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 0603002DHA *I Medical Advanced Technology (AFRRI)*

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	2.460	0.325	0.345	0.352	-	0.352	0.359	0.366	0.373	0.380	Continuing	Continuing
030A: *CSI - Congressional Special Interests*	0.031	0.000	0.000	0.000	-	0.000	0.000	0.000	0.000	0.000	Continuing	Continuing
242A: *Biodosimetry (USUHS)*	1.453	0.195	0.206	0.210	-	0.210	0.214	0.218	0.222	0.226	Continuing	Continuing
242B: *Radiation Countermeasures (USUHS)*	0.976	0.130	0.139	0.142	-	0.142	0.145	0.148	0.151	0.154	Continuing	Continuing

A. Mission Description and Budget Item Justification

For the Uniformed Services University of the Health Sciences/ Armed Forces Radiobiology Research Institute (USUHS/AFRRI), this program supports applied research for advanced development of biomedical strategies to prevent, treat and assess health consequences from exposure to ionizing radiation. It capitalizes on findings under PE 0602787HP, Medical Technology, and from industry and academia to advance novel medical countermeasures into and through pre-clinical studies toward newly licensed products. Program objectives focus on mitigating the health consequences from exposures to ionizing radiation(alone or in combination with other injuries) that represent the highest probable threat to US forces in current tactical, humanitarian and counterterrorism mission environments. Findings from basic and developmental research are integrated into focused advanced technology development studies to produce the following: (1) protective and therapeutic strategies; (2) novel biological markers and delivery platforms for rapid, field-based individual medical assessment; and (3) experimental data needed to build accurate models for predicting casualties from complex injuries involving radiation and other battlefield insults. The AFRRI, because of its multidisciplinary staff and exceptional laboratory and radiation facilities, is uniquely positioned to execute the program as prescribed by its mission.

B. Program Change Summary ($ in Millions)	FY 2019	FY 2020	FY 2021 Base	FY 2021 OCO	FY 2021 Total
Previous President's Budget	0.338	0.345	0.352	-	0.352
Current President's Budget	0.325	0.345	0.352	-	0.352
Total Adjustments	-0.013	0.000	0.000	-	0.000
• Congressional General Reductions	-	-			
• Congressional Directed Reductions	-	-			
• Congressional Rescissions	-	-			
• Congressional Adds	-	-			
• Congressional Directed Transfers	-	-			
• Reprogrammings	-	-			
• SBIR/STTR Transfer	-0.013	-			

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 0603002DHA / *Medical Advanced Technology (AFRRI)*	Project (Number/Name) 030A / *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
030A: *CSI - Congressional Special Interests*	0.031	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 0603002DHA / *Medical Advanced Technology (AFRRI)*	Project (Number/Name) 242A / *Biodosimetry (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
242A: *Biodosimetry (USUHS)*	1.453	0.195	0.206	0.210	-	0.210	0.214	0.218	0.222	0.226	Continuing	Continuing

A. Mission Description and Budget Item Justification

For the Uniformed Services University of the Health Sciences/Armed Forces Radiobiology Research Institute (USU/AFRRI), this program supports applied research for advanced development of biomedical strategies to prevent, treat and assess health consequences from exposure to ionizing radiation. It capitalizes on findings under PE 0602787HP, Medical Technology, and from industry and academia to advance novel medical countermeasures into and through pre-clinical studies toward newly licensed products. Program objectives focus on mitigating the health consequences from exposures to ionizing radiation (alone or in combination with other injuries) that represent the highest probable threat to US forces in current tactical, humanitarian and counterterrorism mission environments. Findings from basic and developmental research are integrated into focused advanced technology development studies to produce the following: (1) protective and therapeutic strategies; (2) novel biological markers and delivery platforms for rapid, field-based individual medical assessment; and (3) experimental data needed to build accurate models for predicting casualties from complex injuries involving radiation and other battlefield insults. The AFRRI, because of its multidisciplinary staff and exceptional laboratory and radiation facilities, is uniquely positioned to execute the program as prescribed by its mission.

