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ARMY RDT&E BUDGET ITEM JUSTIFICATION (R-2 Exhibit)								DATE February 1999																																																									
BUDGET ACTIVITY 3 - Advanced Technology Development				PE NUMBER AND TITLE 0603105A Military Human Immunodeficiency Virus (HIV) Research				PROJECT DH29																																																									
COST <i>(In Thousands)</i>	FY1998 Actual	FY 1999 Estimate	FY 2000 Estimate	FY 2001 Estimate	FY 2002 Estimate	FY 2003 Estimate	FY2004 Estimate	FY2005 Estimate	Cost to Complete	Total Cost																																																							
DH29 Military HIV	17541	5672	5976	5926	5952	6098	6878	6901	Continuing	Continuing																																																							
<p>A. <u>Mission Description and Budget Item Justification:</u> This program element supports research to provide concept exploration of candidate prevention vaccines to include safety and efficacy in model systems to prepare and conduct clinical studies. It funds Congressionally directed Acquired Immune Deficiency Syndrome (AIDS) research to control the infection in military environments, protect the military blood supply and protect military personnel from unusual risks associated with infection. AIDS research is focused on the following thrust areas: diagnosis, natural history, epidemiology, and vaccine development. Efforts are directed to answer militarily unique questions affecting manning, mobilization, and deployment. This program is managed primarily by the U.S. Army Medical Research and Materiel Command. The major contractor is the Henry M. Jackson Foundation for the Advancement of Military Medicine, Rockville, MD. Additional AIDS related research is conducted within the following projects: 0601102A, project S17; 0602787A, project 873; 0603105A, project H29; 0603807A, project 811; and 0604807A, project 812.</p>																																																																	
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<p>Change Summary Explanation: Funding: FY 1998: Congressional special interest funding reprogrammed by DoD to this PE for proper program execution.</p>																																																																	
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BUDGET ACTIVITY 3 - Advanced Technology Development	PE NUMBER AND TITLE 0603105A Military Human Immunodeficiency Virus (HIV) Research	PROJECT DH29
<p>FY 1998 Accomplishments:</p> <ul style="list-style-type: none"> 17541 Began Phase 1/2 clinical trial of a bivalent subtypes B & E human immunodeficiency virus (HIV) recombinant gp120 vaccine in Thailand; successfully enrolled 380 subjects (12 in open portion, 368 in blinded portion of study; study is ongoing. Demonstrated safety in 12 open study volunteers and induction of binding antibody to both subtypes B & E after the third immunization. Analysis of safety and immunogenicity data for the blinded portion of the trial will be completed at the end of the study. Began a Phase 1 clinical trial in U.S. volunteers of oligomeric gp160 vaccine alone or after priming with a live canarypox vector. Successfully vaccinated 29 subjects; no serious adverse events have been reported. Final data analysis awaits study completion. Developed protocols for gene-chip detection of HIV drug resistance that permit consistently accurate detection of drug-resistant isolates at viral loads of less than 2,500 copies/ml, necessary for accurately studying and understanding the implications of breakthrough viremia in HIV-infected patients and for devising clinically relevant protocols for deployment and use of expensive new technology for clinical management of HIV patients. Validated that the performance of newly available gene-chip technology in the detection of HIV drug resistance is equal to that of more traditional sequencing efforts which are time-consuming and more costly. Demonstrated that existing gene-chip technology is unable to accurately detect gene mutations in non-subtype B HIV isolates. Began efforts to alter the composition of the gene-chip to permit analysis of all subtypes of HIV, important for management of soldiers and others with non-subtype B infection. In continuing surveillance and epidemiologic studies, obtained the first full length genome sequences of subtype F from Brazil, Kenya and Zaire and obtained full-length genomes for two new strains of subtype A from Djibouti. These studies are important for continued disease risk assessment and for design of candidate preventive vaccines. Established a panel of 200 sera representing all subtypes of HIV-1 which have been accurately genotype by multiple methods, a necessary tool in the effort to develop a serological assay that can accurately discriminate subtypes of HIV-1, eventually useful to field surveillance and epidemiological studies. Began a study to determine the subtype of all new infections with