agency	Date: April 2022
Appropriation/Budget Activity 0400: *Research, Development, Test & Evaluation, Defense-Wide* / BA 2: *Applied Research*	**R-1 Program Element (Number/Name)** PE 0602115E / *BIOMEDICAL TECHNOLOGY*

COST ($ in Millions)	Prior Years	FY 2021	FY 2022	FY 2023 Base	FY 2023 OCO	FY 2023 Total	FY 2024	FY 2025	FY 2026	FY 2027	Cost To Complete	Total Cost
Total Program Element	-	98.319	108.698	106.958	-	106.958	120.671	141.371	161.215	151.066	-	-
BT-01: *BIOMEDICAL TECHNOLOGY*	-	98.319	108.698	106.958	-	106.958	120.671	141.371	161.215	151.066	-	-

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 resilience to infectious disease, evidence-based techniques for readiness assessment, 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 characterize and assay biological traits driving performance and readiness as well as 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 rapid battlefield triage of injury, development of shelf stable blood products, protection from traumatic brain injury (TBI), 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.

B. Program Change Summary ($ in Millions)	FY 2021	FY 2022	FY 2023 Base	FY 2023 OCO	FY 2023 Total
Previous President's Budget	107.568	108.698	0.000	-	0.000
Current President's Budget	98.319	108.698	106.958	-	106.958
Total Adjustments	-9.249	0.000	106.958	-	106.958
• 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	-5.788	0.000			
• SBIR/STTR Transfer	-3.461	0.000			
• Adjustments to Budget Year	-	-	106.958	-	106.958

Change Summary Explanation

FY 2021: Decrease reflects reprogrammings and SBIR/STTR transfer.

Exhibit R-2, RDT&E Budget Item Justification: PB 2023 Defense Advanced Research Projects Agency	Date: April 2022
Appropriation/Budget Activity 0400: *Research, Development, Test & Evaluation, Defense-Wide* / BA 2: *Applied Research*	**R-1 Program Element (Number/Name)** PE 0602115E / *BIOMEDICAL TECHNOLOGY*

FY 2022: N/A

FY 2023: FY 2023 funding increase reflects the fact that the FY 2022 President's Budget request did not include out-year funding.

C. Accomplishments/Planned Programs ($ in Millions)	FY 2021	FY 2022	FY 2023
Title: Neural Signal Interfaces and Applications (NSIA)	15.074	16.205	9.716
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. ***FY 2022 Plans:*** - Evaluate system ability to input multiple channels of information into a single volume of neural tissue. - Quantify system latency when used in real time. - Assess performance of read and write components on tissue of varying thickness. - Conduct initial in vivo tests evaluating system use for controlling multiple outputs. ***FY 2023 Plans:*** - Conduct studies to collect safety data to enable regulatory approval for clinical system evaluations. - Submit safety evaluation data and documentation to request regulatory approval for further system evaluations. - Conduct refined tests evaluating control of multiple outputs in real-time. - Conduct refined tests evaluating reception of multiple channels of information in real-time. ***FY 2022 to FY 2023 Increase/Decrease Statement:*** The FY 2023 decrease reflects completion of system development activities to focus on final testing and transition activities.			
Title: Pandemic Prevention	19.550	8.521	5.450
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			

Exhibit R-2, RDT&E Budget Item Justification: PB 2023 Defense Advanced Research Projects Agency	Date: April 2022
Appropriation/Budget Activity 0400: *Research, Development, Test & Evaluation, Defense-Wide* / BA 2: *Applied Research*	**R-1 Program Element (Number/Name)** PE 0602115E / *BIOMEDICAL TECHNOLOGY*

