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<b>Exhibit R-2, RDT&amp;E Budget Item Justification:</b> PB 2020 Defense Advanced Research Projects Agency	<b>Date:</b> March 2019
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<b>Appropriation/Budget Activity</b> 0400: <i>Research, Development, Test &amp; Evaluation, Defense-Wide / BA 2: Applied Research</i>	<b>R-1 Program Element (Number/Name)</b> PE 0602715E / <i>MATERIALS AND BIOLOGICAL TECHNOLOGY</i>											
<b>COST (\$ in Millions)</b>	<b>Prior Years</b>	<b>FY 2018</b>	<b>FY 2019</b>	<b>FY 2020 Base</b>	<b>FY 2020 OCO</b>	<b>FY 2020 Total</b>	<b>FY 2021</b>	<b>FY 2022</b>	<b>FY 2023</b>	<b>FY 2024</b>	<b>Cost To Complete</b>	<b>Total Cost</b>
Total Program Element	-	191.880	208.898	223.976	-	223.976	245.397	242.845	265.429	279.273	-	-
MBT-01: <i>MATERIALS PROCESSING TECHNOLOGY</i>	-	85.376	95.676	108.803	-	108.803	129.628	130.738	151.839	161.839	-	-
MBT-02: <i>BIOLOGICALLY BASED MATERIALS AND DEVICES</i>	-	106.504	113.222	115.173	-	115.173	115.769	112.107	113.590	117.434	-	-

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

The Materials and Biological Technology Program Element is budgeted in the Applied Research Budget Activity because its objective is to develop materials and biological technologies that make possible a wide range of new military capabilities.

The major goal of the Materials Processing Technology project is to develop novel materials, fabrication and processing techniques, models, devices and components that will lower the cost, increase the performance, and/or enable new missions for military platforms and systems. Included in this project are efforts across a wide range of technology areas including manufacturing, electronics, sensors, optics, and complex and autonomous systems.

The Biologically Based Materials and Devices project will leverage the growing and pervasive influence of the biological sciences for the development of new DoD capabilities. Contained in this project are thrusts that apply biology's unique fabrication and manufacturing capabilities to produce and detect novel DoD relevant chemicals, materials at scale, and devices for overmatch. Example projects include analyzing biological threats at the cellular and molecular level, mitigating the effect of threat agents on deployed warfighters, and developing remote, persistent sensor systems to detect terrestrial and maritime threats. This project also includes efforts to develop novel technologies for maintaining human combat performance.

<b><u>B. Program Change Summary (\$ in Millions)</u></b>	<b><u>FY 2018</u></b>	<b><u>FY 2019</u></b>	<b><u>FY 2020 Base</u></b>	<b><u>FY 2020 OCO</u></b>	<b><u>FY 2020 Total</u></b>
Previous President's Budget	224.440	226.898	224.572	-	224.572
Current President's Budget	191.880	208.898	223.976	-	223.976
Total Adjustments	-32.560	-18.000	-0.596	-	-0.596
• Congressional General Reductions	-22.544	-18.000			
• 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	-0.667	0.000			
• SBIR/STTR Transfer	-9.349	0.000			
• TotalOtherAdjustments	-	-	-0.596	-	-0.596

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<p><b><u>Change Summary Explanation</u></b></p> <p>FY 2018: Decrease reflects Congressional reduction, SBIR/STTR transfer and reprogrammings.</p> <p>FY 2019: Decrease reflects Congressional reduction.</p> <p>FY 2020: Decrease reflects minor program repricing.</p>		

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<b>Exhibit R-2A, RDT&amp;E Project Justification:</b> PB 2020 Defense Advanced Research Projects Agency	<b>Date:</b> March 2019
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Appropriation/Budget Activity 0400 / 2					R-1 Program Element (Number/Name) PE 0602715E / MATERIALS AND BIOLOGICAL TECHNOLOGY				Project (Number/Name) MBT-01 / MATERIALS PROCESSING TECHNOLOGY			
COST (\$ in Millions)	Prior Years	FY 2018	FY 2019	FY 2020 Base	FY 2020 OCO	FY 2020 Total	FY 2021	FY 2022	FY 2023	FY 2024	Cost To Complete	Total Cost
MBT-01: MATERIALS PROCESSING TECHNOLOGY	-	85.376	95.676	108.803	-	108.803	129.628	130.738	151.839	161.839	-	-

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

The major goal of the Materials Processing Technology project is to develop novel materials, fabrication and processing techniques, models, devices and components that will lower the cost, increase the performance, and/or enable new missions for military platforms and systems. Included in this project are efforts across a wide range of technology areas including manufacturing, electronics, sensors, optics, and complex and autonomous systems.

