Exhibit R-2, RDT&E Budget Item Justification: PB 2021 Defense Health Agency											Date: February 2020	
Appropriation/Budget Activity 0130: *Defense Health Program I* BA 2: *RDT&E*					R-1 Program Element (Number/Name) PE 0601101DHA *I In-House Laboratory Independent Research (ILIR)*							
COST ($ in Millions)	**Prior Years**	**FY 2019**	**FY 2020**	**FY 2021 Base**	**FY 2021 OCO**	**FY 2021 Total**	**FY 2022**	**FY 2023**	**FY 2024**	**FY 2025**	**Cost To Complete**	**Total Cost**
Total Program Element	20.420	3.552	4.013	0.000	-	0.000	0.000	0.000	0.000	0.000	Continuing	Continuing
010A: *CSI - Congressional Special Interests*	1.315	0.000	0.000	0.000	-	0.000	0.000	0.000	0.000	0.000	Continuing	Continuing
240A: *Infectious Disease (USUHS)*	2.630	0.480	0.490	0.000	-	0.000	0.000	0.000	0.000	0.000	Continuing	Continuing
240B: *Military Operational Medicine (USUHS)*	7.869	1.479	1.509	0.000	-	0.000	0.000	0.000	0.000	0.000	Continuing	Continuing
240C: *Combat Casualty Care (USUHS)*	8.356	1.593	2.014	0.000	-	0.000	0.000	0.000	0.000	0.000	Continuing	Continuing
468: *Metabolomics, Exposure Biomarkers, and Health Outcomes (USUHS)*	0.250	0.000	0.000	0.000	-	0.000	0.000	0.000	0.000	0.000	Continuing	Continuing

Note

Funds were adjusted to higher priority programs in FY 2021-2025.

A. Mission Description and Budget Item Justification

For the Uniformed Services of the Health Sciences (USUHS), this program element supports basic medical research at the Uniformed Services University of the Health Sciences (USUHS). It facilitates the recruitment and retention of faculty; supports unique research training for military medical students and resident fellows; and allows the University's faculty researchers to collect pilot data towards military relevant medical research projects in order to secure research funds from extramural sources (estimated $180 million annually). Approximately 48 intramural research projects are active each year, including 18 faculty start-ups. Projects are funded on a peer-reviewed, competitive basis. Results from these studies contribute to the knowledge base intended to enable technical approaches and investment strategies within Defense Science and Technology (S&T) programs. USU enriches the training of the next generation of physicians/scientists who directly benefit the quality, outcomes, and stability of the military health care delivery system.

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Exhibit R-2, RDT&E Budget Item Justification: PB 2021 Defense Health Agency					Date: February 2020
Appropriation/Budget Activity 0130: *Defense Health Program I* BA 2: *RDT&E*		R-1 Program Element (Number/Name) PE 0601101DHA *I In-House Laboratory Independent Research (ILIR)*			
B. Program Change Summary ($ in Millions)	**FY 2019**	**FY 2020**	**FY 2021 Base**	**FY 2021 OCO**	**FY 2021 Total**
Previous President's Budget	3.687	4.013	0.000	-	0.000
Current President's Budget	3.552	4.013	0.000	-	0.000
Total Adjustments	-0.135	0.000	0.000	-	0.000
• Congressional General Reductions	-	-			
• Congressional Directed Reductions	-	-			
• Congressional Rescissions	-	-			
• Congressional Adds	-	-			
• Congressional Directed Transfers	-	-			
• Reprogrammings	-	-			
• SBIR/STTR Transfer	-0.135	-			

Change Summary Explanation

FY 2021: Programmed effort and funding transferred to other higher priority programs.

Exhibit R-2A, RDT&E Project Justification: PB 2021 Defense Health Agency			Date: February 2020
Appropriation/Budget Activity 0130 / 2	**R-1 Program Element (Number/Name)** PE 0601101DHA / *In-House Laboratory Independent Research (ILIR)*	**Project (Number/Name)** 010A / *CSI - Congressional Special Interests*	

COST ($ in Millions)	Prior Years	FY 2019	FY 2020	FY 2021 Base	FY 2021 OCO	FY 2021 Total	FY 2022	FY 2023	FY 2024	FY 2025	Cost To Complete	Total Cost
010A: *CSI - Congressional Special Interests*	1.315	0.000	0.000	0.000	-	0.000	0.000	0.000	0.000	0.000	Continuing	Continuing

A. Mission Description and Budget Item Justification

Because of the CSI annual structure, out-year funding is not programmed.

