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Exhibit R-2, RDT&E Budget Item Justification: PB 2023 Chemical and Biological Defense Program **Date:** April 2022

Appropriation/Budget Activity 0400: <i>Research, Development, Test & Evaluation, Defense-Wide</i> / BA 1: <i>Basic Research</i>	R-1 Program Element (Number/Name) PE 0601384BP / <i>CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)</i>
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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	-	46.644	37.208	34.734	-	34.734	35.341	35.134	39.336	43.853	Continuing	Continuing
LF1: <i>Life Sciences (Basic Research)</i>	-	27.671	19.172	19.199	-	19.199	19.809	19.602	23.804	25.804	Continuing	Continuing
PS1: <i>Physical Sciences (Basic Research)</i>	-	18.973	18.036	15.535	-	15.535	15.532	15.532	15.532	18.049	Continuing	Continuing

A. Mission Description and Budget Item Justification

This program element (PE) resources basic research efforts directed at promoting theoretical and experimental research in Life and Physical Sciences. These efforts are part of an integrated portfolio addressing emerging chemical and biological (CB) threats, and are a key enabler supporting the Mitigate, Protect, and Understand portfolios. Basic research focuses on pursuing fundamental science to advance a greater understanding of threats, improve situational awareness of emerging threats, and support transformative research in emerging research areas that can potentially foster paradigm shifts in the CB defense research arena to a rapid response capability.

Individual projects include:

- Life Sciences (LF1): fundamental efforts to understand living systems' response to biological or chemical agents, to support detection, diagnostics, protection, and medical treatment (e.g. microbiology, biochemistry, pathogenic mechanisms, cell and molecular biology, immunology, nanoscale science, and information science).
- Physical Sciences (PS1): fundamental scientific phenomena to support investigation of physical and chemical properties and interactions for enhanced functionalities important to detection, diagnostics, protection, and decontamination (e.g. chemistry, physics, materials science, nanotechnologies, nanoscale science, and environmental science).

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Appropriation/Budget Activity	R-1 Program Element (Number/Name)
0400: <i>Research, Development, Test & Evaluation, Defense-Wide / BA 1: Basic Research</i>	PE 0601384BP / <i>CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)</i>

B. Program Change Summary (\$ in Millions)	FY 2021	FY 2022	FY 2023 Base	FY 2023 OCO	FY 2023 Total
Previous President's Budget	50.300	34.708	0.000	-	0.000
Current President's Budget	46.644	37.208	34.734	-	34.734
Total Adjustments	-3.656	2.500	34.734	-	34.734
• Congressional General Reductions	-	-			
• Congressional Directed Reductions	-	-			
• Congressional Rescissions	-	-			
• Congressional Adds	0.000	2.500			
• Congressional Directed Transfers	0.000	-			
• Reprogrammings	-1.656	-			
• SBIR/STTR Transfer	-2.000	-			
• Other Adjustments	0.000	-	34.734	-	34.734

Congressional Add Details (\$ in Millions, and Includes General Reductions)

Project: PS1: *Physical Sciences (Basic Research)*

Congressional Add: *Water Jet Technology*

Congressional Add: *Chemically resistant, high-performance military cordage, rope, and webbing.*

Congressional Add Subtotals for Project: PS1

Congressional Add Totals for all Projects

	FY 2021	FY 2022
	5.000	-
	-	2.500
Congressional Add Subtotals for Project: PS1	5.000	2.500
Congressional Add Totals for all Projects	5.000	2.500

Change Summary Explanation

Funding: FY 2021 (-\$1.656 Million): Below threshold reprogramming to Advanced Component Development & Prototypes and RDT&E Management Support efforts.

FY 2021 (-\$2.000 Million): Transfer of funding to support Small Business Innovative Research/Small Business Technology Transfer efforts.

FY 2021 (+\$5.000 Million): Congressional Add for Water Jet Technology is reflected in the Current President's Budget.

FY 2022 (+\$2.500 Million): Congressional Add for chemically resistant, high-performance military cordage, rope and webbing.

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

Schedule: N/A

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0400: <i>Research, Development, Test & Evaluation, Defense-Wide / BA 1: Basic Research</i>	PE 0601384BP / <i>CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)</i>

Technical: N/A

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Exhibit R-2A, RDT&E Project Justification: PB 2023 Chemical and Biological Defense Program **Date:** April 2022

Appropriation/Budget Activity 0400 / 1	R-1 Program Element (Number/Name) PE 0601384BP / CHEMICAL/BIOLOGICAL DEFENSE (BASIC RESEARCH)	Project (Number/Name) LF1 / Life Sciences (Basic Research)
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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
LF1: Life Sciences (Basic Research)	-	27.671	19.172	19.199	-	19.199	19.809	19.602	23.804	25.804	Continuing	Continuing

A. Mission Description and Budget Item Justification

This project (LF1) focuses on fundamental efforts to understand living systems' responses to biological or chemical agents, to support detection, protection, diagnostics, and medical treatment. Research focuses on studying factors which influence the behavior of chemicals, toxins, and pathogens in relation to the host or target. Understanding of host/agent interactions can drive exploration of novel approaches to detect, diagnose or protect against threats. Research also focuses on medical countermeasures for improved efficacy against a wide array of current and future threat agents. This project is a key enabler supporting the Mitigate, Protect, and Understand portfolios.