**B. Accomplishments/Planned Programs (\$ in Millions)**

<b>Title:</b> Materials Processing and Manufacturing	<b>FY 2018</b>	<b>FY 2019</b>	<b>FY 2020</b>
<p><b>Description:</b> The Materials Processing and Manufacturing thrust is exploring new manufacturing and processing approaches that will dramatically lower the cost and decrease the time required to fabricate DoD parts and systems. Constantly changing specifications for DoD platforms combined with recent manufacturing advances, such as 3D printing and manufacture on demand, drive a need for greater efficiency in development and design cycles as well as scalable and reconfigurable manufacturing processes that incorporate advanced materials with superior properties. Research within the Materials Processing and Manufacturing thrust is focused on achieving the following capability objectives: (1) scalable processes to assemble fully 3D devices that include nanometer- to micron-scale components; (2) processes that yield new materials, materials capabilities and parts that cannot be made through conventional processing approaches; (3) efficient, low volume manufacturing; (4) approaches that reduce manufacturing complexity through new material feedstock formats with reconfigurable processing techniques; and (5) material processing that enhances platform survivability in extreme environments.</p> <p><b>FY 2019 Plans:</b></p> <ul style="list-style-type: none"> <li>- Demonstrate pilot-scale production of tailorable, high-performance carbon fiber-based feedstock that meets or exceeds state-of-the-art aerospace materials capability.</li> <li>- Demonstrate that a multifunctional element can be incorporated into the feedstock while maintaining performance.</li> <li>- Demonstrate that a multifunctional component can be formed without degradation of performance in either the structural or the functional component.</li> <li>- Investigate methods for the scale-up of nano- and micro-assembly techniques.</li> <li>- Test and evaluate retention of nanoscale properties when assembly process is scaled-up.</li> <li>- Initiate development of new models for improved understanding of physical, chemical and mechanical properties of high entropy materials.</li> </ul>	17.997	27.678	29.039

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<b>B. Accomplishments/Planned Programs (\$ in Millions)</b>		<b>FY 2018</b>	<b>FY 2019</b>
<ul style="list-style-type: none"> <li>- Identify new processing approaches for manufacturing high temperature materials in large and/or complex shapes.</li> </ul> <p><b>FY 2020 Plans:</b></p> <ul style="list-style-type: none"> <li>- Explore approaches that leverage new computational and manufacturing tools to fabricate large complex structures for enhanced platform survivability in harsh environments.</li> <li>- Leverage recent breakthroughs in metrology to characterize atomic- through meso-scale material behaviors.</li> <li>- Develop model guided testing tools to validate the behavior of new materials under extreme environmental conditions.</li> <li>- Investigate mechanical/physical/chemical properties of high entropy alloys for applications in extreme environments.</li> </ul> <p><b>FY 2019 to FY 2020 Increase/Decrease Statement:</b> The FY 2020 increase reflects minor program repricing.</p>			
<p><b>Title:</b> Functional Materials and Devices</p> <p><b>Description:</b> The Functional Materials and Devices thrust is developing advanced materials, components and systems to improve device performance for DoD sensing, imaging and communication applications. One focus of this thrust involves development of advanced transductional materials that convert one form of energy to another for DoD-relevant applications in areas such as thermoelectrics. While promising transduction materials are known for a variety of applications, integration into devices has not been realized. Another focus area is the development of physics based models that predict material behavior when illuminated by high peak power electromagnetic interference. A third focus area involves development of new multi-functional materials and device designs that will radically decrease the size, weight and power requirements of neutron and gamma sources for high-resolution neutron, gamma and x-ray imaging. Such devices should enable fieldable detection units for non-destructive evaluation of parts, detection of explosives and other DoD-relevant targets.</p> <p><b>FY 2019 Plans:</b></p> <ul style="list-style-type: none"> <li>- Evaluate compositions, fabrication processes and applications of high-performance textured piezoelectric materials.</li> <li>- Perform final integrated compact neutron source prototype testing.</li> <li>- Explore innovative design concepts for intense, mobile, mono-energetic gamma sources.</li> <li>- Identify component technologies with potential for enabling intense, mobile, mono-energetic gamma sources for elemental imaging and advanced diagnostics.</li> <li>- Initiate development of advanced physics-based models for predicting material behaviors under high peak electromagnetic power.</li> </ul> <p><b>FY 2020 Plans:</b></p> <ul style="list-style-type: none"> <li>- Demonstrate performance of compact gamma source component technologies.</li> <li>- Initiate efforts to integrate component technologies into a compact, mono-energetic gamma source prototype.</li> </ul>		10.228	19.215
			20.164