C. Accomplishments/Planned Programs ($ in Millions)	FY 2021	FY 2022	FY 2023
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. ***FY 2022 Plans:*** - Initiate a Phase I clinical safety study of a gene-encoded antibody. - Complete clinical monitoring of patients in a Phase I antibody clinical safety study. - Investigate antibody medical countermeasure products that bind and neutralize more than one target. - Integrate methodologies for mitigating viral mutant escape from candidate antibodies. - Investigate alternative nucleic acid antibody delivery strategies. ***FY 2023 Plans:*** - Investigate novel mRNA formulations for increased stability. - Initiate a Phase I clinical study of an antibody product that binds and neutralizes more than one target. - Complete clinical monitoring of patients in a Phase I gene-encoded antibody clinical safety study. ***FY 2022 to FY 2023 Increase/Decrease Statement:*** The FY 2023 decrease reflects completion of clinical safety study for Phase I gene-encoded antibody.			
Title: Forensic Indicators of Threat Exposure (FITE) ***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. ***FY 2022 Plans:*** - Perform pressure tests to assess the ability to distinguish viral from bacterial host-based epigenetic signatures in clinical samples. - Perform pressure tests to assess the ability to identify time since exposure on collected samples. - Expand the number and type of human exposure signatures based on collected samples. - Build platform prototype and perform initial tests for module integration in field forward device. ***FY 2023 Plans:*** - Finalize development of human exposure signatures based on collected samples. - Finalize analytical methods to increase sensitivity and specificity for validated human exposure signatures.	11.436	12.957	5.251

Exhibit R-2, RDT&E Budget Item Justification: PB 2023 Defense Advanced Research Projects Agency	Date: April 2022
Appropriation/Budget Activity 0400: *Research, Development, Test & Evaluation, Defense-Wide* / BA 2: *Applied Research*	**R-1 Program Element (Number/Name)** PE 0602115E / *BIOMEDICAL TECHNOLOGY*

C. Accomplishments/Planned Programs ($ in Millions)	FY 2021	FY 2022	FY 2023
- Perform tests on platform prototype for module integration and workflow implementation in militarily relevant, field forward settings. - Assess ability of field forward device to analyze epigenetic signatures with optimum sensitivity and specificity from biological samples in the field. ***FY 2022 to FY 2023 Increase/Decrease Statement:*** The FY 2023 decrease reflects completion of significant research efforts to focus on final system and device demonstration.			
Title: Improved Personnel Placement (IPP) ***Description:*** The Improved Personnel Placement (IPP) program aims to improve force lethality and overmatch by identifying and training candidates for specialized military positions and developing biological assays for readiness 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 gene expression circuits driving performance. This knowledge will help individualize training and readiness assessment 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. ***FY 2022 Plans:*** - Refine the mathematical and computational tools used to perform in silico analysis of phenotypic and biological variables. - Refine protocols to measure phenotypic traits and biological features. - Validate phenotypes linked to elite performance. - Validate expression circuits related to detected phenotypes. ***FY 2023 Plans:*** - Finalize and implement protocols for measuring phenotypic traits and biological features. - Demonstrate validated phenotypic and biological measurements linked to elite performance. - Automate data acquisition and computational tools used to perform in silico analysis of phenotypic and biological features. - Research biomarkers that correlate with readiness and identify physical and/or cognitive tasks used as proxies for performance in real-world deployment settings. ***FY 2022 to FY 2023 Increase/Decrease Statement:*** The FY 2023 decrease reflects completion of significant research efforts to focus on system integration and transition activities.	19.317	16.866	14.971
Title: Deployable Medical Countermeasures for Warfighter Readiness	13.578	16.877	16.133

Exhibit R-2, RDT&E Budget Item Justification: PB 2023 Defense Advanced Research Projects Agency	Date: April 2022
Appropriation/Budget Activity 0400: *Research, Development, Test & Evaluation, Defense-Wide* / BA 2: *Applied Research*	**R-1 Program Element (Number/Name)** PE 0602115E / *BIOMEDICAL TECHNOLOGY*

C. Accomplishments/Planned Programs ($ in Millions)	FY 2021	FY 2022	FY 2023
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 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. ***FY 2022 Plans:*** - Determine the most effective methods for nucleic acid synthesis. - Initiate stability studies for enzymes, intermediate nucleic acid products, and/or reaction components. - Demonstrate automation of each of the modules for nucleic acid synthesis, purification, and formulation. - Develop schematics for integration of modules for nucleic acid synthesis, purification, and analysis into an alpha prototype. ***FY 2023 Plans:*** - Demonstrate assembly and amplification of nucleic acids using breadboard instrumentation and large-scale amplification. - Select final formulation characteristics and production process for suitable medical countermeasure safety, efficacy, and stability. - Select full panel of in-line analytical methods. - Initiate development of an integrated alpha-prototype instrument for nucleic acid synthesis and purification. ***FY 2022 to FY 2023 Increase/Decrease Statement:*** The FY 2023 decrease reflects minor program repricing.			
Title: Bridging the Gap after Spinal Cord Injury	15.997	16.754	16.016
Description: The Bridging the Gap after Spinal Cord Injury program is developing and integrating technologies to heal and restore function associated with spinal cord injuries. 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.			