B. Accomplishments/Planned Programs ($ in Millions)

N/A

C. Other Program Funding Summary ($ in Millions)

N/A

Remarks

D. Acquisition Strategy

N/A

Exhibit R-2A, RDT&E Project Justification: PB 2021 Defense Health Agency			Date: February 2020
Appropriation/Budget Activity 0130 / 2	R-1 Program Element (Number/Name) PE 0601101DHA / *In-House Laboratory Independent Research (ILIR)*	Project (Number/Name) 240A / *Infectious Disease (USUHS)*	

COST ($ in Millions)	Prior Years	FY 2019	FY 2020	FY 2021 Base	FY 2021 OCO	FY 2021 Total	FY 2022	FY 2023	FY 2024	FY 2025	Cost To Complete	Total Cost
240A: *Infectious Disease (USUHS)*	2.630	0.480	0.490	0.000	-	0.000	0.000	0.000	0.000	0.000	Continuing	Continuing

A. Mission Description and Budget Item Justification

For the Uniformed Services of the Health Sciences (USUHS), this program element supports basic medical research at the Uniformed Services University of the Health Sciences (USUHS). It facilitates the recruitment and retention of faculty; supports unique research training for military medical students and resident fellows; and allows the University's faculty researchers to collect pilot data towards military relevant medical research projects in order to secure research funds from extramural sources (estimated $180 million annually). Approximately 48 intramural research projects are active each year, including 18 faculty start-ups. Projects are funded on a peer-reviewed, competitive basis. Results from these studies contribute to the knowledge base intended to enable technical approaches and investment strategies within Defense Science and Technology (S&T) programs. USU enriches the training of the next generation of physicians/scientists who directly benefit the quality, outcomes, and stability of the military health care delivery system.

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B. Accomplishments/Planned Programs ($ in Millions)	FY 2019	FY 2020	FY 2021
Title: Infectious Disease	0.480	0.490	0.000
Description: Immunology and molecular biology of bacterial, viral and parasitic disease threats to military operations. These threats include Bartonella bacilliformis, Clostridium difficile, Escherichia coli and their Shiga toxins, Henipaviruses (Hendra & Nipah), Cedar Virus, Hepatitis A, Helicobacter pylori, HIV, HTLV-1, Leishmaniasis, Litomosoides sigmodontis, Malaria, Neisseria gonorrhoeae, Shigella spp., Streptococcus, and Methicillin-resistant Staphylococcus aureus (MRSA). FY19 Accomplishments: The overall goal of this project is to develop a prototype histone deacetylase inhibitor (HDACi) called sulforaphane (SFN) as an epigenetic, adjunctive therapy for treatment of gonorrhea. We have completed the first aim to Identify SFN-induced effectors with activity against N. gonorrhoeae (Ng) by mass spectrometry, PCR-based arrays and mechanistic studies. A manuscript will be published soon. --We have solved the first quest of the proposed research, namely whether the seasonal H1N1 and H3N2 type A and a type B influenza virus (B/Lee strain) can infect a murine lung. Of note, though our humanized DRAGA mouse proposed to be established as an influenza mouse model for human influenza viruses lacks the murine immune system and it has a fully-functional human immune system, its lungs remain 95% of murine origin (5% represented by expression of CD36 human epithelial lung cells). It			

Exhibit R-2A, RDT&E Project Justification: PB 2021 Defense Health Agency		Date: February 2020
Appropriation/Budget Activity 0130 / 2	**R-1 Program Element (Number/Name)** PE 0601101DHA / *In-House Laboratory Independent Research (ILIR)*	**Project (Number/Name)** 240A / *Infectious Disease (USUHS)*