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<b>B. Accomplishments/Planned Programs (\$ in Millions)</b>		<b>FY 2018</b>	<b>FY 2019</b>
<ul style="list-style-type: none"> <li>- Validate experimentally the ability of physics-based models to predict material behaviors under high peak electromagnetic power.</li> <li>- Initiate efforts to incorporate physics-based models in device design tools to improve operational robustness in the presence of noisy electromagnetic environments.</li> </ul> <p><b>FY 2019 to FY 2020 Increase/Decrease Statement:</b> The FY 2020 increase reflects minor program repricing.</p>			
<p><b>Title:</b> Reconfigurable Systems</p> <p><b>Description:</b> In the Reconfigurable Systems thrust, new approaches are being developed to enable more rapid and robust adaptation of defense systems and systems-of-systems to changing mission requirements and unpredictable environments. This includes development of capabilities across sensing, perception, planning and control for autonomous, high-speed operation in cluttered environments without Global Positioning System (GPS) information. This also includes development of capabilities to manipulate and control adversary sensory perception and/or situational awareness. Additional work in this thrust focuses on how sensing systems and military systems-of-systems are designed for real-time resilient response to dynamic, unexpected signals and contingencies. Research is developing a more unified view of system behavior that allows better understanding and exploitation of complex interactions among components, including development of formal mathematical approaches to complex adaptive system composition and design. These capabilities will impact autonomous systems and systems-of-systems, including those that involve humans, in a variety of DoD-relevant contexts.</p> <p><b>FY 2019 Plans:</b></p> <ul style="list-style-type: none"> <li>- Develop capability for self-diagnosis of current system performance from arbitrary set of sensors, behaviors, and constraints.</li> <li>- Demonstrate closed-loop single functional recomposition from a set of sub-system components.</li> <li>- Demonstrate redesign of system function to attrition and environmental change.</li> <li>- Initiate efforts to determine conditions in which special effects can manipulate human and/or machine sensory inputs to control perception.</li> </ul> <p><b>FY 2020 Plans:</b></p> <ul style="list-style-type: none"> <li>- Demonstrate redesign of coordinated functions to achieve maximum resilience.</li> <li>- Demonstrate dynamic adaptive response to achieve system re-design.</li> <li>- Demonstrate system design for adaptive response to a co-evolving threat coupled to attrition and environment change.</li> <li>- Investigate potential for altering human and/or machine perception by leveraging new breakthroughs in projection technologies across the electromagnetic spectrum.</li> </ul> <p><b>FY 2019 to FY 2020 Increase/Decrease Statement:</b></p>		20.280	12.791
			21.058

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B. Accomplishments/Planned Programs (\$ in Millions)		FY 2018	FY 2019	FY 2020
The FY 2020 increase reflects expanded research in the development of capabilities to manipulate and control adversary sensory perception and situational awareness.				
<p><b>Title:</b> Accelerating Discovery and Innovation</p> <p><b>Description:</b> The Accelerating Discovery and Innovation thrust is developing new approaches, tools and technologies to speed the pace of scientific discoveries and technological innovations from idea generation and fundamental research through integration of technologies into fieldable products and systems in production. The path from idea generation to a discovery is a lengthy, complex process involving many unpredictable steps, cycles and stages across fundamental and applied research and development. Research in this thrust is focused on developing and implementing strategies to address many of the challenges and bottlenecks inherent along this path and to speed the rate at which an idea can be advanced into a concrete capability. Specific approaches include advanced multiplayer gaming technologies to catalyze development of new technology concepts, development of tools for data collection and visualization to accelerate fundamental and applied research, and strategies to understand how seemingly benign commercially available technologies may be converted or combined into threats to military operations, equipment or personnel.</p> <p><b>FY 2019 Plans:</b></p> <ul style="list-style-type: none"><li>- Develop software tools to facilitate an analytic multi-disciplinary conversation to facilitate the collective understanding and potential implications of emerging science and technology.</li><li>- Develop software systems to aid in identifying emerging science and technology concepts and applications based on existing understanding.</li><li>- Design and build additional sets of interoperable kits for military applications from easily obtainable components.</li><li>- Design and build a highly capable reconnaissance-strike system that integrates the interoperable kits.</li><li>- Test the reconnaissance-strike system(s) with military partners.</li><li>- Investigate the understanding of what enables projected animations to be perceived as real.</li></ul> <p><b>FY 2020 Plans:</b></p> <ul style="list-style-type: none"><li>- Create software tools to expedite the synthesis of multi-disciplinary conversations about emerging science and technology into evidence supported research proposals.</li><li>- Develop tools that allow for incorporation of the needs of research and development requirement generators with the capabilities of research and development performers.</li></ul> <p><b>FY 2019 to FY 2020 Increase/Decrease Statement:</b> The FY 2020 increase reflects minor program repricing.</p>		16.437	10.630	11.155
<b>Title:</b> Multi-Scale Modeling		-	14.362	27.387

