Exhibit R-2, RDT&E Budget Item Justification: PB 2020 Defense Health Agency	Date: February 2019
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 2018	FY 2019	FY 2020 Base	FY 2020 OCO	FY 2020 Total	FY 2021	FY 2022	FY 2023	FY 2024	Cost To Complete	Total Cost
Total Program Element	2.140	0.320	0.338	0.345	-	0.345	0.352	0.359	0.366	0.373	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)*	1.266	0.187	0.202	0.206	-	0.206	0.210	0.214	0.218	0.222	Continuing	Continuing
242B: *Radiation Countermeasures (USUHS)*	0.843	0.133	0.136	0.139	-	0.139	0.142	0.145	0.148	0.151	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 2018	FY 2019	FY 2020 Base	FY 2020 OCO	FY 2020 Total
Previous President's Budget	0.332	0.338	0.345	-	0.345
Current President's Budget	0.320	0.338	0.345	-	0.345
Total Adjustments	-0.012	0.000	0.000	-	0.000
• Congressional General Reductions	-	-			
• Congressional Directed Reductions	-	-			
• Congressional Rescissions	-	-			
• Congressional Adds	-	-			
• Congressional Directed Transfers	-	-			
• Reprogrammings	-	-			
• SBIR/STTR Transfer	-0.012	-			

Exhibit R-2, RDT&E Budget Item Justification: PB 2020 Defense Health Agency	Date: February 2019
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)*

Change Summary Explanation

FY 2018: Realignment from Defense Health Program, Research, Development, Test and Evaluation (DHP RDT&E), PE 0603002-Advanced Technology (AFRRI) (-$0.012 million) to DHP RDT&E PE 0605502-Small Business Innovation Research (SBIR) / Small Business Technology Transfer (STTR) Program (+$0.012 million).

Exhibit R-2A, RDT&E Project Justification: PB 2020 Defense Health Agency											Date: February 2019	
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 2018**	**FY 2019**	**FY 2020 Base**	**FY 2020 OCO**	**FY 2020 Total**	**FY 2021**	**FY 2022**	**FY 2023**	**FY 2024**	**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

E. Performance Metrics

N/A

Exhibit R-2A, RDT&E Project Justification: PB 2020 Defense Health Agency			Date: February 2019
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 2018	FY 2019	FY 2020 Base	FY 2020 OCO	FY 2020 Total	FY 2021	FY 2022	FY 2023	FY 2024	Cost To Complete	Total Cost
242A: *Biodosimetry (USUHS)*	1.266	0.187	0.202	0.206	-	0.206	0.210	0.214	0.218	0.222	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 2018	FY 2019	FY 2020
Title: Biodosimetry (USUHS)	0.199	0.202	0.206

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 2018 Plans:
FY 2018 plans continue evaluation of radiation-induced biomarkers from the database of baboon studies as a nonhuman primate (NHP) model with utility to predict severity of hematopoietic (i.e. blood elements) acute radiation syndrome. Perform internal assessment of quality control program for radiation dose assessment by cytogenetics platform towards an eventual clinical laboratory certification. Develop algorithm using blood cell counts and biochemical biomarkers in NHP radiation dose response model. Initiate efforts to evaluate human blood samples from radiation therapy patients using panel of radiation-responsive biomarkers. Evaluate effects of radioprotectants on radiation risk categorization (RRIC) algorithm based on blood counts and blood chemistry tests using irradiated nonhuman primate archived data.

FY 2018 Accomplishments:

Exhibit R-2A, RDT&E Project Justification: PB 2020 Defense Health Agency		Date: February 2019
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 2018	FY 2019	FY 2020
-Published report on the utility of radiation-induced biomarker panels used to develop an algorithm based on a baboon TBI vs PBI study to predict the severity of hematopoietic (i.e. blood elements) acute radiation syndrome demonstrating proof-of-concept that prognostic biomarkers can provide early-phase diagnostic information to guide medical treatment decisions for radiological casualties with life-threatening radiation exposures. -Performed an internal self-assessment of the quality control program for radiation dose assessment by cytogenetics to identify remaining tasks to support an eventual request for clinical laboratory certification. -Initiated discussions with radiation oncologists to evaluate human blood samples from radiation therapy patients using a panel of radiation-responsive biomarkers to validate novel approaches for radiation dose and injury assessment. -Reported on the utility of the early-phase changes after radiation exposure on neutrophil to lymphocyte ratio in various animal (i.e., mice, dogs, rhesus monkeys, and baboons) and human radiation model systems to provide the ability to access radiation exposure. -Developed algorithms applying blood cell and/or biochemical markers for assessing the efficacy of radioprotectants, using archived irradiated nonhuman primate data. -Reported on radiation quality effects (i.e., mixed field neutron vs gamma ray exposures) on hematopoietic biomarkers using an archived baboon radiation model. Established an ARS severity scoring system using the baboon model based on hematology changes that permits assessment of radiation injury independent of radiation quality and total vs partial-body exposures. -Participated in interagency collaboration with REAC/TS and the Naval Dosimetry Center to further design the concepts of operation for the US Biodosimetry Network. Reported these efforts at an international biodosimetry conference. - Demonstrated that total body irradiation (TBI) and partial body irradiation (PBI) resulted in decreases in splenocyte counts at a similar level as shown in both deceased minipigs exposed to TBI and survived minipigs exposed to PBI. The major difference was that the levels of circulating insulin-like growth factor in dead animals were remarkably higher than that in living ones. Therefore, IGF-1 could be a good biomarker for radiation exposure and a determinant for lethality. Unlike minipigs, IGF-1 levels in blood of mice did not have such distinct difference between dead living mice. - Demonstrated that ATP decreased after TBI in minipigs and mice. The underlying mechanism with ATP decreases were explored successfully and understood in mice, suggesting that ATP biogenesis and maintenance after irradiation is one of major targets for developing remedial drugs in both minipigs and mice. ***FY 2019 Plans:*** FY 2019 plans continue efforts as outlined in FY 2018. In addition: -Sustain efforts to perform studies to validate the use of multiple parameter biodosimetry assays for optimized radiation injury and dose assessment. -Develop radiation injury risk and dose models based on archived human radiation accident database. -Continue studies to enhance throughput of cytogenetic scoring using the automated dicentric scoring software. -Participate in inter-comparison exercise studies to demonstrate laboratory competencies.			

