Headquartered at the Uniformed Services University (USU) in Bethesda, MD, the Infectious Disease Clinical Research Program (IDCRP) is a worldwide network of Department of Defense (DoD) clinical and research centers that have joined together to investigate infectious disease challenges facing the military. With a presence at the largest DoD medical centers, the IDCRP currently includes 10 military hospitals and 10 military research sites. Working in tandem with active duty investigators at each of these sites, the IDCRP has over 100 employees. Participating centers are partners in the IDCRP’s network Infectious Disease Institutional Review Board (IRB) at USU developed to undertake multicentered investigation with only a single IRB review followed by a secondary review at the Pentagon by a TriService Panel at the DoD Health Affairs. At present, there are over 70 active protocols in the IDCRP’s research portfolio.
In August 2010, I assumed the role of Director of the Infectious Disease Clinical Research Program from Captain Gregory Martin. I’d like to take a moment to thank Captain Martin for his leadership over the past three years. Captain Martin led the IDCRP to grow exponentially into a mature program capable of conducting multi-center research. The number of full-time equivalent personnel grew to over 100 at 10 hospitals. I would also like to thank our sponsors of the program at the Uniformed Services University, the National Institute of Allergy and Infectious Diseases, the Navy Bureau of Medicine and Surgery, the DoD Global Emerging Infections Surveillance and Response System, and the Centers for Disease Control and Prevention.

This was an appropriate time to transition the leadership of the IDCRP. In May, the American Institute of Biological Sciences conducted a five year review of the program with the help of five external scientists. Dr. Adel Mahmoud, former President of Merck Vaccines and currently at Princeton University, chaired the panel. The reviewers commented that “the IDCRP is an excellent, well-managed program addressing important health threats to military preparedness, the nation’s biodefense, and the broader spectrum of infectious diseases. Since its inception, the IDCRP has made impressive beginning strides in developing the infrastructure and network to conduct clinical research, which has allowed the execution of high-quality, programmatically relevant protocols.” As we move into this period of new leadership, we will be assessing and incorporating a number of the report’s recommendations into our strategic planning.

During this past year, our network brought on-line 11 new research studies and published 32 new articles. Key highlights on the General Infectious Diseases side include beginning to see the fruits of our labor in the Trauma Infectious Disease Outcome Study (TIDOS), which now has over 585 subjects enrolled. As we came upon the one-year anniversary of that project, we were able to analyze the first quarter of data, which was presented by Dr. David Tribble at the 2010 Advanced Technology Applications for Combat Casualty Care conference. Both our Staphylococcus aureus phase I/II vaccine study in CONUS and Ebola/Marburg DNA phase II vaccine study in Uganda are fully enrolled and are in the follow-up phases. In addition, we kicked off a study assessing skin and soft tissue infection prevention and incidence at Fort Benning, GA. At this time, over 400 cases of soft tissue infections have been enrolled in that study.

The HIV/Sexually Transmitted Infections working group continues to contribute significantly to the medical literature. The Military HIV Natural History Study (NHS) cohort has enrolled over 5000 subjects and is now in its 24th year. We are grateful for the foresight of the original investigators on that protocol, which has led to numerous publications and scientific contributions for enhancing our understanding of HIV. Highlights include a randomized controlled clinical trial comparing revaccination with pneumococcal conjugate vaccine to polysaccharide vaccine among HIV-infected adults, published in the Journal of Infectious Diseases. Also, data from the NHS study was utilized in the recent Institute of Medicine report to the Social Security Administration on HIV disability. Finally, the newly formed HIV/STI prevention working group was instrumental in facilitating the recent publication in the Medical Surveillance Monthly Report of key data on sexually transmitted infections (STIs) in the military. This data will help generate the appropriate research questions that need to be answered related to STIs in the military population.