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<b>B. Accomplishments/Planned Programs (\$ in Millions)</b>			<b>FY 2018</b>	<b>FY 2019</b>	<b>FY 2020</b>
<p><b>Description:</b> The Multi-Scale Modeling thrust, an outgrowth of the Reconfigurable Systems thrust, is developing advanced, multi-physics models that can predict the effect of disturbances and/or perturbations in the space environment in order to inform operational decisions based on current space environment conditions. Current space environment models are limited to predicting long term climatic averages or regularly occurring phenomena and do not fully account for coupling effects where perturbations in one region of the space environment may produce disturbances in another region. Approaches for addressing these limitations under the Multi-Scale Modeling thrust include the following: (1) development of observation driven/first-principles theory of magnetosphere-ionosphere-thermosphere coupling; (2) creation of an extensible assimilation framework for unifying space environment monitoring systems and data; and (3) non-traditional space environment measurement approaches. These developments will ensure the accuracy and spatiotemporal resolution of space weather models and is sufficient to enable prediction of operationally relevant perturbations and disturbances in the space environment.</p> <p><b>FY 2019 Plans:</b></p> <ul style="list-style-type: none"> <li>- Initiate efforts to explore advanced methods and tools, such as hybridized particle/fluid methods, adaptive mesh computational techniques, and vector processing, to extend capabilities of state-of-the-art "nowcast" space weather predictions.</li> <li>- Initiate efforts to develop fully coupled space environment model suite capable of assimilating high resolution 4D data (observed and synthetic).</li> <li>- Initiate development of an extensible framework to unify traditional and non-traditional ionospheric measurements, both terrestrial and in-situ.</li> <li>- Initiate development of multi-physics models that can predict ionospheric perturbations, such as plasma "holes" and acoustic shock waves, associated with various air and space platform trajectories.</li> </ul> <p><b>FY 2020 Plans:</b></p> <ul style="list-style-type: none"> <li>- Identify promising approaches that dynamically utilize computational architectures (adaptive meshes, vector processing, cloud architecture) to drive down space weather prediction times to the nowcast (hourly) regime.</li> <li>- Demonstrate in simulation the ability to predict and track space weather phenomena with scale lengths as small as one hundred kilometers.</li> <li>- Demonstrate an extensible assimilation framework capable of processing data sources from at least two major space environment observations networks in less than fifteen minutes.</li> <li>- Demonstrate in simulation the ability of multi-physics models to predict ionospheric perturbations, such as plasma "holes" and acoustic shock waves, associated with various air and space platform trajectories.</li> </ul> <p><b>FY 2019 to FY 2020 Increase/Decrease Statement:</b></p>					

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<b>B. Accomplishments/Planned Programs (\$ in Millions)</b>		<b>FY 2018</b>	<b>FY 2019</b>
The FY 2020 increase reflects expansion into demonstrations of the abilities to predict space weather phenomena and ionospheric perturbations.			
<b>Title:</b> Chemical Processing for Force Protection  <b>Description:</b> Research in this thrust is focused on the development of new chemical approaches and technologies across a broad spectrum of DoD needs. One area involves development of innovative approaches for scalable small molecule synthesis coupled with predictive tools for route design, possibly offering a new strategy to discover how to make new molecules such as pharmaceuticals and explosives. Another focus combines existing strategies for destruction of chemical agents with development of new processing methods to provide a remediation system that can process any chemical agent at the site of storage. In addition, investments in this thrust will advance chemical characterization, information management and analysis, and automation.  <b>FY 2019 Plans:</b> <ul style="list-style-type: none"> <li>- Demonstrate continuous flow synthesis of a molecule requiring a convergent approach (e.g., synthesis and subsequent combination of two intermediates).</li> <li>- Adapt continuous flow technology to low cost, portable chemical reactors for distributed manufacturing.</li> <li>- Develop a computational map of synthetic capabilities for existing modules that outlines the potential suite of molecules that can be generated in the automated device.</li> <li>- Demonstrate rapid search of reaction conditions (1,000s of reactions per hour) and initiate integration of these data into route design algorithms.</li> </ul> <b>FY 2019 to FY 2020 Increase/Decrease Statement:</b> The FY 2020 decrease reflects program completion.		20.434	11.000
<b>Accomplishments/Planned Programs Subtotals</b>		85.376	108.803
<b>C. Other Program Funding Summary (\$ in Millions)</b>			
N/A			
<b>Remarks</b>			
<b>D. Acquisition Strategy</b>			
N/A			
<b>E. Performance Metrics</b>			
Specific programmatic performance metrics are listed above in the program accomplishments and plans section.			

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Appropriation/Budget Activity 0400 / 2					R-1 Program Element (Number/Name) PE 0602715E / MATERIALS AND BIOLOGICAL TECHNOLOGY				Project (Number/Name) MBT-02 / BIOLOGICALLY BASED MATERIALS AND DEVICES			
COST (\$ in Millions)	Prior Years	FY 2018	FY 2019	FY 2020 Base	FY 2020 OCO	FY 2020 Total	FY 2021	FY 2022	FY 2023	FY 2024	Cost To Complete	Total Cost
MBT-02: BIOLOGICALLY BASED MATERIALS AND DEVICES	-	106.504	113.222	115.173	-	115.173	115.769	112.107	113.590	117.434	-	-

A. Mission Description and Budget Item Justification

The Biologically Based Materials and Devices project will leverage the growing and pervasive influence of the biological sciences for the development of new DoD capabilities. Contained in this project are thrusts that apply biology's unique fabrication and manufacturing capabilities to produce and detect novel DoD relevant chemicals, materials at scale, and devices for overmatch. Example projects include analyzing biological threats at the cellular and molecular level, mitigating the effect of threat agents on deployed warfighters, and developing remote, persistent sensor systems to detect terrestrial and maritime threats. This project also includes efforts to develop novel technologies for maintaining human combat performance.