Individual efforts in this Project include:

- Research to understand threats focused on illuminating pathogen/host interactions, innate and targeted immune responses, and drug/pathogen interactions that enable development of new medical countermeasures and diagnostic platforms.
- Research in advancing countermeasures to understand underpinnings necessary to advance translational animal models for human disease, to explore artificial intelligence/machine learning (AI/ML) and novel structural biology approaches for enhancing rapid medical defense capabilities, to seek platform technologies with broad flexibility for drug development, and to improve protective factors for increasing therapeutic efficacy.

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

	FY 2021	FY 2022	FY 2023
Title: 1) Life Sciences	27.671	19.172	19.199
Description: Focuses on fundamental efforts to understand living systems' responses to biological agents, providing knowledge and capabilities that support medical countermeasure development for prophylaxis and therapeutic interventions.			
FY 2022 Plans:			
- Animal Models - Transition animal models to applied program for validation.			
- Enabling Technologies - Continue biotechnologies investments into organs-on-a-chip to address mechanisms of actions as well as drug model development as well as high throughput screen purification and screening.			
- Platform Technology - Continue to validate genomic targets for broad anti-alphavirus treatment and establish a screening database of preclinical countermeasures.			
- Artificial Intelligence (AI) for Early Drug Discovery - Continue to explore the application of machine learning, AI, and other computational tools to inform rational drug discovery, design, optimization, decision support, and medical modeling. Develop a machine learning algorithm to aid in identifying optimal candidates for advanced development of monoclonal antibody biologics.			
- Viral Pathogenesis - Continue pathogenesis in mouse models as well as antimicrobial peptide development.			

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B. Accomplishments/Planned Programs (\$ in Millions)	FY 2021	FY 2022	FY 2023
<p>- Biomarkers - Begin assessing gene expression in various tissues after alphavirus exposure. Begin integration of machine learning (ML), to predict cellular binding site targets.</p> <p>- Inflammation Mapping - Initiate comparison of genomic models of expression to inflammatory response data. Assess how RNA regulation changes after exposure to chemical agents. Begin integration of machine learning (ML) to screen small molecule library for potential therapeutics.</p> <p>Program ending in FY22:</p> <p>- STEM - Complete STEM strategic efforts to develop talent across the education continuum to enrich our current and future DoD workforce to meet defense technological challenges.</p> <p>FY 2023 Plans:</p> <p>- Organoid Technology (previously Enabling Technology) - Investigate cellular toxicity and metabolic profiles in organoids and evaluate relevance to animal model data. Determine inflammatory signaling in mouse models that are relevant to human cells.</p> <p>- Pathogenesis (previously Viral Pathogenesis) - Assess peptide protection against multiple subtype viral insult in mouse model. Assess influence of gene expression following viral infection.</p> <p>- Structural Biology (previously Platform Technology) - Investigate efficacy of inhibitor molecules in mouse models. Evaluate anti-alphavirus peptide for efficacy of reduced viral load in animal models. Design synthesis loop for production and testing of small molecules and validate machine-learning predictions.</p> <p>- Artificial Intelligence (AI) for Early Drug Discovery - Develop training datasets for drug combinations and strategy for molecular selection. Evaluate model response to changing conditions and extend forecasting to additional diseases. Use AI model to generate therapeutic Monoclonal antibodies against bacterial targets and screen for efficacy.</p> <p>- Biomarkers - Begin testing machine-learning model to predict cellular binding site targets. Demonstrate screening framework for binders to expanded data set of pathogens.</p> <p>- Inflammation Mapping - Validate gene protection against chemical toxicity and assess neuron regeneration. Continue to integrate machine learning for predicting nerve reactivation and begin selecting molecules for validation.</p> <p>FY 2022 to FY 2023 Increase/Decrease Statement: Minor change due to routine program adjustments.</p>			
Accomplishments/Planned Programs Subtotals	27.671	19.172	19.199

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C. Other Program Funding Summary (\$ in Millions)

Line Item	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
• CB2: <i>Chemical Biological Defense (Applied Research)</i>	95.517	104.362	0.000	-	0.000	0.000	0.000	0.000	0.000	0.000	199.879
• MT2: <i>Mitigate (Applied Research)</i>	0.000	0.000	75.411	-	75.411	71.705	68.483	64.502	70.651	Continuing	Continuing
• PT2: <i>Protect (Applied Research)</i>	0.000	0.000	58.758	-	58.758	59.338	59.855	61.517	63.612	Continuing	Continuing
• TM2: <i>Techbase Medical Defense (Applied Research)</i>	93.525	105.594	0.000	-	0.000	0.000	0.000	0.000	0.000	0.000	199.119
• UN2: <i>Understand (Applied Research)</i>	0.000	0.000	122.028	-	122.028	117.683	105.509	101.577	100.929	Continuing	Continuing