The IDCRP continues to contribute significantly to the USU and greater DoD education mission. Our personnel direct three USU graduate level courses on the Fundamentals of Clinical Research, Research Design and Analysis, and Epidemiology and Control of Infectious Disease. These courses have been greatly enhanced during the last
year by the addition of experienced epidemiologists, statisticians, and research design experts at the Program Coordination Center (PCC). The PCC staff continues to mentor MPH and PhD students through practicum, project, and thesis work supported through the IDCRP research portfolio. Also, several members of the PCC have assisted with the USU School of Medicine curriculum reform process. The IDCRP continues to train infectious disease fellows and junior staff across the entire DoD medical community. One example was the Clinical Research Workshop held prior to and in conjunction with the 2010 Armed Forces Infectious Disease Society (AFIDS) spring meeting.

As I take the reins of the program, I view the upcoming year as one of consolidation and transition. After a period of rapid growth, it is time to reassess how to leverage our strengths and shore up any weaknesses. This past year, we welcomed Dr. Françoise Seillier-Moiseiwitsch as our new Director of Biostatistics and Data Management. She is working with our colleagues at the Military HIV Research Program (MHRP) to transition their data management personnel from the MHRP to the IDCRP, and she is also building up our in-house statistical capabilities. In the long run, these changes will allow us to position ourselves strategically for growth into the future. Over the coming year, we will be reassessing the program’s current structure of independent HIV/STI and GID working groups. Looking forward, we are establishing a new process to evaluate and prioritize new research concepts. We will also be welcoming CDR Timothy Burgess as the new Deputy Program Director in December 2010. I feel very privileged to serve in this new capacity and am awed by the dedication and teamwork exhibited by our network personnel. I am enthusiastic about moving the program to the next level, where we will build upon the foundation for multi-center clinical research that has already been established.

Col Mark Kortepeter, MC, USA

Program Director

**Our Mission**

The IDCRP will design, conduct and publish collaborative clinical Infectious Disease research of importance to the DoD and NIAID through an effective research network that rapidly responds to evolving Infectious Disease threats.

**Our Vision**

Reduce the impact of infectious diseases on the military population.
Table of Contents

Map of IDCRP Network .................................................................................................................... ii
Letter from Program Director ..........................................................................................................1
IDCRP Introduction
   The IDCRP ................................................................................................................................. 4
   IDCRP Structure ......................................................................................................................... 5
   Regulatory Affairs ..................................................................................................................... 6
   Education ................................................................................................................................. 7
   Biostatistics and Data Management .......................................................................................... 9
The General Infectious Diseases Working Group ........................................................................... 10
The HIV/Sexually Transmitted Infections Working Group ............................................................ 19
IDCRP Protocols ............................................................................................................................. 25
Finance ............................................................................................................................................. 28
Publications and Presentations ........................................................................................................ 30
IDCRP at a Glance .......................................................................................................................... 37
The Infectious Disease Clinical Research Program

The IDCRP was formed in 2005 through an Interagency Agreement between the National Institute of Allergy and Infectious Diseases (NIAID) and the Uniformed Services University (USU). Recognizing the operational, strategic and scientific importance of infectious diseases to the US military, the NIAID provided all the support needed to expand the existing DoD HIV clinical network into a diverse team of clinical and research partners from the NIAID and the DoD.

The IDCRP is designed to build broad collaborations among DoD and NIAID investigators as well as develop affiliations with partners from academia and industry. The program operates at USU through the Henry M. Jackson Foundation for the Advancement of Military Medicine (HJF). The IDCRP draws on the unique strengths of both the DoD and the NIAID. The military medical system includes a diverse group of hospitals and clinics throughout the world with access to nearly 9 million beneficiaries. With increasingly useful databases linked to electronic medical records with laboratory and pharmacy data, the DoD patient population is ideal for research. Through the IDCRP, DoD clinicians and investigators treating military beneficiaries now have access to the extensive infectious diseases research experience of NIAID investigators as well as to the robust education, biostatistics, regulatory and clinical trials monitoring activities associated with the NIAID. Research support in the IDCRP is achieved in a different manner than DoD investigators had been accustomed. IDCRP does not “fund” research projects, but, instead incorporates protocols into the network portfolio.