B. Accomplishments/Planned Programs (\$ in Millions)

<div>Title: Enhancing Neuroplasticity</div> <div>Description: The DoD needs tools to rapidly and effectively train military personnel in multifaceted and complex tasks. The Enhancing Neuroplasticity program is exploring and developing peripheral nerve stimulation methods and non-invasive devices to promote synaptic plasticity for improved learning paradigms. Key advances anticipated from this research will both create an anatomical and functional map of the underlying biological circuitry that mediates plasticity and optimize stimulation and training protocols to enable long-term retention for military personnel. Once successfully identified, the underlying mechanisms of targeted plasticity training can be applied to a broad range of cognitive skill training within the DoD, including foreign language learning, or data and intelligence analysis.</div> <div>FY 2019 Plans:</div> <div><div>- Compare effects of various nerve stimulation targets on brain neurophysiology and learning rate in animal models.</div><div>- Assess the combined impacts of neuromodulator receptor optimization with peripheral nerve stimulation to improve cognitive, motor, or sensory task performance in animal models.</div><div>- Determine efficacy of various biomarkers to validate target nerve stimulation in animal models.</div><div>- Initiate human studies of non-invasive nerve stimulation on learning.</div><div>- Identify technologies capable of in vivo characterization of human microbiome systems at the scale of microbial interactions.</div><div>- Characterize how information is passed between microorganisms (microbial communicome) and how that information is passed through generations and their host locations, including gut, brain, and skin.</div></div> <div>FY 2020 Plans:</div> <div><div>- Utilize biomarkers to guide effective engagement of nerve targets in human studies.</div></div>	FY 2018	FY 2019	FY 2020
	19.430	15.222	14.543

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B. Accomplishments/Planned Programs (\$ in Millions)		FY 2018	FY 2019	FY 2020
<ul style="list-style-type: none"><li>- Evaluate combined efficacy of pharmacological neuromodulation with peripheral nerve stimulation for learning in human trials.</li><li>- Assess the longevity of effects of targeted peripheral nerve stimulation on cognitive, motor, or sensory task performance.</li><li>- Demonstrate statistically valid improvement in performance and/or decrease in the time to achieve proficiency after pairing peripheral nerve stimulation with training.</li></ul> <p><b>FY 2019 to FY 2020 Increase/Decrease Statement:</b> The FY 2020 decrease reflects minor program repricing.</p>				
<p><b>Title:</b> Genome Protection Technologies</p> <p><b>Description:</b> The Genome Protection Technologies program is developing advances in critical efforts to generate a biodefense capability to control, counter, and reverse the effects of accidental or malicious misuse of gene editing technologies. This research will investigate new approaches for developing tunable controls to enable the safe and predictable use of synthetic genes and pathways. Additional work will develop protecting measures to prevent or limit unintended genome editing or engineering and develop new tools to recall or reverse engineered changes. Advances within this program will ensure that the U.S. remains at the vanguard of this now widespread, rapidly advancing field that poses potential national security threats due to the large-scale democratization of gene editing technologies.</p> <p><b>FY 2019 Plans:</b></p> <ul style="list-style-type: none"><li>- Conduct laboratory animal model testing for safety and efficacy of small molecule and genetic countermeasures.</li><li>- Use computational models to evaluate efficacy, stability, and fitness of gene editing controllers and countermeasures.</li><li>- Demonstrate efficacy, stability, and fitness of gene editing controllers and countermeasures in laboratory animal models.</li><li>- Characterize failure modes of gene editor controllers and countermeasures.</li></ul> <p><b>FY 2020 Plans:</b></p> <ul style="list-style-type: none"><li>- Conduct advanced in vivo testing of genome editors to include characterization of off-target effects, failure modes, target editing efficiency, and stability.</li><li>- Design safety measures and characterize toxicity and immunogenicity of genome editors.</li><li>- Determine safety and efficacy and characterize off-target effects of genome editor countermeasure candidates in vivo.</li><li>- Incorporate empirical data such as gene flow, fitness, generational stability, and failure modes into advanced computational models.</li><li>- Demonstrate the ability to revert or eliminate target genes in organisms in laboratory environments.</li></ul> <p><b>FY 2019 to FY 2020 Increase/Decrease Statement:</b> The FY 2020 decrease reflects minor program repricing.</p>		11.844	17.357	17.150
<p><b>Title:</b> Defend Against Crop System Attack</p>		10.700	14.018	13.718

