

**Defense Health Program  
Fiscal Year 2006/FY 2007 Budget Estimates  
Exhibit R-2, DHP Budget Item Justification**

Date: January 2005  
R-1 Item Nomenclature: 3  
Medical Advanced Technology (AFRRI) -  
0603002HP

Appropriation/Budget Activity  
Defense Health Program/BA-2

COST (\$ in Millions)	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011
	<u>Actual</u>	<u>Estimate</u>						
Total PE 0603002HP Cost	0.000	0.000	0.783	0.799	0.817	0.836	0.737	0.752
<b>Subtotal Cost</b>	<b>0.000</b>	<b>0.000</b>	<b>0.783</b>	<b>0.799</b>	<b>0.817</b>	<b>0.836</b>	<b>0.737</b>	<b>0.752</b>

**A. Mission Description and Budget Item Justification:**

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 0602787D, 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 that represent the highest probable threat to US forces under current tactical, humanitarian and counter terrorism mission environments. Findings from basic and developmental research are integrated into highly 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 dose assessment; and (3) experimental data needed to build accurate models for predicting casualties from complex injuries involving radiation and other battlefield insults. The Armed Forces Radiobiology Research Institute (AFRRI), because of its multidisciplinary staff and exceptional laboratory and radiation facilities, is uniquely positioned to execute the program as prescribed by its mission. Because national laboratories operated by the Department of Energy no longer support advanced research relevant to military medical radiobiology, AFRRI is currently the only national resource carrying out this mission.

**B. Program Change Summary:**

COST (\$ in Millions)	FY 2004	FY 2005	FY 2006	FY 2007
	<u>Actual</u>	<u>Estimate</u>	<u>Estimate</u>	<u>Estimate</u>
FY06 Budget Estimate Submission RDT&E	0.000	0.000	0.000	0.000
FY06 Budget Estimates RDT&E	0.000	0.000	0.783	0.799
Total Adjustments	0.000	0.000	0.783	0.799
Congressional Program actions				
Congressional rescissions				
Congressional increases				
Reprogramming	0.000	0.000	0.783	0.799
SBIR/STTR Transfer				
Internal Transfer				

**NOTE:** Program transfers effective FY 2006 from RDT&E Defense Agencies, Budget Activity 3, Program Element 0603002D8Z to RDT&E Defense Health Program, Budget Activity 2, Program Element 0603002HP.

**C. Other Program Funding Summary:** Not applicable.

**D. Acquisition Strategy:** Not applicable.

**E. Performance Metrics:**

By FY 2005 obtain "investigational new drug" status for a therapeutic agent to mitigate radiation injury.  
By FY 2006 provide software tools for biodosimetric assessment.  
By FY 2010 transition 4 new drugs for FDA approval for treatment of radiation injury.  
By FY 2010 provide forward-fieldable biodosimetric tools.

**Defense Health Program  
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Exhibit R-2a, DHP Project Justification**

Date: January 2005  
R-1 Item Nomenclature: 3  
Medical Advanced Technology (AFRRI) -  
0603002HP (Continued)

Appropriation/Budget Activity  
Defense Health Program/BA-2

**A. Mission Description and Budget Item Justification**

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 0602787D8Z, Medical Technology, and from industry and academia to advance novel medical countermeasures into and through pre-clinical studies toward newly licensed products.

**NOTE: Program transfers effective FY 2006 from RDT&E Defense Agencies, Budget Activity 3, Program Element 0603002D8Z to RDT&E Defense Health Program, Budget Activity 2, Program Element 0603002HP.**

Cost (in \$ Millions)	FY 2004	FY 2005	FY 2006	FY 2007
Radiation Dose Assessment: Improving the Throughput	0	0	0.083	0.083

FY 2004 Accomplishments: Defined high throughput approaches for dose assessment of mass casualties, to include improvements in quality control and quality assurance with data logging and bar-coding for example. In addition, demonstrated proof of concept that high throughput systems for lymphocyte isolation and metaphase spread preparation will work and are amenable to automation. Supplemental funding from NIAID allowed the purchase of necessary equipment for laboratory automation.  
FY 2005 Plans: Integrate the automation process for dicentric assay, including tracking system and automated assay preparation.  
FY 2006 Plans: Complete a simulated mass exposure dose assessment experiment. Perform intra- and inter-laboratory studies to validate the procedures.  
FY 2007 Plans: Improve automation of lymphocyte isolation. Characterize system for a variety of radiation parameters, including quality of radiation and dose rate.