Exhibit R-2, RDT&E Budget Item Justification: PB 2023 Defense Advanced Research Projects Agency	Date: April 2022
Appropriation/Budget Activity 0400: *Research, Development, Test & Evaluation, Defense-Wide* / BA 2: *Applied Research*	**R-1 Program Element (Number/Name)** PE 0602115E / *BIOMEDICAL TECHNOLOGY*

C. Accomplishments/Planned Programs ($ in Millions)	FY 2021	FY 2022	FY 2023
FY 2022 Plans: - Complete critical design review for implantable devices for spinal cord injury. - Initiate experiments toward achieving regulatory approval for the system sub-components. - Initiate test of system of systems for spinal cord injury stabilization and restoration of function. - Integrate machine learning algorithms and biological data to enable sensors to monitor the spinal cord injury progression and intervene appropriately. ***FY 2023 Plans:*** - Improve device design and performance features based on results from prototype testing. - Integrate risk mitigation strategies for nervous system access to aid functional restoration. - Initiate studies in an animal model to establish safety of prototype devices and therapies to meet regulatory requirements. - Initiate efficacy experiments in an animal model for the integrated system of systems to mitigate spinal cord injury. ***FY 2022 to FY 2023 Increase/Decrease Statement:*** The FY 2023 decrease reflects minor program repricing.			
Title: Distributed Access to Critical Biotherapeutics for Warfighters	-	10.273	10.020
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 MCMs and critical reagents. To achieve this, investments will be made in technologies that enable immediate, high-yield synthesis of bioactive protein MCMs. This technology will allow the DoD to rapidly secure access to therapeutic proteins and to enzymes needed for nucleic-acid based MCM synthesis without reliance on complex supply chains or slow development cycles. ***FY 2022 Plans:*** - Investigate novel biological platforms to produce protein-based MCMs and reagents. - Investigate processes to ensure the quality of protein-based MCMs and reagents. - Initiate development of technologies to increase the production yield of protein-based MCMs and reagents. ***FY 2023 Plans:*** - Determine the yield of multiple classes of protein-based MCMs or reagents using novel production platforms. - Establish baseline lead time to protein production using the novel production platforms. - Establish process that adds one type of protein modification to enhance the quality of the protein-based MCM.			

Exhibit R-2, RDT&E Budget Item Justification: PB 2023 Defense Advanced Research Projects Agency	Date: April 2022
Appropriation/Budget Activity 0400: *Research, Development, Test & Evaluation, Defense-Wide* / BA 2: *Applied Research*	**R-1 Program Element (Number/Name)** PE 0602115E / *BIOMEDICAL TECHNOLOGY*