Exhibit R-2A, RDT&E Project Justification: PB 2020 Defense Health Agency		Date: February 2019
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 2018	FY 2019	FY 2020
-Engage in discussions with the Air Force to evaluate the bioeffects of exposure to high energy LINAC electrons. -Continue to readily offer the suite of AFRRI's Biodosimetry Tools to DOD customers -Initiate efforts to expand upon the AFRRI Biodosimetry Worksheet to address relevant indicators for assessment of late effects of radiation exposure. -Continue to perform the proposed mitochondrial remodeling in brain tissues by investigating fission and fusion protein markers. ***FY 2020 Plans:*** FY 2020 plans to continue efforts as outlined in FY 2019. In addition: -Continue efforts to obtain laboratory certification for radiation dose assessment using multiple biodosimetry assays. ***FY 2019 to FY 2020 Increase/Decrease Statement:*** Pricing Adjustment.			
Accomplishments/Planned Programs Subtotals	0.199	0.202	0.206

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

E. Performance Metrics

By FY2019
-Perform and report on an evaluation to validate the utility of the human biomarker model.
-Report on laboratory's competence in inter-comparison exercises for radiation dose assessment.
- Report on recent developments and use of AFRRI's Biodosimetry Tools.
By FY2020
- Obtain CLIP certification for performance of the dicentric assay for dose assessment.
- Report on use of AFRRI's suite of biodosimetry tools in a radiological exercise.

Exhibit R-2A, RDT&E Project Justification: PB 2020 Defense Health Agency			Date: February 2019
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 2018	FY 2019	FY 2020 Base	FY 2020 OCO	FY 2020 Total	FY 2021	FY 2022	FY 2023	FY 2024	Cost To Complete	Total Cost
242B: *Radiation Countermeasures (USUHS)*	0.843	0.133	0.136	0.139	-	0.139	0.142	0.145	0.148	0.151	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 2018	FY 2019	FY 2020
Title: Radiation Countermeasures (USUHS)	0.133	0.136	0.139

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 2018 Plans:
FY 2018 plans to continue development studies in animal models for acute radiation syndrome drug discovery and development to further characterize the efficacy and safety profile of promising drug substances and products and to elucidate their mechanism of action as radiation countermeasures. Radiation countermeasure candidates such CDX-301, TPOm, PrC-210, BBT059 at various stages of preclinical development will be evaluated for advances towards clinical studies and application.

FY 2018 Accomplishments:
-Evaluated dose-dependence of radioprotective efficacy of BMT-LIPO-GT3, a new and proprietary formulation of gamma-tocotrienol (GT3), in mice.

Exhibit R-2A, RDT&E Project Justification: PB 2020 Defense Health Agency		Date: February 2019
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 2018	FY 2019	FY 2020
-Mice experimentation conducted with a radioprotectant drug, amifostine and a PARP inhibitor, Talazoparib, for metabololomic and lipidomic studies to establish their pharmacological profiles and potential impact on radiation effects. ***FY 2019 Plans:*** FY 2019 plans continue efforts as outlined in FY 2018. In addition, there will be a continued gathering of preclinical data from animal models natural history studies for radiation toxicity and for the discovery and development of radiation countermeasures. -Detailed analysis of the metabololomic and lipidomic studies will be conducted with the samples collected in mice experiments with amifostine and a PARP inhibitor, Talazoparib. -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 2020 Plans:*** -FY 2020 plans continue efforts as outlined in FY 2019. In addition, metabolomic and lipidomic studies will be conducted with BMT-LIPO-GT3 in mice. ***FY 2019 to FY 2020 Increase/Decrease Statement:*** Pricing Adjustment.			
Accomplishments/Planned Programs Subtotals	0.133	0.136	0.139

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

E. Performance Metrics

By FY 2019
- Evaluate Nrf1, Nrf2, and ATP as biomarkers in various tissues in minipigs after 1.75 Gy.
- Evaluate Nrf1, Nrf2, and ATP as biomarkers in various tissues in mice after 9.5 Gy.

By FY 2020
- Evaluate TFAM, DRP1, OPA1 and Mfn1 as biomarkers in various tissues in minipigs after 1.75 Gy.
- Evaluate TFAM, DRP1, OPA1 and Mfn1 as biomarkers in various tissues in mice after 9.5 Gy.