Research concepts brought to the IDCRP are focused on clinical infectious disease questions of importance to the DoD. A concept is brought to one of the IDCRP working groups where the idea is discussed and formulated into a research protocol that is performed primarily by network uniformed and civilian investigators. Collaborating labs and clinics within and outside the IDCRP may also be incorporated. Protocols are crafted by IDCRP working groups and then submitted to the IDCRP Scientific Review Board (SRB) for a rigorous appraisal. Projects obtaining SRB approval are then reviewed by the Regulatory Affairs Department of IDCRP and often the NIAID monitors for regulatory and ethical considerations. After completion of regulatory review the protocol is submitted to the Infectious Disease Institutional Review Board (IRB) at USU. The ID IRB is comprised of members drawn from participating partners. Prior to implementation at the sites, some protocols may undergo additional regulatory review by the NIAID and a second level review by DoD Health Affairs. After local command authorization is obtained studies commence and continue to be executed and monitored through the IDCRP Working Groups up through completion, presentation and publication. The goal is to provide support and training in clinical infectious diseases research while conducting high quality multicentered investigations that ultimately impact and inform DoD Force Health Protection.
As the diagram above illustrates, the IDCRP is comprised of many individuals representing various organizations. The IDCRP ultimately answers to DoD and NIAID stakeholders who may interact with the Steering Committee members, or directly with Program Coordination Center (PCC) staff, regarding the scope of projects in the IDCRP portfolio. Regardless of where they are initiated, study concepts are brought to the Working Group Directors for consideration. Each Working Group (WG) is composed of PCC staff and network investigators who consider whether the research question is appropriate for the IDCRP. In this early stage a concept sheet is developed and vetted by the WG, then sent to the Senior Advisory Group and the Steering Committee for a decision about whether further development of the concept is warranted at that time. Once approved by both bodies, the concept undergoes development through the WG as its resource requirements are determined by IDCRP Operations and Finance and it is subsequently submitted to the Scientific Review Board (SRB). The SRB is composed of PCC staff, a statistician, IDCRP affiliated investigators and invited Subject Matter Experts who review and score proposals. Through this process, protocols are carefully honed and reviewed for regulatory compliance and statistical rigor prior to submission to the ID IRB at USU. The process of protocol development involves many supporting partners within and external to USU and IDCRP.
The IDCRP Regulatory Affairs team consists of staff at the network’s Military Treatment Facilities and IDCRP Program Coordination Center (PCC). They perform essential duties throughout the IDCRP protocol development and execution process and are led by the Head of Regulatory Affairs. Staff assist in protocol development, conduct intensive review of all IRB submissions to check for compliance with federal, local and IRB policies and procedures, consult with investigators during IRB review, coordinate with IRB staff to address any problems, perform on-site monitoring, track study milestones and maintain regulatory documents for the program.

In the coming year, Regulatory Affairs staff will expand their duties to perform quality management and internal auditing of IDCRP studies. As an additional layer of protection, the quality management will verify that the research data are generated, collected, analyzed and reported according to the protocol and study manual.

NIAID RCHSPB Monitors

The Regulatory Affairs staff at the IDCRP PCC, often in collaboration with the NIAID Regulatory Compliance and Human Subject’s Protection Branch (RCHSPB), conduct a thorough review of all IDCRP protocols to ensure protocols are ready for IRB review. The rigorous review focuses on ensuring regulatory integrity, compliance with local, federal and USU regulations and procedures, and consistency within the protocol and informed consent documents. The aim of this review is to provide the ID IRB with a high quality submission and reduce the post-review stipulations issued by the IRB. Provisions are made to review all research protocols, consent and HIPAA documents, recruitment material and case report forms for required elements as well as additional human subjects considerations.

Early in the protocol development stage, Regulatory Affairs staff and study monitors begin to refine the protocol and its associated documents in preparation for IRB review and study execution. RCHSPB serve as monitors of prospective IDCRP protocols. The monitoring ensures the protection of human subjects, validates the integrity of data collection and capture, compliance with ICH/GCP and applicable regulations.

The USU ID IRB

The USU Infectious Disease Institutional Review Board (ID IRB) is a DoD Infectious Diseases community IRB centered at USU. The ID IRB was established via a Memorandum of Understanding (MOU) in January 2008. This MOU, signed by the Assistant Secretary of Defense (Health Affairs), the Surgeon General for each service, and the President of Uniformed Services University, created a single review pathway for multicenter ID research, eliminating the need for multiple and repetitive scientific, ethical and second level reviews. Having this streamlined review process effectively made possible multicenter collaborative research without the impediments and delays of the past.

