Exhibit R-2, RDT&E Budget Item Justification Fiscal Year (FY) 2005 Budget Estimates						Date: February 2004	
Appropriation/Budget Activity RDT&E, D BA 3			R-1 Item Nomenclature: Medical Advanced Technology, PE 0603002D8Z				
Cost ($ in millions)	FY 2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009
Total PE Cost	0.000	5.941	2.063	2.539	2.590	2.644	2.700
Medical Adv. Technology/P506 Subtotal Cost	0.000	5.941	2.063	2.539	2.590	2.644	2.700

A. Mission Description and Budget Item Justification:

(U) 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:** (Show total funding, schedule, and technical changes for the program element that have occurred since the previous President's Budget Submission)

	2003	2004	2005
Previous President's Budget	0	0	0
Current FY 2005 President's Budget	0	5.941	2.063
Total Adjustments		5.941	2.063
Congressional program reductions			
Congressional rescissions			
Congressional increases			
Reprogrammings			
SBIR/STTR Transfer			
Other			

C. Other Program Funding Summary: Not applicable

D. Execution: Armed Forces Radiobiology Research Institute, Bethesda, MD

Exhibit R-2a, RDT&E Project Justification Fiscal Year (FY) 2005 Budget Submission	Date: February 2004
Appropriation/Budget Activity RDT&E, D BA 3	Project Name and Number Medical Advanced Technology, P506 PE-0603002D8Z

Cost ($ in millions)	FY 2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009
Project/Thrust Cost	0.000	5.941	2.063	2.539	2.590	2.644	2.700

A. (U) Mission Description and Budget Item Justification:

(U) 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.

B. (U) Accomplishments/Planned Program:

Cost (in $ Millions)	FY 2003	FY 2004	FY 2005
5-AED Preclinical Studies	0	1.559	.120

FY 2003: In compliance with FDA requirements, safety and toxicity studies for 5-androstenediol were initiated in a large animal model through contract with a GLP certified laboratory.
FY 2004: Obtain results from toxicology studies. Contract out GLP efficacy studies on primates.
FY 2005: Transition to advanced development for Phase I clinical trials. Submit IND application to FDA/CDER.

Cost (in $ Millions)	FY 2003	FY 2004	FY 2005
Ex-Rad Radioprotectant (Congressional add)	0	1.000	0

FY 2003: Initiated a collaboration with Onconova Therapeutics to evaluate the cellular and molecular mechanism by which Ex-Rad ON01210 exerts its radioprotective effects.

FY 2004: Evaluate the efficacy, toxicity, and pharmacology of the radioprotectant.			
Cost (in $ Millions)	FY 2003	FY 2004	FY 2005
Radiation Dose Assessment: Development and Protocol Evaluation	0	.545	.194
FY 2003: Improved lymphocyte isolation procedures for better mitotic yield. Conducted radiation dose assessment in radiation accidents from 12 samples. **FY 2004:** Define high throughput approaches for dose assessment of mass casualties, to include lymphocyte isolation system, metaphase spread preparation, and automation equipment for metaphase spread preparation. **FY 2005:** Complete a simulated mass exposure dose assessment experiment. Perform intra- and inter-laboratory studies to validate the procedures.			
Cost (in $ Millions)	FY 2003	FY 2004	FY 2005
Biodosimetry PCC Assay Validation	0	.505	.255
FY 2003: Completed in vivo validation of the premature chromosome condensation (PCC) assay using samples from the accident in Thailand. Acquired blood samples from radiotherapy patients for assessment. **FY 2004:** Complete time-course study to determine the effect of sampling delay on the PCC assay. Continue validation of assay using samples from accident victims and radiotherapy patients. Complete analysis from 8 radiotherapy patients. Optimize an immuno-enzymatic bright field method for detecting chromosome aberrations involving specific chromosomes in mouse for persistency study. **FY 2005:** Establish multicolor chromosome aberration analysis. Continue validation of assay using samples from accident victims and radiotherapy patients.			
Cost (in $ Millions)	FY 2003	FY 2004	FY 2005
Early-Response Gene Expression Markers	0	.783	.583

FY 2003: Demonstrated that gene expression changes can be measured in less than 3 hours after sample processing using devices capable of nucleic acid analysis through gene amplification on a platform deployable to a field laboratory.
FY 2004: Evaluate dose-dependent changes in multiple gene targets from single donors (samples irradiated ex vivo) for intra-individual comparisons. Complete study of inter-individual comparisons using ex-vivo irradiation of samples. Initiate validation of assay using gene expression in rodent models exposed to radiation in vivo.
FY 2005: In animal model test the influence of radioprotectants on gene expression markers to determine if the use of these pharmacological agents will influence the biodosimetric assay endpoints. Develop proof-of-principle fieldable protocols for major component of the nucleic acid analysis assay.

Cost (in $ Millions)	FY 2003	FY 2004	FY 2005
Biodosimetry Assessment Tool (BAT) and Blood Markers	0	.438	.138

FY 2003: Initiated efforts to design a version of BAT for a PDA. Obtained an updated database of bioassay data on lymphocyte and monocyte counts from the REAC/TS accident registry to support the enhancement of the BAT dose prediction models.
FY 2004: Initiate evaluation of a new hematology analyzer and perform reliability, accuracy and dynamic range studies. Initiate design for blood counter data storage system. For BAT, update neutron criticality data for onset of vomiting. Complete development of integrated help screens. Update BAT software to version 1.0. Transition selected BAT utilities to Palm Pilot platform – beta version.
FY 2005: Complete hematology protocol development and exercise deployable hematology system. Evaluate time window requirements to determine dose using lymphocyte depletion kinetics. Incorporate neutron criticality lymphocyte depletion data set into BAT. Complete PDA version 1.0 of BAT software application.

Cost (in $ Millions)	FY 2003	FY 2004	FY 2005
Assessment of uranium exposure	0	.111	.023

FY 2003: Initiated development of analytical techniques to increase the sensitivity of methodology for the rapid detection of uranium in urine. These approaches require the uranium in the urine to be concentrated. Began synthesis of imprinted polymer resin to be used for concentrating uranium in the urine. Identified potential compounds for uranium chelation chromatography.
FY 2004: Assess the utility of commercially available resins to concentrate urinary uranium. Continue synthesis of imprinted polymers capable of sequestering uranium.
FY 2005: Assess the utility of imprinted polymers to concentrate urinary uranium. Assess the utility of chelation chromatography methodologies for the concentration of uranium in urine.

Cost (in $ Millions)	FY 2003	FY 2004	FY 2005
Infection Therapies	0	1.000	.750

FY 2003: Determined the efficacy of several antibiotics including ceftriazone and gentamicin and three quinolones (trovafloxacin, gatifloxacin, and moxifloxacin) to protect against opportunistic infection with K. pneumoniae in sublethally irradiated mice.
FY 2004: Continue studies with most promising antibiotics to optimize dose regimens to protect against opportunistic infection with K. pneumoniae in sublethally irradiated mice.
FY 2005: Determine the optimal dose regimens for quinolones against a polymicrobial infection from endogenous pathogens with lethal doses of radiation.

C. Other Program Funding Summary: N/A.