Exhibit R-2, RDT&E Budget Item Justification: PB 2019 Defense Health Agency	Date: February 2018
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 2017	FY 2018	FY 2019 Base	FY 2019 OCO	FY 2019 Total	FY 2020	FY 2021	FY 2022	FY 2023	Cost To Complete	Total Cost
Total Program Element	1.841	0.299	0.332	0.338	-	0.338	0.345	0.352	0.359	0.366	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)*	1.087	0.179	0.199	0.202	-	0.202	0.206	0.210	0.214	0.218	Continuing	Continuing
242B: *Radiation Countermeasures (USUHS)*	0.723	0.120	0.133	0.136	-	0.136	0.139	0.142	0.145	0.148	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 2017	FY 2018	FY 2019 Base	FY 2019 OCO	FY 2019 Total
Previous President's Budget	0.310	0.332	0.338	-	0.338
Current President's Budget	0.299	0.332	0.338	-	0.338
Total Adjustments	-0.011	0.000	0.000	-	0.000
• Congressional General Reductions	-	-			
• Congressional Directed Reductions	-	-			
• Congressional Rescissions	-	-			
• Congressional Adds	-	-			
• Congressional Directed Transfers	-	-			
• Reprogrammings	-	-			
• SBIR/STTR Transfer	-0.011	-			

Exhibit R-2, RDT&E Budget Item Justification: PB 2019 Defense Health Agency	Date: February 2018
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) (-$0.011 million) to DHP RDT&E PE 0605502-Small Business Innovation Research (SBIR) / Small Business Technology Transfer (STTR) Program (+$0.011 million).

Exhibit R-2A, RDT&E Project Justification: PB 2019 Defense Health Agency			Date: February 2018
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 2017	FY 2018	FY 2019 Base	FY 2019 OCO	FY 2019 Total	FY 2020	FY 2021	FY 2022	FY 2023	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 2019 Defense Health Agency			Date: February 2018
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 2017	FY 2018	FY 2019 Base	FY 2019 OCO	FY 2019 Total	FY 2020	FY 2021	FY 2022	FY 2023	Cost To Complete	Total Cost
242A: *Biodosimetry (USUHS)*	1.087	0.179	0.199	0.202	-	0.202	0.206	0.210	0.214	0.218	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 2017	FY 2018	FY 2019
Title: Biodosimetry (USUHS)	0.179	0.199	0.202
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: 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 2019 Plans: FY 2019 plans continue efforts as outlined in FY 2018 in addition to the following:			

Exhibit R-2A, RDT&E Project Justification: PB 2019 Defense Health Agency		Date: February 2018
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 2017	FY 2018	FY 2019
-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. -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. ***FY 2018 to FY 2019 Increase/Decrease Statement:*** Pricing Adjustment.			
Accomplishments/Planned Programs Subtotals	0.179	0.199	0.202

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 2017
-Report on development and use of AFRRI's FRAT application for utility in triage diagnostics of suspected radiation casualties.
-Test ability of PCC assay for assessment of high-dose partial-body exposures.
-Continue evaluating new predictive radiation-responsive biomarkers in NHP models for ARS outcome and their applicability in humans.
-Continue to create human baseline database for evaluated biomarkers for use in human radiation accident cases.
-Establish large animal models (i.e., baboon, Rhesus monkey) radiation biomarker database archive linked to severity of acute radiation syndrome.
By FY2018
-Model radiation risk and injury categorization (RRIC) algorithm using large animal models (i.e., baboon, Rhesus monkey) radiation dose response databases to predict hematopoietic ARS; initiate comparison of RRIC algorithm with human radiation accident data.
-Report use of multiple radiation-responsive endpoints using premature chromosome condensation assay for radiation dose assessment.
-Provide enhanced and updated radiation software application.

Exhibit R-2A, RDT&E Project Justification: PB 2019 Defense Health Agency		Date: February 2018
Appropriation/Budget Activity 0130 / 2	**R-1 Program Element (Number/Name)** PE 0603002DHA / *Medical Advanced Technology (AFRRI)*	**Project (Number/Name)** 242A / *Biodosimetry (USUHS)*

By FY2019
-Perform and report on an evaluation to validate the utility of the human biomarker model.
-Delivery an updated software tools incorporating human radiation risk and dose tool.
-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 2019 Defense Health Agency			Date: February 2018
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 2017	FY 2018	FY 2019 Base	FY 2019 OCO	FY 2019 Total	FY 2020	FY 2021	FY 2022	FY 2023	Cost To Complete	Total Cost
242B: *Radiation Countermeasures (USUHS)*	0.723	0.120	0.133	0.136	-	0.136	0.139	0.142	0.145	0.148	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 2017	FY 2018	FY 2019
Title: Radiation Countermeasures (USUHS)	0.120	0.133	0.136
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: 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 2019 Plans: FY 2019 plans continue efforts as outlined in FY 2018 in addition to a continued gathering of preclinical data from animal models natural history studies for radiation toxicity and for the discovery and development of radiation countermeasures.			
FY 2018 to FY 2019 Increase/Decrease Statement:			

Exhibit R-2A, RDT&E Project Justification: PB 2019 Defense Health Agency		Date: February 2018
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 2017	FY 2018	FY 2019
Pricing Adjustment.			
Accomplishments/Planned Programs Subtotals	0.120	0.133	0.136

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 2017
- Complete DRF (dose reduction factor) of TPOm, BBT-059 and PrC-210 drug products.
- Study effect of TPOm drug products on radiation-induced endothelial dysfunction.
- Study downstream effect of CDX-301 drug product on signaling targets of ERK, MAP2K, and Smad2/3
- Evaluate efficacy of Phenyl butyrate in CD2F1 mice.
- Identify lncRNAs in spleen from mice treated with CDX-301 drug product.
- Complete evaluation of peg-G-CSF and Alxn4100TPO drug products as co-therapy after irradiation-wound combined injury.
- Evaluate cellular PGC-1α, NF-KB, and MAPK measurements in spleen, ileum, lung, and heart of mice and minipigs after irradiation.

By FY 2018
- Understand molecular pathways involved in radioprotection by the drug product TPOm and BBT-059.
- Understand molecular pathways involved in radioprotection by BBT-059 drug product.
- Understand effect of PrC-210 on recovery of radiation-induced depletion of peripheral blood cells and bone marrow progenitor cells.
- Characterize dynamic changes in miRNA regulation in radiation-wound combined injured mice treated with ghrelin.
- Measure IL-18 and IL-BP biomarkers in serum and various tissues in minipigs after 1.75 Gy.
- Measure cytokines and chemokines biomarkers in serum and various tissues in mice after 9.5 Gy.

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.

Exhibit R-2A, RDT&E Project Justification: PB 2019 Defense Health Agency		Date: February 2018
Appropriation/Budget Activity 0130 / 2	**R-1 Program Element (Number/Name)** PE 0603002DHA / *Medical Advanced Technology (AFRRI)*	**Project (Number/Name)** 242B / *Radiation Countermeasures (USUHS)*

- Evaluate TFAM, DRP1, OPA1 and Mfn1 as biomarkers in various tissues in mice after 9.5 Gy.

By FY 2021

- Evaluate miRNA-696 biomarker in serum and various tissues in minipigs after 1.75 Gy.
- Evaluate miRNA-696 biomarker in serum and various tissues in mice after 9.5 Gy.

By FY 2022

- Predict miRNA targeted signaling pathways using IPA in minipigs after 1.75 Gy.
- Predict miRNA targeted signaling pathways using IPA in mice after 9.5 Gy.
- Compare two species for their similarities and differences.