The ID IRB composition ensures local representation via the inclusion of members representing military treatment and research facilities participating in the IDCRP as well as additional members who provide representation and/or advocacy for particular subgroups. The ID IRB is headed by CAPT Trueman Sharp, Chairman of the Department of Military and Emergency Medicine at USU. In the ID IRB he chairs a diverse group of individuals from a variety of scientific and non-scientific backgrounds. Members of the ID IRB are drawn from over eight military medical centers from across the United States and the National Institutes of Health. With them comes a wealth of expertise in fields that include Preventive Medicine, Pediatric Infectious Disease, Adult Infectious Disease, Pediatric and Adolescent Medicine and Hematology and Oncology. Also serving as members are scientists who are subject matter experts in Immunology, Virology and Neuroscience. To ensure that the voice of the community is represented, there are non-scientist members who range from enlisted service members to chaplains. The ID IRB also draws upon the USU General Counsel and consultants who are authorities in clinical and research bioethics. With all these resources and a unique military perspective behind them, the USU ID IRB fulfills their duty in safeguarding the rights and welfare of human subjects.
The military services’ mandate for second level ethical review of human research is met by the Office of the Under Secretary of Defense for Personnel and Readiness [USD(P&R)]/ Triservice Headquarters Panel (HQ Panel). This HQ Panel provides administrative review of ID IRB determinations of Food and Drug Administration (FDA)-regulated, greater than minimal risk and international research. Due to the collaboration of service representatives and USD(P&R), the HQ Panel eliminates the need for separate reviews by USD(P&R) and each participating service.

By consolidating the number of required reviews for multicenter research, the ID IRB has served an integral role in allowing the IDCRP to respond rapidly to infectious disease threats affecting military populations. To further streamline its processes, USU has adopted a fully electronic protocol submission and review system (IRBNet) to automate much of the previously paper-centric IRB procedures. Since its creation, the USU ID IRB has reviewed over 50 domestic and international research protocols.

The IDCRP Regulatory Affairs staff, RCHSPB monitors, and ID IRB staff continue to work collaboratively to advance multicenter, militarily-relevant infectious disease research.

**Education**

**IDCRP Support for USU Based Programs and Initiatives**

The educational contributions of the IDCRP continue to focus on two broad areas of activities. The first involves the IDCRP’s close relationship with the Uniformed Services University, and its support of primary and graduate medical education for the three active duty services as well as the U.S. Public Health Service (USPHS). The IDCRP continues to direct three graduate level courses for Masters of Public Health (MPH) students, residents, and fellows. These include courses in the Fundamentals of Clinical Research, Research Design and Analysis, and Epidemiology and Control of Infectious Disease. These graduate level courses are taught by Drs Martin Ottolini, Ken Wilkins, and David Tribble, respectively. These courses have been greatly enhanced in scope and depth during the last year by the addition of...
experienced epidemiologists, statisticians, and research design experts at the fully staffed Program Coordinating Center (PCC), along with our NIAID partners.

In addition, the PCC staff has reached out to mentor a greater number of MPH and PhD students through these courses and practicum, project, and thesis work, supported by the IDCRP’s research portfolio. The IDCRP is committed to the continued success of the USU F. Edward Hébert School of Medicine. Members have supported search committees to fill senior academic positions, served as advisors on critical academic committees, and accepted a large variety of teaching and administrative duties associated with the Departments of Preventive Medicine and Biometrics, Internal Medicine, Pediatrics, Emerging Infectious Diseases, and Microbiology and Immunology. Several members are assisting in the multi-year curriculum reform process mandated this year by the USU leadership.

