Exhibit R-2, RDT&E Budget Item Justification: PB 2025 Chemical and Biological Defense Program	Date: March 2024
Appropriation/Budget Activity 0400: *Research, Development, Test & Evaluation, Defense-Wide* / BA 1: *Basic Research*	**R-1 Program Element (Number/Name)** PE 0601384BP / *Chemical and Biological Defense Program*

COST ($ in Millions)	Prior Years	FY 2023	FY 2024	FY 2025 Base	FY 2025 OCO	FY 2025 Total	FY 2026	FY 2027	FY 2028	FY 2029	Cost To Complete	Total Cost
Total Program Element	0.000	38.999	36.235	37.812	0.000	37.812	43.264	49.270	50.188	50.188	Continuing	Continuing
LF1: *Life Sciences (Basic Research)*	-	18.485	20.335	21.125	0.000	21.125	26.206	29.030	29.575	29.575	Continuing	Continuing
PS1: *Physical Sciences (Basic Research)*	-	20.514	15.900	16.687	0.000	16.687	17.058	20.240	20.613	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).

Exhibit R-2, RDT&E Budget Item Justification: PB 2025 Chemical and Biological Defense Program	Date: March 2024
Appropriation/Budget Activity 0400: *Research, Development, Test & Evaluation, Defense-Wide* / BA 1: *Basic Research*	**R-1 Program Element (Number/Name)** PE 0601384BP / *Chemical and Biological Defense Program*

B. Program Change Summary ($ in Millions)	FY 2023	FY 2024	FY 2025 Base	FY 2025 OCO	FY 2025 Total
Previous President's Budget	39.734	36.235	37.812	-	37.812
Current President's Budget	38.999	36.235	37.812	-	37.812
Total Adjustments	-0.735	0.000	0.000	-	0.000
• Congressional General Reductions	-	-			
• Congressional Directed Reductions	-	-			
• Congressional Rescissions	-	-			
• Congressional Adds	-	-			
• Congressional Directed Transfers	-	-			
• Reprogrammings	-	-			
• SBIR/STTR Transfer	-0.735	-			
• Other Adjustments	-	-	0.000	-	0.000

Congressional Add Details ($ in Millions, and Includes General Reductions)	FY 2023	FY 2024
Project: PS1: *Physical Sciences (Basic Research)*		
Congressional Add: *Waterless solutions for decontamination*	5.000	-
Congressional Add Subtotals for Project: PS1	5.000	-
Congressional Add Totals for all Projects	5.000	-

Change Summary Explanation

Funding: FY 2023 (-$0.735 Million): Transfer of funding to support Small Business Innovative Research/Small Business Technology Transfer efforts.

Schedule: N/A

Technical: N/A

Exhibit R-2A, RDT&E Project Justification: PB 2025 Chemical and Biological Defense Program											Date: March 2024	
Appropriation/Budget Activity 0400 / 1					R-1 Program Element (Number/Name) PE 0601384BP / *Chemical and Biological Defense Program*				Project (Number/Name) LF1 / *Life Sciences (Basic Research)*			
COST ($ in Millions)	**Prior Years**	**FY 2023**	**FY 2024**	**FY 2025 Base**	**FY 2025 OCO**	**FY 2025 Total**	**FY 2026**	**FY 2027**	**FY 2028**	**FY 2029**	**Cost To Complete**	**Total Cost**
LF1: *Life Sciences (Basic Research)*	-	18.485	20.335	21.125	0.000	21.125	26.206	29.030	29.575	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 2023	FY 2024	FY 2025
Title: 1) Life Sciences	18.485	20.335	21.125
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 2024 Plans:*** - 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. - 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. - 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.			