B. Accomplishments/Planned Programs ($ in Millions)	FY 2019	FY 2020	FY 2021
Title: Biodosimetry (USUHS)	0.195	0.206	0.210

Description: Biodosimetry (USUHS): For the Uniformed Services University of the Health Sciences (USUHS), this program supports applied research for advanced development of biomedical and biophysical strategies to assess health consequences from exposure to ionizing radiation. It capitalizes on findings under PE 0602787HP, Medical Technology, and from industry and academia to advance novel biological markers and delivery platforms for rapid, field-based individual dose assessment and experimental data needed to build accurate models for predicting casualties from complex injuries involving radiation and other battlefield insults.

FY 2019 Accomplishments:
Attained major technical advances using “automated dicentrics scoring” to enhance radiation dose assessment to include: submission of technical publication reporting on the establishment of dose-response calibration curves following exposure to three different dose rates of 60Co gamma rays; established x-ray calibration curve (i.e., 250 kvP, 0.6 Gy/min); and automated dicentrics scoring performance evaluation using well-defined blind tests samples that showed an overall scoring of 103 ± 3.8 %, which justifies use of the automated dicentrics scoring in triage dose assessments.
-Reported on findings from inter-laboratory exercise triage (n=50 spreads) dose assessments from AFRRI and institutional collaborator from Health Canada. Preliminary findings from this exercise (INTCO6-2018) showed accurate dose predictions within 0.6 Gy of the actual dose. These findings expand AFRRI’s verified dicentrics scorers and demonstrate laboratory competence,

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 0603002DHA / *Medical Advanced Technology (AFRRI)*	**Project (Number/Name)** 242A / *Biodosimetry (USUHS)*

B. Accomplishments/Planned Programs ($ in Millions)	FY 2019	FY 2020	FY 2021
consistent with the guidance from the relevant (International Organization for Standardization) ISO standards. Results from AFRRI's 3-4 years' experience participating in the inter-comparison exercises with Health Canada is being written up for publication. -Introduced a novel parameter, Hematological Index of Radiation Injury (HIRI), to distinguish individuals from exposure to <2 Gy vs. >2 Gy of radiation by a single CBC with differential in the early time period after a suspected exposure. Validated the HIRI algorithm using archived data from both an animal model (i.e., Macaque nonhuman primate exposed to 60Co gamma rays) and human radiation accidents. Filed an invention disclosure that was followed by the submission of a provisional patent application linking the HIRI algorithm with applications on hand-held and benchtop blood cell counters to aide first-response in triaging suspected individuals exposed to ionizing radiation. Reported research findings on MicroRNA 34a (MiR-34a) as applicable biomarker for increased expression in small intestine of mice that were exposed to mixed-field (neutrons+gamma) radiation. ***FY 2020 Plans:*** FY 2020 plans continue efforts to validate the use of multiple parameter biodosimetry assays for optimized radiation injury and dose assessment in addition to the following: Continue to develop and validate the HIRI algorithm for use in triaging suspected radiological casualties; sustain cytogenetic biodosimetry laboratory participation in inter-comparison exercises performing dose assessment to document laboratory proficiency; obtain dose-responses for automated scoring of dicentric yields in blood exposed to high-energy LINAC electrons; and continue efforts to obtain laboratory certification for radiation dose assessment using multiple biodosimetry assays. ***FY 2021 Plans:*** FY 2021 plans continue efforts as outlined in FY 2020 in addition to the following: expand the validation of cytogenetic assays for dose assessment using the premature chromosome condensation (PCC) assay as a secondary endpoint for radiation dose and partial-body assessment; iInvestigate differential effects on organ injury such as bone marrow and small intestine between males and females after mixed-field and pure gamma radiation will be evaluated; and initiate 25 cytokine profile measurements for correlation with effects of radiation exposure. ***FY 2020 to FY 2021 Increase/Decrease Statement:*** Pricing adjustment for inflation.			
Accomplishments/Planned Programs Subtotals	0.195	0.206	0.210

C. Other Program Funding Summary ($ in Millions)

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 0603002DHA / *Medical Advanced Technology (AFRRI)*	**Project (Number/Name)** 242A / *Biodosimetry (USUHS)*

C. Other Program Funding Summary ($ in Millions)

Remarks

The program element 0602787DHA for AFRRI in addition to the three program elements: 0601115HPPE, 0602115HPPE, and 0603115HP are coordinated and integrated into the portfolio management by the Joint Program Committee-7/ Radiation Health Effects Research Program (RHERP).