Remarks

D. Acquisition Strategy

N/A

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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
PS1: <i>Physical Sciences (Basic Research)</i>	-	18.973	18.036	15.535	-	15.535	15.532	15.532	15.532	18.049	Continuing	Continuing

A. Mission Description and Budget Item Justification

This project (PS1) advances fundamental scientific knowledge in physical science areas that include chemistry, physics, materials science, environmental science, and nanotechnology that could potentially lead to transformational CB defensive capabilities enhancing Warfighter performance and safety. This project is a key enabler supporting the Mitigate, Protect, and Understand portfolios.

Individual efforts in this Project include:

- Innovative materials focuses on understanding the physics, physical properties, fabrication pathways, and characterization methods related to material classes that would enable novel, advanced capabilities for decontamination, protection and detection of chemical and biological (CB) threats.
- Novel sensing research to improve the understanding of elementary physics or fundamental materials properties to construct novel platforms and approaches for detection, diagnostics, hazard mitigation and protection.
- Modeling sciences research to explore the potential of AI/ML computational approaches for hazard mitigation, stand-off physio-monitoring, rational and rapid design of medical countermeasures, and novel materials with enhanced efficacy.

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

	FY 2021	FY 2022	FY 2023
Title: 1) Physical Sciences	13.973	15.536	15.535
Description: Focuses on fundamental scientific phenomena including chemistry, physics, materials science, environmental science, and nanotechnology.			
FY 2022 Plans:			
- Multifunctional Materials - Continue to synthesize polymer compositions and modify structures based on mechanical analysis. Begin understanding requirements for scale-up of synthesis and integration into woven fibers.			
- Design Rules for Materials - Continue investigating the effects of topology and pore size of metal organic frameworks, and test against simulant molecules. Revise computational models to predict material reaction rates.			
- Biomimetic - Continue understanding design rules for catalytic hydrolysis of target molecules. Continue characterization of polymers through simulation and comparison to experimental data.			
- Novel Destruction - Continue developing a kinetic rates model for organic compounds and Chemical Warfare Agent (CWA) surrogates. Continue investigating new nano-catalyst synthesis method to reduce material costs and improve catalytic activity.			
- Photocatalysis - Begin to evaluate thermal chemistry of various materials for baseline metrics. Model performance metrics of material characteristics and kinetics with and without chemical simulants.			

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B. Accomplishments/Planned Programs (\$ in Millions)	FY 2021	FY 2022	FY 2023
<p>Programs ending in FY22:</p> <ul style="list-style-type: none"> - Bio Characterization - Complete determination for drivers of genetic change and behavior of pathogens in a nonculturable state. Complete conditions that determine that resuscitate bacteria and assess virulence after resuscitation. - Photonics - Complete characterization of photonic component sensitivity and integration of multi-agent chemical sensing. Complete assessment of selectivity needs and testing against mixture vapors. - Chemical Reactivators - Complete mechanistic and structural studies of the aged reactivator complexes. <p>FY 2023 Plans:</p> <ul style="list-style-type: none"> - Multifunctional Materials - Design experiments to predict high-performing materials. Synthesize and characterize materials for stability in preparation for live agent testing. - Design Rules for Materials - Evaluate surface interactions of the metal organic framework against simulant molecules. Expand model to incorporate kinetics and thermodynamic interactions of chemical decomposition based on simulant work. - Biomimetic - Complete: design and validate macroscale biomimetic membrane. Demonstrate application of stabilized enzymes and optimization of kinetic and structural features. - Photocatalysis - Synthesize metal organic framework (MOF) and evaluate surface characteristics to determine strategy for tuning properties. Perform studies using simulants and model energetic effects. - Novel Destruction - Continue developing a kinetic rates model for organic compounds and CWA surrogates. Continue investigating new nano-catalyst synthesis method to reduce material costs and improve catalytic activity. <p>FY 2022 to FY 2023 Increase/Decrease Statement: Minor change due to routine program adjustments.</p>			
Accomplishments/Planned Programs Subtotals	13.973	15.536	15.535

	FY 2021	FY 2022
Congressional Add: Water Jet Technology	5.000	-
FY 2021 Accomplishments: - Developed and tested Water Jet Technology for the destruction of chemical agent munitions using a stream of high pressure water.		
Congressional Add: Chemically resistant, high-performance military cordage, rope, and webbing.	-	2.500
FY 2022 Plans: Chemically resistant, high-performance military cordage, rope, and webbing.		
Congressional Adds Subtotals	5.000	2.500

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Remarks

D. Acquisition Strategy

N/A