C. Accomplishments/Planned Programs ($ in Millions)	FY 2021	FY 2022	FY 2023
- Determine ability of novel biological platform to produce therapeutic proteins that are equivalent to state of the art in terms of functionality and quality. ***FY 2022 to FY 2023 Increase/Decrease Statement:*** The FY 2023 decrease reflects minor program repricing.			
Title: Next-Generation Combat Casualty Care ***Description:*** The Next-Generation Combat Casualty Care program will develop advances in critical efforts to preserve warfighter life and well-being 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 stabilization missions. Advances within this program will ensure that the U.S. remains able to care for service members in peer and near-peer conflict by addressing gaps in combat casualty care. ***FY 2022 Plans:*** - Begin to develop in vitro models for rapid product prototyping, testing, and evaluation. - Begin to investigate approaches for stabilizing the products to enable storage in field conditions. - Begin to investigate key biological functions of a whole blood substitute for trauma settings. - Develop initial therapeutic formulations. ***FY 2023 Plans:*** - Initiate efficacy assessments of therapeutic formulations against hemorrhage using in vitro models. - Demonstrate safety of stabilized products using in vitro models. - Provide initial proof-of-concept for stabilization and manufacturing approach of products. - Prepare for initial in vivo studies to demonstrate efficacy against hemorrhage. ***FY 2022 to FY 2023 Increase/Decrease Statement:*** The FY 2023 increase reflects minor program repricing.	-	10.245	10.733
Title: Rapid Battlefield Triage ***Description:*** The Rapid Battlefield Triage program will advance capabilities to quickly triage warfighters requiring urgent life-saving medical intervention and enable medical resources to provide an appropriate response in current and future battlefields. Today, triage at point-of-injury is limited by subjective assessments, tools that are manually intensive, and physiological signatures with little diagnostic and prognostic value. This program will build on recent biomarker discoveries and innovations in sensing platforms to develop field-portable technologies that support triage in the most challenging operational environments. By optimizing allocation of scarce medical resources and scaling to multiple casualties, these devices will help far-forward units	-	-	8.907

Exhibit R-2, RDT&E Budget Item Justification: PB 2023 Defense Advanced Research Projects Agency	Date: April 2022
Appropriation/Budget Activity 0400: *Research, Development, Test & Evaluation, Defense-Wide* / BA 2: *Applied Research*	**R-1 Program Element (Number/Name)** PE 0602115E / *BIOMEDICAL TECHNOLOGY*

C. Accomplishments/Planned Programs ($ in Millions)	FY 2021	FY 2022	FY 2023
maximize their fighting strength against adversaries that inflict large numbers of casualties and constrain evacuation to advanced medical facilities. ***FY 2023 Plans:*** - Investigate novel physiological signatures of injury type and severity. - Begin to develop algorithms to clean and process sensor data. - Correlate physiological signatures of injury and severity with sensor outputs. - Develop experimental models to test sensor technologies. ***FY 2022 to FY 2023 Increase/Decrease Statement:*** The FY 2023 increase reflects program initiation.			
Title: Neuroprotection from Brain Injury ***Description:*** Building upon technologies discovered under the Restoring Cognitive Capability program (budgeted in PE 0602715E, Project MBT-02), the Neuroprotection from Brain Injury program will transform our defense against traumatic brain injury (TBI), for example as a result of exposure to blast. This program will further develop a mechanistic understanding of early molecular events following injury. Additionally, the program will develop technologies to rapidly deliver prophylactic countermeasures, ultimately preventing severe brain injury. These novel technologies will change the paradigm for treatment of TBI by preventing injury rather than attempting to reverse or repair it. ***FY 2023 Plans:*** - Evaluate biological events immediately following TBI. - Identify candidate biological events that can be targeted for developing protective or immediate treatment countermeasures. - Link the first biological events to downstream cellular or molecular cascades known to result in cognitive, psychological, or behavioral symptoms of TBI. ***FY 2022 to FY 2023 Increase/Decrease Statement:*** The FY 2023 increase reflects program initiation.	-	-	9.761
Title: Restoration of Auditory and Visual Function After Injury ***Description:*** The Restoration of Auditory and Visual Function After Injury program developed neurotechnology to mitigate the effects of physical injury to the auditory and visual systems of military personnel. Research focused on understanding various forms of sensing and actuation to improve outcomes. Technologies developed through this program provided foundational neural interface technology for restoring lost capability, improving situational awareness, and enhancing cognitive and physical effectiveness.	3.367	-	-

Exhibit R-2, RDT&E Budget Item Justification: PB 2023 Defense Advanced Research Projects Agency	Date: April 2022
Appropriation/Budget Activity 0400: *Research, Development, Test & Evaluation, Defense-Wide* / BA 2: *Applied Research*	**R-1 Program Element (Number/Name)** PE 0602115E / *BIOMEDICAL TECHNOLOGY*

C. Accomplishments/Planned Programs ($ in Millions)	FY 2021	FY 2022	FY 2023
Accomplishments/Planned Programs Subtotals	98.319	108.698	106.958

D. Other Program Funding Summary ($ in Millions)

N/A

Remarks

E. Acquisition Strategy

N/A