B. Accomplishments/Planned Programs ($ in Millions)	FY 2019	FY 2020	FY 2021
was thus essential to carry out preliminary experiments to determine whether the murine lung (in our case, BALB/c mouse) can be infected with the seasonal influenza viruses mentioned above. Together, the BALB/c experiments demonstrate that (i) the murine lung (and thus expectedly the lungs of DRAGA mouse) can be infected with all the type A and B influenza viruses tested in the lab; (ii) a primary, non-lethal infection with H3N2 seasonal viruses can fully protect against a secondary infection with a highly infectious H1N1 virus. ***FY 2020 Plans:*** Efforts will continue within the Infectious Disease research area in FY 2020. Specific investigator-initiated projects compete for funding each year, usually with two to three-year project periods. Therefore, no detailed description of the research is possible at this time. ***FY 2021 Plans:*** Funds were adjusted to higher priority programs. ***FY 2020 to FY 2021 Increase/Decrease Statement:*** As a result of directed RDT&E program reductions and reprioritization, ILIR PE 0601101 funding was eliminated.			
Accomplishments/Planned Programs Subtotals	0.480	0.490	0.000

C. Other Program Funding Summary ($ in Millions)

N/A

Remarks

D. Acquisition Strategy

N/A

Exhibit R-2A, RDT&E Project Justification: PB 2021 Defense Health Agency			Date: February 2020
Appropriation/Budget Activity 0130 / 2	R-1 Program Element (Number/Name) PE 0601101DHA / *In-House Laboratory Independent Research (ILIR)*	Project (Number/Name) 240B / *Military Operational Medicine (USUHS)*	

COST ($ in Millions)	Prior Years	FY 2019	FY 2020	FY 2021 Base	FY 2021 OCO	FY 2021 Total	FY 2022	FY 2023	FY 2024	FY 2025	Cost To Complete	Total Cost
240B: *Military Operational Medicine (USUHS)*	7.869	1.479	1.509	0.000	-	0.000	0.000	0.000	0.000	0.000	Continuing	Continuing

A. Mission Description and Budget Item Justification

For the Uniformed Services of the Health Sciences (USUHS), this program element supports basic medical research at the Uniformed Services University of the Health Sciences (USUHS). It facilitates the recruitment and retention of faculty; supports unique research training for military medical students and resident fellows; and allows the University's faculty researchers to collect pilot data towards military relevant medical research projects in order to secure research funds from extramural sources (estimated $180 million annually). Approximately 48 intramural research projects are active each year, including 18 faculty start-ups. Projects are funded on a peer-reviewed, competitive basis. Results from these studies contribute to the knowledge base intended to enable technical approaches and investment strategies within Defense Science and Technology (S&T) programs. USU enriches the training of the next generation of physicians/scientists who directly benefit the quality, outcomes, and stability of the military health care delivery system.

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B. Accomplishments/Planned Programs ($ in Millions)	FY 2019	FY 2020	FY 2021
Title: Military Operational Medicine	1.479	1.509	0.000
Description: Sustainment of individual performance; mapping and managing deployment and operational stressors; cognitive enhancement; use of dietary and nutritional supplements and military and medical training readiness. FY19 Accomplishments: -- Developed a network within the MHS to systematically, efficiently and effectively manage and triage (from initial medical care to tertiary care) all patients presenting with ERi [i.e. EHi and/or ER] (project 1). The primary focus is on safe return to full duty. We also intend to determine the contribution of intrinsic and extrinsic risk factors associated with ERi, and create a scoring system to triage Service Members to early return to duty or further specialty evaluation for recurrence risk (project 2), and to develop genetic and biologic screening tools for ERi that can be deployed as far forward as possible with the ultimate goal of differentiating those at risk for recurrence and those who can be returned to full duty (project 3). While projects 1 and 2 are moving forward, patients are still referred for clinical workup through the current word of mouth process. Based on case history, some of the patients are offered enrollment in the genetic screening protocol of project 3. This protocol has been ongoing for several years and compares the genome of cases of exertional injuries with the markers of malignant hyperthermia (MH) susceptibility. During the project period, we have enrolled 8 index case individuals in project 3 of the study, and genetic analysis has been started.			