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B. Accomplishments/Planned Programs (\$ in Millions)		FY 2018	FY 2019	FY 2020
<p><b>Description:</b> The Defend Against Crop System Attack program is developing a platform technology aimed at increasing the speed of DoD response to state or non-state actor release of biological threats directed at our crop systems. Conventional methods to defend against these threats are generally slow and ineffective. This program will leverage recent advances in molecular and synthetic biology to enable rapid delivery of gene therapies to plants for large-scale trait modification, improving resilience against adversary attack or emerging natural threats. Research within this program will develop an agnostic, scalable capability for protecting entire crop systems from emerging threats posed to food security by U.S. adversaries.</p> <p><b>FY 2019 Plans:</b></p> <ul style="list-style-type: none"><li>- Scale deployment of flexible plant transformation platforms in a controlled greenhouse setting.</li><li>- Initiate integration of novel and existing failsafe capabilities for the trait delivery platform.</li><li>- Investigate new approaches to increase the efficacy of genetic transmission.</li><li>- Demonstrate predictable and repeatable transmission of genetic materials to plants.</li></ul> <p><b>FY 2020 Plans:</b></p> <ul style="list-style-type: none"><li>- Ensure two week-long stable viral transformation resulting in gene-based protection in plant target.</li><li>- Determine adequate virus concentration to achieve adult plant transformation.</li><li>- Perform risk mitigation of potential delivery challenges within complex laboratory environments.</li><li>- Integrate virus delivery approach to achieve adult plant transformation.</li></ul> <p><b>FY 2019 to FY 2020 Increase/Decrease Statement:</b> The FY 2020 decrease reflects minor program repricing.</p>				
<p><b>Title:</b> Persistent Terrestrial Living Sensors</p> <p><b>Description:</b> The Persistent Terrestrial Living Sensors program is developing engineered biological sensor platforms capable of detecting land-based threats (e.g., chemicals, radiation, explosives) and relaying unique signals to existing DoD ground, air, and space assets. Unlike conventional methods that passively monitor threats and are limited by sensor energy needs, these biological sensors are effectively energy independent, increasing the potential for wide distribution and environmental robustness. Resulting platforms developed within this program will enable a variety of remote, persistent monitoring and reporting capabilities to address threat scenarios relevant for national security, including detecting improvised explosive devices (IEDs) and protecting infrastructure. These sensors will provide a flexible suite to complement conventional sensor systems within the DoD.</p> <p><b>FY 2019 Plans:</b></p> <ul style="list-style-type: none"><li>- Develop a quantitative model to guide plant-based sensor resilience and environment flexibility.</li><li>- Demonstrate the feasibility of combining high-specificity detection traits with physiological response traits by first exploring plant cell expression and quantitative modeling, and then by altering the physiology of plants.</li></ul>		3.000	12.582	13.174

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Appropriation/Budget Activity 0400 / 2	R-1 Program Element (Number/Name) PE 0602715E / MATERIALS AND BIOLOGICAL TECHNOLOGY	Project (Number/Name) MBT-02 / BIOLOGICALLY BASED MATERIALS AND DEVICES		
B. Accomplishments/Planned Programs (\$ in Millions)		FY 2018	FY 2019	FY 2020
<ul style="list-style-type: none"><li>- Begin production of plants with individual sense and report traits.</li><li>- Investigate methods to use soil-based microorganisms to sense subterranean events and propagate signals to the soil surface.</li></ul> <p><b>FY 2020 Plans:</b></p> <ul style="list-style-type: none"><li>- Demonstrate genetic modification of plant-expressed sensory proteins associated with DoD-relevant compounds.</li><li>- Demonstrate genetic modification of plant-expressed reporting signals at detectable levels.</li><li>- Identify internal plant resource issues that will have to be addressed to develop a real-world detection platform.</li><li>- Identify external biotic and abiotic challenges that need to be addressed to avoid practical use of plants as sensors.</li><li>- Test methods for stand-off detection of signals produced by microorganisms in response to subterranean sensing.</li></ul> <p><b>FY 2019 to FY 2020 Increase/Decrease Statement:</b> The FY 2020 increase reflects minor program repricing.</p>				
<p><b>Title:</b> Preemptive Expression of Protective Alleles (PREPARE)*</p> <p><b>Description:</b> *Formerly Transient CBRN Threat Defense</p> <p>The Preemptive Expression of Protective Alleles (PREPARE) program is creating a transient, near immediate prophylaxis to protect military personnel and civilians against public health and national security threats. Currently, protection against chemical, biological, and radiological threats relies on physical barrier technology. This program will include research to develop novel transient and reversible gene modulator therapies to bolster intrinsic host defenses. Work within this project will provide novel solutions that extend beyond the DoD's limited protective capabilities to respond to re-emerging, newly emerging, or engineered threats.</p> <p><b>FY 2019 Plans:</b></p> <ul style="list-style-type: none"><li>- Begin development of bioinformatics tools and validation methods that will improve the design and specificity of transient gene therapy strategies.</li><li>- Demonstrate genetic basis for cellular stress resistance in vitro.</li><li>- Characterize effective delivery tools for gene modulators that enable stress resistance.</li><li>- Characterize specificity of transient gene therapy in animal models.</li><li>- Demonstrate effectiveness of stress resistance constructs to specific threats.</li><li>- Initiate development of platform capabilities for scalable and adaptable threat response platform.</li></ul> <p><b>FY 2020 Plans:</b></p> <ul style="list-style-type: none"><li>- Demonstrate multiplexed targeting of multiple cellular resistance genes to confer resistance to multiple threats.</li><li>- Demonstrate and optimize specificity and duration of modulation of gene modulators in animal models.</li><li>- Optimize delivery tool specificity for gene modulators.</li></ul>		8.510	15.712	16.097

