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Exhibit R-2, RDT&E Budget Item Justification: PB 2024 Chemical and Biological Defense Program **Date:** March 2023

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 and Biological Defense Program</i>
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COST (\$ in Millions)	Prior Years	FY 2022	FY 2023	FY 2024 Base	FY 2024 OCO	FY 2024 Total	FY 2025	FY 2026	FY 2027	FY 2028	Cost To Complete	Total Cost
Total Program Element	0.000	35.327	39.734	36.235	0.000	36.235	37.812	43.264	49.270	50.188	Continuing	Continuing
LF1: <i>Life Sciences (Basic Research)</i>	-	19.114	19.199	20.335	0.000	20.335	21.125	26.206	29.030	29.575	Continuing	Continuing
PS1: <i>Physical Sciences (Basic Research)</i>	-	16.213	20.535	15.900	0.000	15.900	16.687	17.058	20.240	20.613	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 Understand, Protect, and Mitigate 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 the 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</i> / BA 1: <i>Basic Research</i>	PE 0601384BP / <i>Chemical and Biological Defense Program</i>

B. Program Change Summary (\$ in Millions)	FY 2022	FY 2023	FY 2024 Base	FY 2024 OCO	FY 2024 Total
Previous President's Budget	37.208	34.734	35.341	-	35.341
Current President's Budget	35.327	39.734	36.235	-	36.235
Total Adjustments	-1.881	5.000	0.894	-	0.894
• Congressional General Reductions	-	-			
• Congressional Directed Reductions	-	-			
• Congressional Rescissions	-	-			
• Congressional Adds	-	5.000			
• Congressional Directed Transfers	-	-			
• Reprogrammings	-1.022	-			
• SBIR/STTR Transfer	-0.859	-			
• Other Adjustments	-	-	0.894	-	0.894

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

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

Congressional Add: *Physical Sciences*

	FY 2022	FY 2023
	2.500	5.000
Congressional Add Subtotals for Project: PS1	2.500	5.000
Congressional Add Totals for all Projects	2.500	5.000

Change Summary Explanation

Funding: FY 2022 (+\$2.500 Million): Congressional Add for chemically resistant, high-performance military cordage, rope and webbing is included in the Previous President's Budget total.

FY 2022 (-\$1.022 Million): Below threshold reprogramming to support priority protection and hazard mitigation efforts within Advanced Technology Development.

FY 2022 (-\$0.859 Million): Transfer of funding to support Small Business Innovative Research/Small Business Technology Transfer efforts.

FY 2023 (+\$5.000 Million): Congressional Add for waterless solutions for decontamination.

FY 2024 (+\$0.894 Million): Basic Research enhancements for strategic competition (+\$0.722 Million) and Departmental inflation rate adjustments (+\$0.172 Million).

Schedule: N/A

Technical: N/A

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Exhibit R-2A, RDT&E Project Justification: PB 2024 Chemical and Biological Defense Program **Date:** March 2023

Appropriation/Budget Activity 0400 / 1	R-1 Program Element (Number/Name) PE 0601384BP / <i>Chemical and Biological Defense Program</i>	Project (Number/Name) LF1 / <i>Life Sciences (Basic Research)</i>
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COST (\$ in Millions)	Prior Years	FY 2022	FY 2023	FY 2024 Base	FY 2024 OCO	FY 2024 Total	FY 2025	FY 2026	FY 2027	FY 2028	Cost To Complete	Total Cost
<i>LF1: Life Sciences (Basic Research)</i>	-	19.114	19.199	20.335	0.000	20.335	21.125	26.206	29.030	29.575	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 that influence the behavior of chemicals, toxins, and pathogens in relation to the host or target. Understanding host/agent interactions can drive the 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 Understand, Protect, and Mitigate 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 the 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 2022	FY 2023	FY 2024
Title: 1) Life Sciences	19.114	19.199	20.335
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 2023 Plans:			
- Organoid 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.			
- Pathogenesis - Assess peptide protection against multiple subtype viral insult in mouse model. Assess influence of gene expression following viral infection.			
- Structural Biology - 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.			

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B. Accomplishments/Planned Programs (\$ in Millions)	FY 2022	FY 2023	FY 2024
<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 2024 Plans:</p> <p>- Organoid Technology - Continue to investigate cellular toxicity and metabolic profiles in organoids and evaluate relevance to animal model data. Determine primary metabolite production in mouse cells.</p> <p>- Pathogenesis - Continue to assess peptide protection against multiple subtype viral insult in mouse model. Evaluate the impact of transcriptional changes on neuronal cell death in vitro.</p> <p>- Structural biology - Continue investigating efficacy of inhibitor molecules in mouse models. Characterize resistance to anti-alphavirus peptide to describe mechanism of action. Generate experimental data for testing of small molecules and validate machine-learning predictions.</p> <p>- Artificial Intelligence (AI) for Early Drug Discovery - Develop active learning strategy to guide selection and molecular screening. Continue to evaluate model response to changing conditions and extend forecasting to additional diseases. Use AI model to combine small molecule and therapeutic Monoclonal antibodies against bacterial targets and screen for efficacy.</p> <p>- Biomarkers - Begin iterative improvement of machine-learning model to predict cellular binding site targets. Integrate machine-learning architecture and sampling for iterative experimental design.</p> <p>- Inflammation Mapping - Begin testing of novel medical countermeasures in an in vitro nerve model. Begin validation of select molecules and demonstrate molecular design against in vitro data.</p> <p>FY 2023 to FY 2024 Increase/Decrease Statement: Minor change due to routine program adjustments.</p>			
Accomplishments/Planned Programs Subtotals	19.114	19.199	20.335