Exhibit R-2A, RDT&E Project Justification: PB 2021 Defense Health Agency		Date: February 2020
Appropriation/Budget Activity 0130 / 2	**R-1 Program Element (Number/Name)** PE 0601101DHA / *In-House Laboratory Independent Research (ILIR)*	**Project (Number/Name)** 240B / *Military Operational Medicine (USUHS)*

B. Accomplishments/Planned Programs ($ in Millions)	FY 2019	FY 2020	FY 2021
--Continued development of a self-test kit for rapid diagnosis of hygiene-related urogenital infections. Our comprehensive, MWRUHSQ survey questionnaire is being used to systematically evaluate the impact of varying water and sanitation resources on urogenital health and health behaviors in active duty service women (ADSW), and their views of the female urinary diversion device (FUDD) as a way to mitigate some challenges while in the field for the purpose of enhancing our understanding of ADSW's gender-specific health needs in austere environments. Preliminarily analyzed data collected from the initial 152 participants and we have submitted a data-based manuscript describing not only our psychometric characterization (to-date), but also our findings. -- Developed predictive models for female Marine officer performance at The Basic School (TBS), including musculoskeletal injury (MSK-I) & graduation outcomes. Enrolled 153 Female & 1217 Males from 7 training Companies (enrolled 80% of eligible Females; exceeded estimate of 120/yr). Completed post-testing on 4 Companies: Female grad rate 89% vs. 98% for Males in our cohort. Data analysis ongoing; injury & graduation outcomes being tracked. Four research abstracts presented at national conferences. -- Made significant progress in elucidating and validating the role of SREBP in mediating the effect of histone deacetylase inhibitors to increase KATP channel subunit expression. We now have convincing data that 1) correlates cellular cholesterol with SUR2 gene expression, 2) demonstrates cleavage and translocation of the SREBP transcription factor, and 3) selective SREPB-dependent activation of the SUR2 promoter. In addition, we have data implicating HDI-dependent decrease in cholesterol uptake pathways (LDL receptor) and marked increase in PCSK9 (an enzyme that promotes degradation of LDL receptor suggesting a mechanism by which histone deacetylase inhibitors cause a decrease in cellular cholesterol). Finally, dominant negative suppression of SREBP function inhibits the action of histone deacetylase inhibitors. ***FY 2020 Plans:*** Efforts will continue within the Military Operational Medicine research area in FY 2020. Specific investigator-initiated projects compete for funding each year, usually with two to three-year project periods. Therefore, no detailed description of the research is possible at this time. ***FY 2021 Plans:*** Funds were adjusted to higher priority programs. ***FY 2020 to FY 2021 Increase/Decrease Statement:*** As a result of directed RDT&E program reductions and reprioritization, ILIR PE 0601101 funding was eliminated.			
Accomplishments/Planned Programs Subtotals	1.479	1.509	0.000

C. Other Program Funding Summary ($ in Millions)

N/A

Remarks

Exhibit R-2A, RDT&E Project Justification: PB 2021 Defense Health Agency		Date: February 2020
Appropriation/Budget Activity 0130 / 2	**R-1 Program Element (Number/Name)** PE 0601101DHA / *In-House Laboratory Independent Research (ILIR)*	**Project (Number/Name)** 240B / *Military Operational Medicine (USUHS)*

D. Acquisition Strategy

N/A

Exhibit R-2A, RDT&E Project Justification: PB 2021 Defense Health Agency			Date: February 2020
Appropriation/Budget Activity 0130 / 2	R-1 Program Element (Number/Name) PE 0601101DHA / *In-House Laboratory Independent Research (ILIR)*	Project (Number/Name) 240C / *Combat Casualty Care (USUHS)*	

COST ($ in Millions)	Prior Years	FY 2019	FY 2020	FY 2021 Base	FY 2021 OCO	FY 2021 Total	FY 2022	FY 2023	FY 2024	FY 2025	Cost To Complete	Total Cost
240C: *Combat Casualty Care (USUHS)*	8.356	1.593	2.014	0.000	-	0.000	0.000	0.000	0.000	0.000	Continuing	Continuing