HIV that occur in U.S. military personnel, important for documenting global dispersal of HIV subtypes and for determining and designing vaccines for prevention of infection among U.S. forces. Began a study to determine the temporal trends of non-subtype B infection in the U.S. using HIV positive sera (unlinked to any identifiers) obtained during the past 14 years from recruit screening programs. Demonstrated that the molecular epidemiology of new HIV infections in Nigeria reflects that the majority of new infections consist of HIV hybrid subtypes (subtype G/A), raising the likelihood that evermore complex strains of HIV may occur. This effort is important for understanding and defining disease risk assessment for U.S. forces deployed in such regions and for design of preventive candidate vaccines. Demonstrated that the genetic diversity of HIV-1 in Thailand has increased since 1990 when HIV was first isolated and sequenced, important for understanding and defining virological and immunological events in vaccine trials and for the design of vaccines for prevention of HIV infection. Standardized multiple assays for subtype E HIV-1, including neutralization assay, cytotoxic T lymphocyte assay, lymphoproliferation assay, and viral culture. This effort is important for evaluation of vaccine-induced immune response in clinical vaccine trials in Thailand. Began a seroconverter study to identify and evaluate all new infections with HIV-1 among military healthcare beneficiaries to document risk behaviors associated with HIV infection among military service members; to design prevention interventions; and to document and define the extent of non-subtype B infection and viral drug resistance among military service members. Enrolled 263 subjects in the first year of study and documented non-subtype B infection in 10 of 208 subjects (7 subtype E). Documented that 20% of subjects with new HIV infection have a drug-resistant strain. 		
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<p>FY 1998 Accomplishments: (continued)</p> <p>Demonstrated that immunization with recombinant gp160 had no benefit for subjects already infected with HIV-1. Demonstrated that re-infusion of <i>ex vivo</i> expanded autologous CD4 lymphocytes into HIV infected patients is safe and resulted in raising of measured CD4 lymphocyte counts and normalization CD4/CD8 ratios. This may offer additional treatment options for infected patients. Additional studies are necessary to understand long-term clinical implications and long-term fate and function of re-infused cells. Demonstrated that a targeted behavioral intervention program [STD/HIV Intervention Program (SHIP)] can significantly decrease self-reported risk behaviors for HIV-1 infection. Transitioned the SHIP intervention to the Marine Security Guard School and the Navy Preventive Medicine Technician School. Began a cohort feasibility study at a family planning clinic in Thailand to prepare for future Phase 3 vaccine trials of preventive HIV vaccines in Thailand. Reached target enrollment of 1,008 subjects within 5 months of study implementation.</p> <p>Total 17541</p> <p>FY 1999 Planned Program:</p> <ul style="list-style-type: none"> • 5521 Establish laboratory infrastructure in Thailand for support of efficacy vaccine trial. Conduct Phase 1/0 study of DNA vaccine candidate in the U.S. Transition to advanced development a candidate bivalent vaccine with potential to prevent HIV infection in 70 percent of immunized personnel. Conduct Phase 0/1 study of avipox-vectored gp160 vaccine in Thailand. Complete Phase 1/2 study of bivalent gp120 vaccine in Thailand. • 151 Small Business Innovation Research/Small Business Technology Transfer (SBIR/STTR) Programs <p>Total 5672</p> <p>FY 2000 Planned Program:</p> <ul style="list-style-type: none"> • 5976 Define the correlates of immunity to HIV, necessary for vaccine design. Establish genetic and phenotypic correlates of drug resistance among HIV-1 clinical isolates, necessary for establishing drug treatment strategies for military dependents. Evaluate and validate a rapid test for field diagnosis of HIV infection. Conduct clinical studies to slow progression and prevent immune deficiency related to HIV infection. Develop a vaccine process to prevent HIV infection of all genotypes of HIV-1. Define the correlates of immunity to HIV. Establish the genetic and phenotypic correlates of drug resistance as a clinical tool. <p>Total 5976</p> <p>FY 2001 Planned Program:</p> <ul style="list-style-type: none"> • 5926 Transition to advanced development a test for simple and rapid forward diagnosis of HIV infection. Conduct Phase 0/1 study of novel vaccine vector for the prevention of HIV-1. Conduct Phase 0/1 study of oligomeric protein vaccines. Clinical evaluation of novel methodologies for detection antiretroviral drug resistance. <p>Total 5926</p>		
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