RDT&E BUDGET ITEM JUSTIFICATION SHEET (R-2 Exhibit)									DATE June 2001	
APPROPRIATION/BUDGET ACTIVITY RDT&E, Defense Wide/BA 1							R-1 ITEM NOMENCLATURE In-House Laboratory Independent Research (ILIR) **PE 0601101D8Z**			
COST *(In Millions)*	FY2000	FY2001	FY2002						Cost to Complete	Total Cost
Total Program Element (PE) Cost	2.019	1.989	2.097						Continuing	Continuing
ILIR/P503	2.019	1.989	2.097						Continuing	Continuing

(U) A. Mission Description and Budget Item Justification

(U) BRIEF DESCRIPTION OF ELEMENT

(U)This program element supports basic medical research at the Uniformed Services University of the Health Sciences (USUHS) and provides the only programmed research funds received by the University. In addition, this program facilitates the recruitment and retention of faculty; supports unique research training for military medical students and resident fellows; and allows the University`s faculty researchers to collect pilot data in order to secure research funds from extramural sources (estimated $25-$30 million annually). Eighty to 100 intramural research projects are active each year, including 20-25 new starts. Projects are funded on a peer-reviewed, competitive basis. Results from these studies contribute to the fund of knowledge intended to enable technical approaches and investment strategies within Defense Science and Technology (S&T) programs.

(U)The ILIR program at USUHS is designed to answer fundamental questions of importance to the military medical mission of the Department of Defense in the areas of Combat Casualty Care (CCC), Infectious Diseases (ID), and Military Operational Medicine (MOM). The portfolio of research projects will vary annually because this research is investigator-initiated. Examples of typical research efforts are:

Combat Casualty Care: Ischemia and reperfusion injury, traumatic brain and peripheral nerve injury, neural control of pain, endotoxic shock, malignant hyperthermia, inflammation and wound healing.

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Infectious Diseases: Immunology and molecular biology of bacterial, viral and parasitic disease threats to military operations. These threats include E. coli and their shiga toxins, HIV, HTLV-1, strongyloides, gonorrhea, streptococcus, hepatitis A, typhoid, influenza A, Venezuelan equine encephalitis (VEE), malaria, and bartonellosis.

Military Operational Medicine: Sustainment of individual performance, deployment and operational stressors, cognitive enhancement, military & medical training readiness.

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(U) Project Number and Title: P503 ILIR

(U) PROGRAM ACCOMPLISHMENTS AND PLANS

(U) FY 2000 Accomplishments:

(U) Combat Casualty Care: This program provides support for 16 projects that investigate various aspects of wounding and wound healing. Emphasis currently falls on the roles that inflammatory mediators play in these processes. Investigation of endotoxin sensitivity at the cellular level has characterized the cascade of activation and influx of inflammatory cells in gram-negative sepsis in response to LPS, an important step in identifying targets for controlling sepsis-based inflammation. Work toward mapping the activation mechanism of opioid receptors led to identification of specific G proteins responsible for diminishing the ability of opioids to relive pain. Investigation of transcriptional control of differentiation in neural cells established that Myt-1 proteins may facilitate repair in the central nervous system. ($ 0.370 million)

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(U) Infectious Diseases: As in previous years, infectious disease research was one of the most active fields at USUHS, with 27 projects underway during FY00. Militarily relevant biological threat agents such as E. coli and its toxins, influenza A, typhoid and HIV all garnered significant resources. A study comparing neutralizing antibody responses to HIV and VEE completed its first phase, where in vivo safety tests elicited no adverse reactions to intracerebral administration of the replicon vaccine. Results from an ongoing investigation of lactobacillus as a possible pro- biotic agent against gonorrhea suggested that, during infection, N. Gonorrhea generates high amounts of an enzyme that can combat the H2O2 produced by lactobacilli. Work on a family of protocols investigating the transmission of Bartonellosis in Peru expanded to include a newly discovered epidemic population, a useful model for the experience of a military population entering an infectious region. A protocol to develop a candidate vaccine for HIV-1, new in FY00, generated HIV-1 envelope glycoproteins for in vivo testing in a mouse model during FY01.
($ 0.653 million)

(U) Military Operational Medicine: The forty-one projects in the MOM program included on-going work on identifying the causes of stress fractures, particularly among active women, and the response of endocrine function to (1) emotional stress and (2) strenuous physical exertion. A study of the role of melanopsin in regulating circadian rhythm showed that polarized and non-polarized light are equally effective in controlling acute pineal melatonin suppression. Investigation of the role of neuromodulators in the amygdala in rats with elevated basal level of endogen-ous norepinephrine suggested that beta-blockers can help diminish formation of traumatic emotional memories. A cultured-cell study of glutaminergic processes found preliminary indications that NMDA protects against neuronal cell death. Investigation of pituitary responses to dexamethasone and disulfiram in vivo found that the regulation of PHM`s expression and catalytic efficiency serve as coordinated physiological mechanisms for maintaining appropriate levels of alpha-amidating activity, although the response to the two drugs occurs via different mechanisms.
($ 0.996 million)

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(U) FY 2001 Plans:

(U) Infectious Diseases: Work continues toward development of vaccines for HIV, gonorrhea, and other STDs; understanding of the pathogenesis of VEE, HTLV-1, and influenza A; and effective management of infections by H. pylori and Bartonellosis. New studies include the next stage of an investigation of shiga-like toxins of E. coli; neutralizing antibody response to VEE and HIV replicons; and identification of a new possible transmission vector for Bartonellosis. ($ 0.725 million)

(U) Military Operational Medicine: New projects supported in FY00 include analysis of the circadian photoentrainment pathway in a murine model; regulation of peptide amidation; and immediate early gene requirements for long-term potentiation and learning. Studies of stress in relation to eating disorders, nicotine use, physical exertion, and immunosuppression will all continue, as will investigation of transcriptional control of neural cell differentiation, the role of AP-1 proteins in synergistic signaling, and the role of neuromodulators in neuroplasticity in the amygdala. ($ 0.841 million)

(U) Combat Casualty Care: Ongoing projects include a family of studies of malignant hyperthermia, aimed primarily at developing a reliable genetic marker; investigation of signal transduction; and endotoxins. New projects in FY01 will pursue a noninvasive diagnostic test for malignant hyperthermia and investigate the mechanism of liver failure in a disulfiram-based model.
($ 0.423 million)

(U) FY 2002 Plans:

(U) Efforts will continue in all of USUHS`s major research areas (CCC, ID, and MOM) in FY01. Since specific, investigator-initiated projects compete for funding each year, no detailed description of the research is possible at this time. ($ 2.097 million)

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(U) B. Program Change Summary	**FY2000**	**FY2001**	**FY2002**	**Total Cost**
Previous President's Budget Submit	2.029	2.007	2.086	Continuing
Appropriated Value		2.007		Continuing
Adjustments to Appropriated Value				
a. Congressionally Directed Undistributed Reduction	0.000	-0.018	0.000	
b. Rescission/Below-threshold Reprogramming, Inflation Adjustment	-0.010	0.000	0.011	
c. Other	0.000	0.000	0.000	
Current President's Budget	2.019	1.989	2.097	Continuing

Change Summary Explanation

(U) Funding: FY 2000 funding changes are due to reprogramming adjustments. FY 2001 reductions reflect Section 8086 adjustments.

(U) Schedule: N/A

(U) Technical:

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(U) C. OTHER PROGRAM FUNDING SUMMARY COST: N/A

(U) D. ACQUISITION STRATEGY: N/A

(U) E. SCHEDULE PROFILE: N/A