Cost (in \$ Millions)	FY 2004	FY 2005	FY 2006	FY 2007
Biodosimetry Assay Validation of PCC Assay	0	0	0.098	0.100

FY 2004 Accomplishments: Initiated collaborative studies to assess the effect of sampling delay on the persistency of chromosome damage using the mouse. Continued validation of PCC assay using samples from accident victims and radiotherapy patients.  
FY 2005 Plans: Complete time-course study to determine the effect of sampling delay on the PCC assay. Establish multicolor chromosome aberration analysis. Continue validation of assays using samples from accident victims and radiotherapy patients.  
FY 2006 Plans: Complete analysis from radiotherapy patient samples for detecting partial-body exposures and estimating doses. Initiate assessment of radioprotective drugs on cytological markers.  
FY 2007 Plans: Quantify the effect of radioprotective drugs on the cytological biomarkers using most promising drug candidates.

Cost (in \$ Millions)	FY 2004	FY 2005	FY 2006	FY 2007
Biodosimetry Assay Validation of Molecular Markers	0	0	0.187	0.189

FY 2004 Accomplishments: Demonstrated that the gene expression markers developed in peripheral blood lymphocytes irradiated ex vivo were up regulated in vivo in an animal model and in human radiotherapy patients. Developed a 4 target QRT-PCR assay for gene expression to increase assay throughput, increase the number of observable targets, conserve sample, and reduce assay cost.  
FY 2005 Plans: Using radiotherapy patients whenever possible continue to validate the assays for both protein and gene expression markers. Initiate validation studies for gene expression and protein biomarkers in rodent exposed to radiation in vivo. Initiate studies to assess the responses follow partial body exposures. Begin development of fieldable protocols for blood collection, stabilization of sample, sample isolation, and assay.  
FY 2006 Plans: Continue studies validating radiation sensitivity of molecular biomarkers in patients and animal models under a variety of conditions. Assess the time-dependency of the sampling following radiation in an animal model. Improve characteristics of the protocol to improve fieldability.  
FY 2007 Plans: Continue to optimize and validate field assays.

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Cost (in \$ Millions)	FY 2004	FY 2005	FY 2006	FY 2007
Biodosimetry Assessment Tool (BAT) and Blood Markers for biodosimetry	0	0	0.085	0.089

FY 2004 Accomplishments: Created the preliminary version of the "First Responder Radiological Assessment Triage" (FRAT) which is the PDA version of the software tool for dose prediction "Biodosimetry Assessment Tool" (BAT). Evaluated accuracy of hematology analyzer and initiated testing of reliability, accuracy and dynamic range. Initiated development of hematology protocol with necessary quality control. Created hematology database from REAC/TS accident registry including photon and criticality exposure scenarios and initiated analysis of lymphocyte depletion kinetics for consideration to use to expand BAT and FRAT.  
FY 2005 Plans: Incorporate dose-dependent time window on lymphocyte depletion data analysis in to BAT. Incorporate neutron criticality lymphocyte depletion data set into BAT. Complete FRAT software application. Complete hematology protocol development and exercise deployable hematology system.  
FY 2006 Plans: Maintain BAT and FRAT software providing enhancements as appropriate.  
FY 2007 Plans: Maintain BAT and FRAT software providing enhancements as appropriate.

Cost (in \$ Millions)	FY 2004	FY 2005	FY 2006	FY 2007
Assessment of uranium exposure	0	0	0.024	0.023

FY 2004 Accomplishments: Began assessment of commercially available resins to concentrate urinary uranium to increase the sensitivity of methodology for the rapid detection. Continued synthesis of imprinted polymers capable of sequestering uranium.  
FY 2005 Plans: Assess the utility of imprinted polymers to concentrate urinary uranium. Assess the utility of chelation chromatography methodologies for the concentration of uranium in urine.  
FY 2006 Plans: Prepare and assess microcrystalline naphthalene conjugates for the concentration of urinary uranium. Assess the potential of the technique of cloud point extraction for use as a urine uranium concentration method.  
FY 2007 Plans: Using most effective concentration method, optimize assay for measurement of urinary uranium.

Cost (in \$ Millions)	FY 2004	FY 2005	FY 2006	FY 2007
Infection Therapies	0	0	0.306	0.315

FY 2004 Accomplishments: Demonstrated a non-specific biological response modifier (beta-1,3-1,6 glucan) and the antimicrobial agent ceftriazone enhanced survival of opportunistic infection with K. pneumoniae in sublethally irradiated mice. The combination therapy was superior to either the beta glucan or the antibiotic alone.  
FY 2005 Plans: Determine the pharmacokinetics of gatifloxacin, ciprofloxacin, and moxifloxacin in mice after irradiation. Evaluate a variety of antibiotics for their efficacy to treat gram-positive and gram-negative infections that result after lethal irradiation.  
FY 2006 Plans: Determine the optimal dose regimens for quinolones against a polymicrobial infection from endogenous pathogens with lethal doses of radiation.  
FY 2007 Plans: Initiate efficacy studies under GLP specifications to obtain an FDA indication for use of quinolones for radiation injury.

**B. Other Program Funding Summary:** Not applicable.

**C. Acquisition Strategy:** Not applicable.

**D. Major Performers:** Armed Forces Radiobiology Research Institute, Bethesda, MD.