RDT&E BUDGET ITEM JUSTIFICATION SHEET (R-2 Exhibit)								DATE February 2000	
APPROPRIATION/BUDGET ACTIVITY RDT&E, Defense Wide/BA 1							R-1 ITEM NOMENCLATURE In-House Laboratory Independent Research (ILIR) PE 0601101D8Z		
COST*(In Millions)*	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	FY 2004	FY 2005	Cost to Complete	Total Cost
Total Program Element (PE) Cost	2.146	2.029	2.007	2.086	2.081	2.123	2.165	Continuing	Continuing
ILIR/P503	2.146	2.029	2.007	2.086	2.081	2.123	2.165	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. This program facilitates the recruitment and retention of faculty, supports state-of-the-art capabilities for training military medical students and resident fellows, and allows the collection of pilot data by the University`s faculty researchers. Pilot data allow the faculty 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), Military Operational Medicine (MOM), and Nuclear, Biological and Chemical (NBC) Medical Defense. 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.
- 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.
- Nuclear, Biological and Chemical Defense: basic research questions concerning nerve agent intoxication and treatment.

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(U) Project Number and Title: P503 ILIR

(U) PROGRAM ACCOMPLISHMENTS AND PLANS

(U) FY1999 Accomplishments:

(U)Combat Casualty Care: The objective of this program continues to provide support for a significant number of new and continuing projects in Combat Casualty Care. The program continued to investigate various aspects of wounding and wound healing and the roles that inflammatory mediators play in these processes. Projects to elucidate cellular and molecular mechanisms in endotoxic shock and its treatment are an important area of research. Other major thrust areas included peripheral nerve injury, mechanisms of repair and traumatic brain injury, based on animal models and nerve cells in culture. Included in this program is the investigation of low-power laser therapy to decrease programmed cell death when motor nerves are severed.
($ 0.643 Million)
(U)Infectious Diseases: This broad area continued to be emphasized within the USUHS; approximately 30 protocols are supported within this area. Militarily relevant bacterial threat agents such as E. coli and its toxins, gonococcus and streptococcus garnered significant available resources. Mobilization of macrophages and antibody production continued to be studied within the context of Venezuelan equine encephalitis. The initiative to study typhoid fever with the development of an animal model continues. Research continued on the study of bartonellosis by examining the vector and the animal reservoir, and by performing studies on the epidemiology of this parasitic disease. Comparison of two inactivated hepatitis A vaccines was completed with the final results impacting the decision for vaccination of military personnel.
($ 0.644 Million)

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(U)Military Operational Medicine: FY1999 funds supported research in training and military readiness as a critical area within Military Operational Medicine. Training practices and their effects on exertional heat illness of enlisted basic training recruits continued to be examined, as well as the study of the effects of exercise and exertion on the immune system. Studies to determine the effects of stress, nicotine intake and dysfunctional eating habits also continued. New work to delineate neural mechanisms underlying post-traumatic stress disorder (PTSD) was initiated. Studies in animal models of the role of neurotrophins in protecting higher brain functions and reversal of functional deficits by administration of nerve growth factor were begun.
($ 0.665 Million)
(U)Nuclear, Biological and Chemical Medical Defense: Multiple basic research projects in this threat area were supported. Analysis of the chemical breakdown of different isomers of 1,4 benzodiazepines, such as Valium, and other chiral drugs used as antidotes to central nervous system effects of nerve agent poisoning continue. Study of the pattern of sensory input to the frontal cortex was supported. The organism that exhibits extraordinary resistance to ionizing radiation, *Deinococcus radiodurans*, was examined to better understand what gives it this unique ability. A study was initiated to examine the role of mitochondrial membrane proteins in agent-induced cell death.
($ 0.194 Million)

(U) FY2000 Plans:

(U)**Combat Casualty Care:** The objective of this program is to provide support for a significant number of new and continuing projects that investigate various aspects of wounding and wound healing and the roles that inflammatory mediators play in these processes. Elucidation of cellular and molecular mechanisms in endotoxic shock and its treatment continue to be important research goals. Other major thrust areas include investigation of injury to and repair of the brain and peripheral nerves using animal models and nerve cells in culture, and identifying the cellular mechanisms behind malignant hyperthermia in order to develop new diagnosis and treatment options. ($0.428 M)
(U) **Infectious Diseases:** As in previous years, infectious disease is one of the most active fields of research at USUHS. Militarily relevant biological threat agents such as E. coli and its toxins, influenza A, typhoid and HIV all garner significant resources. A three-pronged study of bartonellosis in Peru continues, its primary focus on identification of the disease transmission vectors. A study comparing the neutralizing antibody responses to HIV and VEE is nearing completion, as is comparison of two inactivated hepatitis A vaccines. ($0.684 M)
(U) **Military Operational Medicine:** New projects supported by FY2000 funds include exploration of factors possibly contributing to the higher incidence stress fractures in women; the role of melanopsin in regulating circadian rhythm; and the neural and endocrine mechanisms that underlie PTSD. Ongoing projects include the investigation of endocrine & immune response to stress and exertion; the interaction between stress and nicotine intake; and the correlation of body composition, dietary options, and activity patterns with dysfunctional eating habits. ($0.678 M)

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(U) **Nuclear, Biological and Chemical Medical Defense:** Projects initiated in FY2000 focus on health issues related to exposure to chemical warfare compounds, emphasizing development of methods for rapid diagnosis and effective treatment. In addition, work continues on identifying the function of the outer mitochondrial membrane protein in protecting against tissue injury and cell death due to radiation expsoure, and on analyzing patterns of sensory input to the frontal cortex, with particular attention to the roles of the dopaminergic system and neocortical cholinergic depletion. (0.239 M)

(U) FY2001 Plans:

(U)Efforts will continue in all the major research areas (CCC, ID, MOM, and NBC) for FY2001. Specific projects compete for funding each year, therefore, detailed description of the research is impossible at this time.
($ 2.007 Million)

(U) B. Program Change Summary	**FY1999**	**FY2000**	**FY2001**	**Total Cost**
Previous President's Budget	2.167	2.033	2.021	Continuing
Appropriated Value	0.000	0.000	0.000	Continuing
Adjustments to Appropriated Value				
a. Congressionally Directed Undistributed Reduction	0.000	0.000	0.000	
b. Rescission/Below-threshold Reprogramming, Inflation Adjustment	(.023)	(.004)	(.014)	
c. Other	0.000	0.000	0.000	
Current President's Budget	2.146	2.029	2.007	Continuing

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Change Summary Explanation:

(U) **Funding:** Funding changes are due to inflation reductions and the government wide rescission.

(U) **Schedule:** N/A

(U) **Technical:** N/A

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

(U) **D.** **ACQUISITION STRATEGY:** N/A

(U) **E.** **SCHEDULE PROFILE:** N/A