C. Other Program Funding Summary (\$ in Millions)											
Line Item	FY 2022	FY 2023	FY 2024 Base	FY 2024 OCO	FY 2024 Total	FY 2025	FY 2026	FY 2027	FY 2028	Cost To Complete	Total Cost
• CB2: <i>Chemical Biological Defense (Applied Research)</i>	97.410	-	-	-	-	-	-	-	-	0.000	97.410
• MT2: <i>Mitigate (Applied Research)</i>	-	73.321	66.371	-	66.371	63.832	51.426	59.920	64.824	Continuing	Continuing

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

<u>Line Item</u>	<u>FY 2022</u>	<u>FY 2023</u>	<u>FY 2024</u> <u>Base</u>	<u>FY 2024</u> <u>OCO</u>	<u>FY 2024</u> <u>Total</u>	<u>FY 2025</u>	<u>FY 2026</u>	<u>FY 2027</u>	<u>FY 2028</u>	<u>Cost To</u> <u>Complete</u>	<u>Total Cost</u>
• PT2: <i>Protect (Applied Research)</i>	-	58.091	55.057	-	55.057	56.153	57.817	61.452	61.452	Continuing	Continuing
• TM2: <i>Techbase Medical Defense (Applied Research)</i>	107.608	-	-	-	-	-	-	-	-	0.000	107.608
• UN2: <i>Understand (Applied Research)</i>	-	112.952	119.182	-	119.182	111.773	107.842	107.193	107.193	Continuing	Continuing

Remarks

D. Acquisition Strategy

N/A

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COST (\$ in Millions)	Prior Years	FY 2022	FY 2023	FY 2024 Base	FY 2024 OCO	FY 2024 Total	FY 2025	FY 2026	FY 2027	FY 2028	Cost To Complete	Total Cost
<i>PS1: Physical Sciences (Basic Research)</i>	-	16.213	20.535	15.900	0.000	15.900	16.687	17.058	20.240	20.613	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 Understand, Protect, and Mitigate 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 Artificial Intelligence/Machine Learning (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 2022	FY 2023	FY 2024
Title: 1) Physical Sciences	13.713	15.535	15.900
Description: Focuses on fundamental scientific phenomena including chemistry, physics, materials science, environmental science, and nanotechnology.			
FY 2023 Plans:			
- Multifunctional Materials - Design experiments to predict high-performing materials. Synthesize and characterize materials for stability in preparation for 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.			

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B. Accomplishments/Planned Programs (\$ in Millions)	FY 2022	FY 2023	FY 2024
- 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. FY 2024 Plans: -Multifunctional Materials - Begin development of peptoid-based ultrathin membranes with customized reactivation sites. Establish design, methodology and assembly protocols for fusion tag system and surface binding functionality at various densities. -Design Rules for Materials - Complete characterization and testing of bi-functional materials. Develop synthetic process for design of metal organic framework with high adsorption capacity and selectivity. -Biomimetic - Investigate scalability of protein designs and test membrane-protein against simulants. Begin synthesis of polymer coating to nylons and characterization of mechanical properties. -Photocatalysis - Characterize individual components of hybrid catalysts and their interactions with simulants, in light and dark. Continue studies of aerogels using simulants and model energetic effects. -Novel Destruction - Investigate binding specificity of enzymes for catalytic activity and improved sensitivity. Experiment with photochemical activity and determine oxidation capacity of materials. FY 2023 to FY 2024 Increase/Decrease Statement: Minor change due to routine program adjustments.			
Accomplishments/Planned Programs Subtotals	13.713	15.535	15.900

	FY 2022	FY 2023
Congressional Add: Physical Sciences	2.500	5.000
FY 2022 Accomplishments: Chemically resistant, high-performance military cordage, rope, and webbing. FY 2023 Plans: Waterless solutions for decontamination.		
Congressional Adds Subtotals	2.500	5.000

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

Line Item	FY 2022	FY 2023	FY 2024 Base	FY 2024 OCO	FY 2024 Total	FY 2025	FY 2026	FY 2027	FY 2028	Cost To Complete	Total Cost
• CB2: <i>Chemical Biological Defense (Applied Research)</i>	97.410	-	-	-	-	-	-	-	-	0.000	97.410
• MT2: <i>Mitigate (Applied Research)</i>	-	73.321	66.371	-	66.371	63.832	51.426	59.920	64.824	Continuing	Continuing
• PT2: <i>Protect (Applied Research)</i>	-	58.091	55.057	-	55.057	56.153	57.817	61.452	61.452	Continuing	Continuing

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<u>Line Item</u>	<u>FY 2022</u>	<u>FY 2023</u>	<u>FY 2024</u> <u>Base</u>	<u>FY 2024</u> <u>OCO</u>	<u>FY 2024</u> <u>Total</u>	<u>FY 2025</u>	<u>FY 2026</u>	<u>FY 2027</u>	<u>FY 2028</u>	<u>Cost To</u> <u>Complete</u>	<u>Total Cost</u>
• TM2: <i>Techbase Medical Defense (Applied Research)</i>	107.608	-	-	-	-	-	-	-	-	0.000	107.608
• UN2: <i>Understand (Applied Research)</i>	-	112.952	119.182	-	119.182	111.773	107.842	107.193	107.193	Continuing	Continuing

Remarks

D. Acquisition Strategy

N/A