Exhibit R-2A, RDT&E Project Justification: PB 2025 Chemical and Biological Defense Program		Date: March 2024
Appropriation/Budget Activity 0400 / 1	**R-1 Program Element (Number/Name)** PE 0601384BP / *Chemical and Biological Defense Program*	**Project (Number/Name)** LF1 / *Life Sciences (Basic Research)*

B. Accomplishments/Planned Programs ($ in Millions)	FY 2023	FY 2024	FY 2025
- 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. - Biomarkers - Begin iterative improvement of machine-learning model to predict cellular binding site targets. Integrate machine-learning architecture and sampling for iterative experimental design. - 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. ***FY 2025 Plans:*** - Organoid Technology – Continue investigating cellular toxicity and metabolic profiles in organoids and evaluate relevance to animal model data. Determine inflammatory signaling in rat models that are relevant to human cells. - Pathogenesis – Evaluate small molecule inhibitor on viral gene expression in vivo. Evaluate how hemorrhagic fever viruses alter biological activity of host cells. - Structural biology – Investigate efficacy of inhibitor molecule in an organ-on-chip platform. Begin training models to predict structural features for small molecules based on experimental data. - Artificial Intelligence (AI) for Early Drug Discovery – Characterize promising protein binding candidates based on model predictions. Validate predictive models ability to identify specific metabolic properties to enhance host immunity. Apply multi-learning prediction to molecular binding to expand general application drug design. - Biomarkers – Evaluation of machine-learning model to predict strain specific binding targets. Complete machine-learning architecture and sampling for iterative experimental design and begin validation of amino acid sequence capture. - Inflammation Mapping – Evaluate inflammatory pathways activated by chemical exposure using multiple characterization techniques. Validate potential medical countermeasure candidates in an in vitro nerve model. ***FY 2024 to FY 2025 Increase/Decrease Statement:*** Increase due to additional investment in Artificial Intelligence (AI) for Early Drug Discovery on a new topic in data science focusing on data standardization, FDA regulatory considerations, and machine learning (ML) specifications.			
Accomplishments/Planned Programs Subtotals	18.485	20.335	21.125

C. Other Program Funding Summary ($ in Millions)

Line Item	FY 2023	FY 2024	FY 2025 Base	FY 2025 OCO	FY 2025 Total	FY 2026	FY 2027	FY 2028	FY 2029	Cost To Complete	Total Cost
• UN2: *Understand (Applied Research)*	106.499	119.182	97.205	-	97.205	107.842	107.193	107.193	107.193	Continuing	Continuing
• PT2: *Protect (Applied Research)*	66.409	55.057	49.328	-	49.328	54.817	59.861	58.452	58.452	Continuing	Continuing

Exhibit R-2A, RDT&E Project Justification: PB 2025 Chemical and Biological Defense Program		Date: March 2024
Appropriation/Budget Activity 0400 / 1	**R-1 Program Element (Number/Name)** PE 0601384BP / *Chemical and Biological Defense Program*	**Project (Number/Name)** LF1 / *Life Sciences (Basic Research)*

C. Other Program Funding Summary ($ in Millions)

Line Item	FY 2023	FY 2024	FY 2025 Base	FY 2025 OCO	FY 2025 Total	FY 2026	FY 2027	FY 2028	FY 2029	Cost To Complete	Total Cost
• MT2: *Mitigate (Applied Research)*	67.108	66.371	55.744	-	55.744	55.426	66.420	68.824	68.824	Continuing	Continuing

Remarks

D. Acquisition Strategy

N/A

Exhibit R-2A, RDT&E Project Justification: PB 2025 Chemical and Biological Defense Program											Date: March 2024	
Appropriation/Budget Activity 0400 / 1					R-1 Program Element (Number/Name) PE 0601384BP / *Chemical and Biological Defense Program*				Project (Number/Name) PS1 / *Physical Sciences (Basic Research)*			
COST ($ in Millions)	**Prior Years**	**FY 2023**	**FY 2024**	**FY 2025 Base**	**FY 2025 OCO**	**FY 2025 Total**	**FY 2026**	**FY 2027**	**FY 2028**	**FY 2029**	**Cost To Complete**	**Total Cost**
PS1: *Physical Sciences (Basic Research)*	-	20.514	15.900	16.687	0.000	16.687	17.058	20.240	20.613	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 2023	FY 2024	FY 2025
Title: 1) Physical Sciences	15.514	15.900	16.687
Description: Focuses on fundamental scientific phenomena including chemistry, physics, materials science, environmental science, and nanotechnology. ***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.			