A. Mission Description and Budget Item Justification

For the Uniformed Services of the Health Sciences (USUHS), this program element supports basic medical research at the Uniformed Services University of the Health Sciences (USUHS). It facilitates the recruitment and retention of faculty; supports unique research training for military medical students and resident fellows; and allows the University's faculty researchers to collect pilot data towards military relevant medical research projects in order to secure research funds from extramural sources (estimated $180 million annually). Approximately 48 intramural research projects are active each year, including 18 faculty start-ups. Projects are funded on a peer-reviewed, competitive basis. Results from these studies contribute to the knowledge base intended to enable technical approaches and investment strategies within Defense Science and Technology (S&T) programs. USU enriches the training of the next generation of physicians/scientists who directly benefit the quality, outcomes, and stability of the military health care delivery system.

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B. Accomplishments/Planned Programs ($ in Millions)	FY 2019	FY 2020	FY 2021
Title: Combat Casualty Care	1.593	2.014	0.000
Description: Regenerative medicine, rehabilitation, neurological, limb loss, pain management, readiness, resilience. FY19 Accomplishments: - sought to understand the mechanisms underlying cognitive deficits that are reported to affect non-native subjects following their prolonged stay and/or work at high altitude (HA). Found that exposure to hypobaric-hypoxia triggers maladaptive responses inducing cognitive deficits and suggests potential mechanisms underlying the adverse impacts of staying or traveling at high altitude. --Training in the WAVE requires large expenses of the environment to be modeled. We developed algorithms to automatically generate complex terrain and we have also developed algorithms that permit avatars to exhibit humanly plausible reactions to environmental stimuli. Stimuli regions of interest and danger. -- Analyzing both cross sectional and prospective data to evaluate acute and longer term health outcomes. As stated above, we are utilizing Cox Proportional Hazards Regressions to compare risk for various health outcomes between different exposure groups in our cohort of Coast Guard responders who were involved in the Deepwater Horizon response. We have been analyzing the long term health data from this study. Recently, we have focused mainly on the dermal and respiratory health systems.			

Exhibit R-2A, RDT&E Project Justification: PB 2021 Defense Health Agency		Date: February 2020
Appropriation/Budget Activity 0130 / 2	**R-1 Program Element (Number/Name)** PE 0601101DHA / *In-House Laboratory Independent Research (ILIR)*	**Project (Number/Name)** 240C / *Combat Casualty Care (USUHS)*

B. Accomplishments/Planned Programs ($ in Millions)	FY 2019	FY 2020	FY 2021
FY 2020 Plans: Efforts will continue within the Combat Casualty Care research area in FY 2020. Specific investigator-initiated projects compete for funding each year, usually with two to three-year project periods. Therefore, no detailed description of the research is possible at this time. ***FY 2021 Plans:*** Funds were adjusted to higher priority programs. ***FY 2020 to FY 2021 Increase/Decrease Statement:*** As a result of directed RDT&E program reductions and reprioritization, ILIR PE 0601101 funding was eliminated.			
Accomplishments/Planned Programs Subtotals	1.593	2.014	0.000

C. Other Program Funding Summary ($ in Millions)

N/A

Remarks

D. Acquisition Strategy

N/A

Exhibit R-2A, RDT&E Project Justification: PB 2021 Defense Health Agency			Date: February 2020
Appropriation/Budget Activity 0130 / 2	R-1 Program Element (Number/Name) PE 0601101DHA / *In-House Laboratory Independent Research (ILIR)*	Project (Number/Name) 468 / *Metabolomics, Exposure Biomarkers, and Health Outcomes (USUHS)*	

COST ($ in Millions)	Prior Years	FY 2019	FY 2020	FY 2021 Base	FY 2021 OCO	FY 2021 Total	FY 2022	FY 2023	FY 2024	FY 2025	Cost To Complete	Total Cost
468: *Metabolomics, Exposure Biomarkers, and Health Outcomes (USUHS)*	0.250	0.000	0.000	0.000	-	0.000	0.000	0.000	0.000	0.000	Continuing	Continuing

A. Mission Description and Budget Item Justification

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B. Accomplishments/Planned Programs ($ in Millions)

N/A

C. Other Program Funding Summary ($ in Millions)

N/A

Remarks

D. Acquisition Strategy

N/A