**IDCRP Support for DoD-Wide Infectious Disease Educational Initiatives**

The second group of activities relate to the IDCRP’s continued outreach to help educate and mentor infectious disease fellows and junior staff across the entire DoD medical community. IDCRP staff extensively support our service members training within the three internal medicine and the pediatric infectious disease fellowship programs in San Diego, San Antonio, and the National Capital Consortium. IDCRP-sponsored activities at the annual Armed Forces Infectious Disease Society meeting have expanded to include a separate “Clinical Research Workshop” held prior to the 2010 meeting in Annapolis, MD, attended by nearly 20 fellows and junior staff. In addition, the IDCRP sponsored a symposium on Acute Respiratory Infections as part of this meeting, which showcased a diverse portfolio of research presentations by six IDCRP-sponsored researchers. IDCRP education and research staff have presented research updates at several regional military continuing medical education (CME) activities.

The IDCRP is committed to nurturing the next generation of infectious disease clinical researchers by supporting development, execution, analysis, and presentation of results from a diverse portfolio of fellow and junior staff research protocols in a supportive environment. Recent accomplishments include:

- **LCDR Chris Duplessis** compared the immunogenicity of H1N1 vaccination between HIV infected and HIV uninfected persons (IDCRP-053), under the mentorship of Dr. Nancy Crum-Cianflone. He presented initial results at the spring AFIDS meeting. He presented further data comparing the immunogenicity of live vs. inactivated vaccine in this study cohort at the 2010 Infectious Disease Society of America (IDSA) meeting in Vancouver. His initial manuscript has been accepted for publication in *Clinical Infectious Diseases*.

- **LTC James Mancuso**’s analysis of the value of latent tuberculosis screening in US Army recruits (IDCRP-021) is serving as a major component of his Doctor of Public Health thesis work, which he defended this fall under the mentorship of Dr. David Tribble.

- **MAJ Erica Johnson**’s study of the epidemiology and outcomes of community-acquired pneumonia (IDCRP-000-20), and CPT Jeff Sherwood’s study of the association of vitamin D and testosterone levels with bone loss in the US Military HIV Study Cohort (IDCRP-000-22), are undergoing final analysis.

- **LT David Byers**’ proposed study of the pharmacokinetics of colistin (IDCRP-039) has received funding support from the Deployment Related Medical Research Program (DRMRP) and is moving forward, while CPT Kris Paolino’s proposal to use protein microarrays to evaluate host and pathogen responses to gram negative bacteremia has advanced to IRB review.

All of these studies are moving forward under the extensive support from our HIV/STI and GID research staff, our clinical research associates and site managers, statistical consultants, scientific reviewers, and regulatory affairs staff.
Biostatistics and Data Management

IDCRP biostatisticians and data managers provide expertise to principal investigators for the conceptualization, design, execution, analysis, and publication of research studies, be they retrospective, prospective, observational, laboratory-based or interventional. Until recently, these extensive activities have been coordinated by the Deputy Director of Biostatistics and Data Management, Dr. Kenneth Wilkins, and services have been provided by the IDCRP team at San Antonio Military Medical Center (SAMMC), the Data Analysis Center (DAC), and the Data Coordinating and Analysis Center (DCAC).

The DAC, housed in the Coordinating Center for Biometric Research within the Division of Biostatistics at the University of Minnesota’s School of Public Health, is contracted to provide statistical and epidemiological support to IDCRP investigators. DAC personnel work closely with investigators throughout concept and protocol development, provide monitoring for prospective studies, carry out statistical analyses of prospective and retrospective studies, and participate in writing abstracts and manuscripts. DAC personnel are also involved in statistical reviews during the working group review and scientific review of IDCRP protocols, and consult on data collection practices, case report form (CRF) design, and grant writing.

The DCAC, housed in the Military HIV Research Program (MHRP) of the Division of Retrovirology at the Walter Reed Army Institute of Research functions as the IDCRP’s data management center. DCAC roles include CRF and database development, data entry, data quality control, and preparation of research data sets for analysis. DCAC personnel also assist IDCRP investigators with exploratory data queries to assess research concepts for feasibility.