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<b>Exhibit R-2A, RDT&amp;E Project Justification:</b> PB 2020 Defense Advanced Research Projects Agency		<b>Date:</b> March 2019	
<b>Appropriation/Budget Activity</b> 0400 / 2	<b>R-1 Program Element (Number/Name)</b> PE 0602715E / MATERIALS AND BIOLOGICAL TECHNOLOGY	<b>Project (Number/Name)</b> MBT-02 / BIOLOGICALLY BASED MATERIALS AND DEVICES	
<b>B. Accomplishments/Planned Programs (\$ in Millions)</b>		<b>FY 2018</b>	<b>FY 2019</b>
<ul style="list-style-type: none"> <li>- Demonstrate target-agnostic platform that can address multiple threats using a common set of gene modulation and delivery components.</li> <li>- Investigate timing of optimal countermeasure administration to maximize therapeutic and prophylactic performance.</li> </ul> <p><b>FY 2019 to FY 2020 Increase/Decrease Statement:</b> The FY 2020 increase reflects minor program repricing.</p>			
<p><b>Title:</b> Persistent Aquatic Living Sensors</p> <p><b>Description:</b> The Persistent Aquatic Living Sensors program will develop novel capabilities to sense and surveil submersibles (e.g., submarines, unmanned underwater vehicles) and divers in littoral waters using living organisms present in the environment. This effort will focus on characterizing marine biological behavior in response to targets of interest and developing the hardware, software, and algorithms that will translate organism behavior into DoD actionable information. By harnessing the unique capabilities of biology, including adaptation, response, and replication, work in this program will enable persistent dominance in contested waters. Results from this research will enhance security for maritime activities and provide DoD naval operations with new sensing paradigms to complement current sensor technologies used in traditionally challenging regions across the world.</p> <p><b>FY 2019 Plans:</b></p> <ul style="list-style-type: none"> <li>- Investigate organism response to targets of interest in a laboratory environment using benchtop instrumentation.</li> <li>- Initiate research to convert organism response into robust sensing system by developing algorithms to classify organism response in relation to targets.</li> <li>- Research new reporting schemes to communicate signal detection and actionable information to existing DoD systems.</li> </ul> <p><b>FY 2020 Plans:</b></p> <ul style="list-style-type: none"> <li>- Characterize biological responses to targets and confounders at greater distances and in more realistic environments.</li> <li>- Investigate approaches to evoke biological responses in marine organisms.</li> <li>- Harden engineered components for persistent deployments, and perform validation testing on system endurance.</li> <li>- Develop fully integrated seaworthy prototype combining biology and engineered components.</li> <li>- Demonstrate system ability to detect and classify targets and confounders in ecosystem-style aquaria or open waters, analyze results, and produce alerts via satellite link.</li> </ul> <p><b>FY 2019 to FY 2020 Increase/Decrease Statement:</b> The FY 2020 increase reflects ongoing research and development efforts, construction of seaworthy prototype, and prototype demonstration, as well as new efforts initiated to evoke biological responses in marine organisms.</p>		-	18.799
<b>Title:</b> Expanding Human Resiliency		-	13.425

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Appropriation/Budget Activity 0400 / 2	R-1 Program Element (Number/Name) PE 0602715E / MATERIALS AND BIOLOGICAL TECHNOLOGY	Project (Number/Name) MBT-02 / BIOLOGICALLY BASED MATERIALS AND DEVICES		
B. Accomplishments/Planned Programs (\$ in Millions)		FY 2018	FY 2019	FY 2020
<p><b>Description:</b> The Expanding Human Resiliency program aims to maximize warfighter performance and resiliency by leveraging the signals of the human microbiome to improve physiology. This program will develop new technologies to control and manipulate the microbiome to enable peak human performance. Current state-of-the-art approaches are focused on metagenomics to inventory and categorize the microbes in a given sample. In order to have more precise and on-demand control of the human microbiome, technologies will be developed to elucidate the complex interactions between the microorganisms and their human host as well as the interactions between consortia of adapted and evolved microorganisms. Additional work will be performed to facilitate human functions (e.g., immunity to disease, metabolic performance, tolerance to chemical exposure, etc.) and behaviors (e.g., mood, decision making, ability to work as a cohesive team, etc.) using specific microbial consortia living in the gastrointestinal tract, respiratory tract, skin or mouth. Advances in this area will both develop novel technologies to interrogate complex microbial communities in human systems and discover ways to beneficially harness microbiomes to expand warfighter resiliency and performance.</p> <p><b>FY 2020 Plans:</b></p> <ul style="list-style-type: none"><li>- Investigate ways to improve methods for interpretation and prediction of microbial interactions and their ability to regulate host function.</li><li>- Initiate testing of methods to alter chemical production by microbiomes.</li><li>- Begin longitudinal studies to track host function and behavior with changes in the microbiome.</li><li>- Begin development of initial microbiome modulation approaches and assess host functional response.</li></ul> <p><b>FY 2019 to FY 2020 Increase/Decrease Statement:</b> The FY 2020 increase reflects program initiation.</p>				
<p><b>Title:</b> Living Foundries</p> <p><b>Description:</b> The goal of the Living Foundries program is to create a revolutionary, biologically-based manufacturing platform for the DoD and the Nation. With its ability to perform complex chemistries, be flexibly programmed through DNA code, scale, adapt to changing environments, and self-repair, biology represents one of the most powerful manufacturing platforms known. Living Foundries seeks to develop the foundational technological infrastructure to transform biology into an engineering practice, speeding the biological design-build-test-learn cycle and expanding the complexity of systems that can be engineered. Ultimately, Living Foundries aims to provide game-changing manufacturing paradigms for the DoD, enabling adaptable, on-demand production of critical and high-value molecules.</p> <p>Research thrusts focus on the development and demonstration of open technology platforms to prove out capabilities for rapid (months vs. years) design and construction of new bio-production systems. The result will be an integrated, modular infrastructure across the areas of design, fabrication, debugging, analysis, optimization, and validation -- spanning the entire development life-</p>		17.020	6.298	-