Exhibit R-2A, RDT&E Project Justification: PB 2025 Chemical and Biological Defense Program		Date: March 2024
Appropriation/Budget Activity 0400 / 1	**R-1 Program Element (Number/Name)** PE 0601384BP / *Chemical and Biological Defense Program*	**Project (Number/Name)** PS1 / *Physical Sciences (Basic Research)*

B. Accomplishments/Planned Programs ($ in Millions)	FY 2023	FY 2024	FY 2025
-Novel Destruction - Investigate binding specificity of enzymes for catalytic activity and improved sensitivity. Experiment with photochemical activity and determine oxidation capacity of materials. ***FY 2025 Plans:*** - Multifunctional Materials – Demonstrate surface agnostic coating with selective moisture vapor transport. Optimize and characterize nano-sheet degradation of simulants with high throughput assay. - Design Rules for Materials – Begin testing feasibility of scaling 2D film deposition methods and operational limits. Begin mechanistic studies to evaluate structural characters and reactivity of fibers with impregnated metal organic framework composites. Utilize microscopy to evaluate elasticity of graphene fibers coated onto garment surfaces. - Biomimetic – Investigate scalability of protein designs and test membrane-protein against simulants. - Photocatalysis – Synthesize photo-reactor and begin characterization of chemical reactivity. Perform studies of simulants and modeling energetic effects. Demonstrate sustained degradation activity in the dark. - Artificial Intelligence (AI) for Materials Discovery – Investigate computational approaches for material discovery, design, and parameters for catalytic and reactive decomposition of chemical threats. ***FY 2024 to FY 2025 Increase/Decrease Statement:*** Increase in funding will apply to a new program in Artificial Intelligence (AI) for Material Discovery.			
Accomplishments/Planned Programs Subtotals	15.514	15.900	16.687

	FY 2023	FY 2024
Congressional Add: Waterless solutions for decontamination	5.000	-
FY 2023 Accomplishments: - Identified and validated spectroscopic and other analytical methods for quality assessment and developed manufacturing scale-up and supply chain management plans. Perform Design of Experiments to test novel oxidant and type and source of zirconium hydroxide impact on formulation physical properties and decontamination effectiveness and assess potential manufacturing equipment and processes.		
Congressional Adds Subtotals	5.000	-

C. Other Program Funding Summary ($ in Millions)

Line Item	FY 2023	FY 2024	FY 2025 Base	FY 2025 OCO	FY 2025 Total	FY 2026	FY 2027	FY 2028	FY 2029	Cost To Complete	Total Cost
• UN2: *Understand (Applied Research)*	106.499	119.182	97.205	-	97.205	107.842	107.193	107.193	107.193	Continuing	Continuing
• PT2: *Protect (Applied Research)*	66.409	55.057	49.328	-	49.328	54.817	59.861	58.452	58.452	Continuing	Continuing

Exhibit R-2A, RDT&E Project Justification: PB 2025 Chemical and Biological Defense Program			Date: March 2024
Appropriation/Budget Activity 0400 / 1	**R-1 Program Element (Number/Name)** PE 0601384BP / *Chemical and Biological Defense Program*	**Project (Number/Name)** PS1 / *Physical Sciences (Basic Research)*	

C. Other Program Funding Summary ($ in Millions)

Line Item	FY 2023	FY 2024	FY 2025 Base	FY 2025 OCO	FY 2025 Total	FY 2026	FY 2027	FY 2028	FY 2029	Cost To Complete	Total Cost
• MT2: *Mitigate (Applied Research)*	67.108	66.371	55.744	-	55.744	55.426	66.420	68.824	68.824	Continuing	Continuing

Remarks

D. Acquisition Strategy

N/A