Over the last six months, the Biostatistics and Data Management team has undergone rapid changes, starting with the hiring of its new Director, Dr. Françoise Seillier-Moiseiwitsch, and a new name, Data Coordination and Analysis Center. The PCC group has grown from one to five (two MS-level biostatisticians, two Ph.D.-level biostatisticians and one senior scientific programmer), with an additional member slated to join early in FY11. This group’s function is to meet the statistical needs of all GID and new HIV/STI studies. The MHRP DCAC has been reorganized with the personnel now formally part of the IDCRP and teams have been formed according to function rather than according to the traditional structure of HIV/STI and GID working groups. The new DCAC consists of the following teams: Oracle (SAMMC), IT Infrastructure and Development (PCC), Data Management (including data entry, Rockville), Data Configuration (Rockville), SAS Programming (Rockville) and Biostatistics (PCC and DAC).

Plans for the new fiscal year include: transition to an IT infrastructure independent from MHRP, migration of studies from the RSS and ClinWorks data management systems to ClinPlus and the deployment of electronic data capture (eCRF’s and web-based questionnaires) to replace paper CRF’s.
The IDCRP General Infectious Diseases (GID) Working Group, now in its fourth year, has seen success in the execution of major multisite efforts, such as the Trauma Infectious Disease Outcomes Study (TIDOS) and the Acute Respiratory Infection Consortium (ARIC), completion of high impact projects, and continued growth of priority initiatives. The GID Working Group has completed and/or initiated 26 active protocols representing a diverse range of research designs including retrospective cohorts, laboratory-based translational studies, prospective observational cohorts, community-based interventional trials, and FDA-regulated randomized controlled trials.

The diversity of research methods is enhanced by the multi-disciplinary nature of the IDCRP network and its partners, where collaborations between Infectious Disease clinicians (adult and pediatric), Preventive Medicine physicians, Microbiologists, Trauma/Orthopedic Surgeons, Epidemiologists, and Statisticians continued to be solidified. GID collaborative projects have brought together research teams at the military treatment facilities (in the US and international), research commands (in the US and international), preventive medicine commands, recruit training commands, Veteran’s Affairs medical centers, industry partners, the CDC, and the NIH.

The continued growth and success of the Working Group has been made possible by the expanding sponsorship and direct financial support of a number of projects through several sources including the NIAID, CDC, US Navy Bureau of Medicine and Surgery (BUMED), DoD Global Emerging Infections Surveillance and Response System (DoD-GEIS), and the US Army Medical Research Materiel Command (USAMRMC-Deployment Related Medical Research Program). Indirect support has also been substantial, as collaborators have leveraged significant resources in support of several projects including US Army Public Health Command (formerly USACHPPM), US Army Institute for Surgical Research (USAISR), Brooke Army Medical Center (BAMC) Department of Clinical Investigation, Nabi Biopharmaceuticals, and GlaxoSmithKline Biologicals.

The GID Working Group portfolio is currently comprised of five research focus areas:

- Trauma-related infections (particularly combat injuries) epidemiology, prevention and management/ Hospital-acquired infections with focus on multidrug-resistant organisms (MDRO) management challenges
- Skin and soft tissue infections (SSTI) epidemiology, prevention and management with focus on community-associated methicillin resistant Staphylococcus aureus (CA-MRSA) infections in military training and operational settings
- Acute respiratory infection epidemiology, prevention and management with focus on pandemic influenza, adenoviruses, and other respiratory pathogens which impact military populations
- Deployment/travel associated infections epidemiology, prevention and management, evidence based support for DoD policy related to ID screening/surveillance/prophylaxis and treatment
- Vaccines of military importance with focus on infections with high impact on military populations (such as S. aureus, respiratory infections, and infections with bioterrorism potential implications)

Current research efforts addressing these priority areas are detailed in the following sections.
Focus Area 1: Trauma related infections (particularly combat injuries) epidemiology, prevention and management/Hospital-acquired infections with focus on MDRO management challenges

The current conflicts combined with ever challenging antimicrobial resistance dramatically emphasize the critical need for ongoing research efforts to improve prevention and management of infections following traumatic injury. Recent advances in battlefield surgical practice and technology, including rapid evacuation, have fortunately led to an increased number of survivors following combat-associated traumatic injuries. Infections are common complications of the many complex poly-trauma cases now seen in military treatment facilities (MTF) and can lead to significant morbidity and mortality. Treatment of these infections, primarily hospital-associated, is clinically challenging, as many are caused by multidrug-resistant organisms (MDRO), and there is a lack of evidence-based recommendations to guide clinicians toward effective treatment and prevention methods. Developing a responsive research portfolio to address these concerns has been the single highest priority for the GID Working Group. Approaching this complex challenge requires a diverse and robust mix of research initiatives that employ various methodologies including prospective and retrospective cohorts, translational studies investigating antibiotic susceptibility, genetic relatedness of microbial pathogens, applied laboratory studies of current surgical management approaches, and reconsideration of once optimal older therapeutic agents as the evolution of antimicrobial resistance continues to limit the options for effective agents.