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<b>B. Accomplishments/Planned Programs (\$ in Millions)</b>		<b>FY 2018</b>	<b>FY 2019</b>
<p>cycle and enabling the ability to rapidly assess and improve designs. Success is predicated on tight coupling of computational design, fabrication of systems, debugging using multiple characterization data types, analysis, and further development such that iterative design and experimentation will be accurate, efficient and controlled. Demonstration platforms will be challenged to build a variety of DoD-relevant, novel molecules with complex functionalities, such as synthesis of advanced, functional chemicals, materials precursors, and polymers (those tolerant of harsh environments). This program has basic research efforts funded in PE 0601101E, Project TRS-01.</p> <p><b>FY 2019 Plans:</b></p> <ul style="list-style-type: none"> <li>- Demonstrate a fully automated infrastructure pipeline capable of prototyping and generating DoD-relevant molecules.</li> <li>- Demonstrate ability to scale production of molecules from multi-gram to kilogram scale using biology.</li> <li>- Investigate methods to generate molecules that have not been previously synthesized using traditional chemistry.</li> </ul> <p><b>FY 2019 to FY 2020 Increase/Decrease Statement:</b> The FY 2020 decrease reflects program completion.</p>			
<p><b>Title:</b> Adaptive Immunomodulation-Based Therapeutics</p> <p><b>Description:</b> The Adaptive Immunomodulation-Based Therapeutics program is developing platform technologies to interrogate and define the biological pathways that will enhance operational readiness for DoD personnel. This program will aid the warfighter by improving immune response, minimizing inflammation, and restoring critical organ function post trauma. One approach to achieve this capability will require the development of new tools to stimulate and measure responses of the nervous system in order to harness the bioelectric code, enabling targeted therapy without the need for pharmacological products, ultimately reducing logistical requirements. An additional approach involves characterizing the host response in patients with severe infections, which provides a quantitative framework to guide therapy. Algorithms will be developed to evaluate and predict various physiological conditions for military personnel. Advances made under the Adaptive Immunomodulation-Based Therapeutics program will improve the response capabilities against severe biological threats and offer new avenues for treating disease or organ function to improve force readiness.</p> <p><b>FY 2019 Plans:</b></p> <ul style="list-style-type: none"> <li>- Quantify on-target responses to neurostimulation to validate feedback biomarkers, evaluate therapeutic benefit, and demonstrate circuit specificity.</li> <li>- Implement computational models of integrated neuromodulation and biomarker signaling for feedback control of health status.</li> <li>- Demonstrate sustained functionality of novel bio-interfaces for neuromodulatory control of health status in animal models.</li> </ul>		16.212	13.234
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<b>B. Accomplishments/Planned Programs (\$ in Millions)</b>		<b>FY 2018</b>	<b>FY 2019</b>	<b>FY 2020</b>
- Initiate clinical studies of feedback-controlled neuromodulation system to treat inflammation, pain, and the effects of Post-traumatic stress disorder (PTSD).				
<b>FY 2019 to FY 2020 Increase/Decrease Statement:</b> The FY 2020 decrease reflects program completion.				
<b>Title:</b> BioDesign  <b>Description:</b> BioDesign employed system engineering methods in combination with advances in biological and chemical technologies to create novel methods for threat response. This thrust developed new high-throughput technologies for monitoring the function of cellular machinery at the molecular level and the response(s) of that machinery to physical, chemical, or biological threats. While conventional approaches typically require decades of research, new high-throughput approaches permit rapid assessment of the impact of known or unknown threats on identified biomolecules and cell function. Successful research in this thrust both reduced the time required to understand the mechanism of action for new pharmaceutical compounds and enhanced response capabilities for emerging and engineered threats.		9.747	-	-
<b>Title:</b> Biological Robustness in Complex Settings (BRICS)  <b>Description:</b> The Biological Robustness in Complex Settings (BRICS) program developed innovative approaches to engineer forensic microbial systems, creating unique microbial signatures for environmental forensic operations and modulation of host function. Integrating the fundamental component technologies developed under PE 0601101E, TRS-01, this program focused on engineering microbial communities, detection signatures, and mechanisms of robustness. This deeper knowledge helped assemble the constructs needed for new microbial systems that could be used for DoD relevant applications including forensics and warfighter health and performance.		10.041	-	-
<b>Accomplishments/Planned Programs Subtotals</b>		106.504	113.222	115.173
<b>C. Other Program Funding Summary (\$ in Millions)</b> N/A				
<b>Remarks</b>				
<b>D. Acquisition Strategy</b> N/A				
<b>E. Performance Metrics</b> Specific programmatic performance metrics are listed above in the program accomplishments and plans section.				