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 0603002DHA / *Medical Advanced Technology (AFRRI)*	Project (Number/Name) 242B / *Radiation Countermeasures (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
242B: *Radiation Countermeasures (USUHS)*	0.976	0.130	0.139	0.142	-	0.142	0.145	0.148	0.151	0.154	Continuing	Continuing

A. Mission Description and Budget Item Justification

Radiation Countermeasures (USU): For the Uniformed Services University of the Health Sciences (USU), this program supports applied research for advanced development of biomedical strategies to prevent and treat health consequences from exposure to ionizing radiation. It capitalizes on findings under PE 0602787HP, Medical Technology, and from industry and academia to advance novel medical countermeasures into and through pre-clinical studies toward newly licensed products. Program objectives focus on preventing or mitigating the health consequences from exposures to ionizing radiation alone or in combination with other injuries, in the context of probable threats to US forces in current tactical, humanitarian and counterterrorism mission environments. Findings from basic and developmental research are integrated into highly focused advanced technology development studies yielding protective and therapeutic strategies.

B. Accomplishments/Planned Programs ($ in Millions)	FY 2019	FY 2020	FY 2021
Title: Radiation Countermeasures (USUHS)	0.130	0.139	0.142

Description: Radiation Countermeasures (USU): For the Uniformed Services University of the Health Sciences (USU), this program supports applied research for advanced development of biomedical strategies to prevent and treat health consequences from exposure to ionizing radiation. It capitalizes on findings under PE 0602787HP, Medical Technology, and from industry and academia to advance novel medical countermeasures into and through pre-clinical studies toward newly licensed products. Program objectives focus on preventing or mitigating the health consequences from exposures to ionizing radiation alone or in combination with other injuries, in the context of probable threats to US forces in current tactical, humanitarian and counterterrorism mission environments. Findings from basic and developmental research are integrated into highly focused advanced technology development studies yielding protective and therapeutic strategies.

FY 2019 Accomplishments:
- Demonstrated an important finding that radiation injury (RI) and combined radiation injury (CI) significantly reduced nuclear respiratory factor 1 and 2 (NRF1/2) and mitochondrial complexes I-V, thereby leading to decreases in energy production in mouse brain.
-Reported data on RI and CI decreased dynamin-related protein 1 (DRP1) and mitofusin 1 (Mfn1), resulting in mitochoondial remodeling in mouse brain. In addition, reported data showed RI and CI decreased AKT activation in mouse brain.
- Reported data on combinational therapy of Ghrelin and Neulasta recovered energy production by recovering NRF1/2, mitochondrial complex III, shape integrity and pro-survival signal molecules in mouse brain.

FY 2020 Plans:

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 0603002DHA / *Medical Advanced Technology (AFRRI)*	**Project (Number/Name)** 242B / *Radiation Countermeasures (USUHS)*

B. Accomplishments/Planned Programs ($ in Millions)	FY 2019	FY 2020	FY 2021
-FY 2020 plans are: continued gathering of preclinical data from animal models natural history studies for radiation toxicity and for the discovery and development of radiation countermeasures; conduct detailed analysis of the metabololomic and lipidomic studies with the samples collected in mice experiments with amifostine and a PARP inhibitor, Talazoparib; and determination of dose reduction factor (DRF) with optimal formulation dose with BMT-LIPO-GT3 and time in relation to irradiation, study of cytokine induction in unirradiated as well as irradiated mice, and hematopoietic recovery in animals exposed to radiation. ***FY 2021 Plans:*** FY 2021 plans continue efforts as outlined in FY 2020 in addition to the following: Commence investigation of energy production in mouse small intestine exposed to high-LET radiation. ***FY 2020 to FY 2021 Increase/Decrease Statement:*** Pricing adjustment for inflation.			
Accomplishments/Planned Programs Subtotals	0.130	0.139	0.142

C. Other Program Funding Summary ($ in Millions)

N/A

Remarks

The program element 0602787DHA for AFRRI in addition to the three program elements: 0601115HPPE, 0602115HPPE, and 0603115HP are coordinated and integrated into the portfolio management by the Joint Program Committee-7/ Radiation Health Effects Research Program (RHERP)

D. Acquisition Strategy

N/A