The “Departments of Defense and Veterans Affairs Multi-center Cohort Study Evaluating Infection-Associated Clinical Outcomes in Hospitalized Medical Evacuees following Traumatic Injury” (IDCRP-024) is at the center of the effort to address these concerns. This multicenter observational cohort study, referred to as TIDOS (Trauma Infectious Disease Outcome Study), is a collaborative effort between several MTFs [Landstuhl Regional Medical Center (LRMC), Walter Reed Army Medical Center (WRAMC), National Naval Medical Center (NNMC), and Brooke Army Medical Center (BAMC)], DoD research commands [US Army Institute for Surgical Research (USAISR), Walter Reed Army Institute of Research (WRAIR)], the Veterans Administration (St. Louis VAMC), and the Uniformed Services University. The US Navy Bureau of Medicine and Surgery (BUMED), through the Wounded Warrior Initiative, have provided funding to support this major initiative. The TIDOS project is the first prospective evaluation of infectious disease complications, risk factors, and long-term outcomes among patients with combat-related traumatic injuries. A notable strength of this study is the use of predefined standardized methodology, combined with a comprehensive evaluation of clinical management, surgical and medical care (i.e. antimicrobial therapy), and clinical microbiology results across various levels of care, medical facilities, and stages of outpatient follow-up.

The TIDOS project officially began enrollment and data collection in June 2009. As of September 2010, clinical data and clinical microbiology isolate collection has been completed on approximately 2000 patients admitted through LRMC, 1100 of whom have been transferred to a participating military hospital in the United States. Over half of these patients (N = 585) have enrolled in the TIDOS cohort. A detailed analysis of the initial 3-month cohort was presented in August 2010 at the premier DoD Trauma Research annual meeting. This analysis documented the common occurrence of infectious complications among all patients, during initial hospitalization at Level IV care in LRMC/Germany (5.9%), and an increasing proportion (24.5%) during Level V care in the United States. Notably, 22% of the study participants were documented to have incident infections following initial US-based
hospitalization. Overall, the most commonly observed infections were wound infections (34.6%), bloodstream infections (17.3%), and osteomyelitis (16.5%). Among the patients documented to have sustained an infectious complication during the hospitalization period, greater than 50% of those individuals experienced two or more infections and 10% had 4 or more infections. Forty percent of the study population had already left the DoD and registered for medical care in the VA. Additional analyses as well as continued enrollment are ongoing to better define risk factors for infection, and to determine optimal methods of prevention and care of infections, particularly focusing on MDRO infections.

To date, the TIDOS project provides the most comprehensive assessment of infectious complications following traumatic injury within the Department of Defense and emphasizes the significant impact of infectious complications on wounded military personnel. In addition to fulfilling the research objectives, the collaborative effort forged with the USAISR has led to the development of the Joint Theater Trauma Registry (JTTR) Infectious Disease supplemental module, a critical tool for combat-related health event/outcome analysis secondary to trauma-related infections during wartime. Moreover, this is the first IDCRP study to initiate successful research collaboration with the Veterans Administration. For participants enrolled in the study, the linkage of DoD and VA medical records will be critical to the long-term evaluation of infectious complications among these injured military personnel.

Infections due to Gram negative multidrug resistant organisms (MDRO) continue to increase, prompting urgent efforts to investigate strategies for diagnosis, therapy, and infection control. IDCRP investigators at BAMC and WRAMC have focused attention on *Acinetobacter baumannii-calcoaceticus* complex (ABC) as well as other MDRO. Troops medevaced from combat areas have had an extraordinarily high incidence of ABC infections that have been acquired as patients move across levels of care. Furthermore, these wound infections have demonstrated serious problems with multidrug resistance. At BAMC, a highly productive study has focused on characterization of ABC antimicrobial susceptibility for a range of old and new therapeutic agents (IDCRP-005). The BAMC team is performing investigations of assay interpretative criteria using established and new diagnostic methods, healthcare related topical biocidal susceptibility, and changes in antibiotic susceptibility patterns over time along with the genetic basis of resistance.

Colistin is an older antibiotic that has been resurrected as an “antibiotic of last resort” in many MDRO infections but is lacking important pharmacokinetics/pharmacodynamics (PK/PD) data that can inform optimized management. To provide clinicians the information they need to most effectively use colistin, a multicenter study (IDCRP-039), led by investigators at the National Naval Medical Center, will start in late 2010. This study, funded through the USAMRMC intramural Deployment Related Medical Research Program, will investigate colistin pharmacokinetic and pharmacodynamic (PK/PD) relationships in patients with Gram negative MDRO serious infections. At WRAMC, additional investigations (IDCRP-027) are underway to assess ABC susceptibility to an aminoglycoside agent licensed in Japan, arbekacin, which has a broad spectrum of activity against many gram-negative and gram-positive bacteria with preliminary data suggesting potential clinical utility against MDR ABC. This effort has now extended to investigate arbekacin in vitro activity against extended spectrum beta-lactamase (ESBL)-producing *Escherichia coli* and *Klebsiella pneumoniae*, AmpC beta-lactamase producing *Enterobacter* species, MDR *Pseudomonas aeruginosa*, and methicillin resistant *Staphylococcus aureus* (MRSA).

Retrospective analysis of existing JTTR data (IDCRP-006) has demonstrated that approximately one third of trauma patients in the initial periods of OIF were affected by infectious complications. Follow-up investigations have built upon this effort to more fully assess infection rates over broader periods of time.
including risk factor analysis. Commencing in late 2010, DoD and VA investigators will launch a multisite retrospective cohort study to focus on a major concern of acute and long-term morbidity, trauma-associated osteomyelitis (IDCRP-044). This large-scale effort is supported though the BUMED Wounded Warrior Initiative. The majority of injuries sustained during OIF/OEF have been orthopedic and are frequently open, complex fractures and prone to infection. The actual number of infectious complications associated with these orthopedic injuries is not known but the serious problem with antimicrobial resistance in these injuries is a widely recognized clinical problem that has required utilization of some older antibiotic regimens.

Focus Area 2: Skin and soft tissue infections (SSTI) epidemiology, prevention and management with focus on community-associated methicillin-resistant Staphylococcus aureus (CAMRSA) infections in military training and operational settings

Staphylococcal infections, most commonly skin and soft tissue infections (SSTI), have been common among active duty military members for decades. The recent global emergence of community-associated methicillin-resistant Staphylococcus aureus (CA-MRSA) has had dramatic impact on military populations, particularly during close-quartered intense training periods. According to a 4-year (2002-2005) US Army Medical Surveillance Monthly Report, there were 181,311 diagnoses of SSTI with an overall incidence rate of 32.4 per 1,000 person years. An increasing proportion of SSTIs in service members are caused by CA-MRSA. The DoD Service components have issued guidelines for the diagnosis, treatment, prevention, and control of SSTI caused by CA-MRSA; however, incidence remains high, evidence-based recommendations have been lacking and effective prevention strategies are sorely needed. The IDCRP has prioritized SSTI (particularly CA-MRSA) prevention as a critical component of the GID research portfolio. A multifactorial prevention approach addressing personal hygiene, educational messages, and environmental cleansing is certainly required; however, adjunctive measures are needed that may include efforts to decolonize S. aureus from reservoir sites on individuals and/or primary prevention through S. aureus vaccination.

The IDCRP’s first randomized controlled trial, conducted within a military training setting, evaluated whether 2% chlorhexidine-impregnated cloths (CHG) could reduce SSTI rates and S. aureus colonization in Marine Corps Officer candidates during 6-10 weeks of training (IDCRP-001). This intervention was not effective in reducing infection rates, prompting ongoing research to determine effective prevention and inform DoD prevention policies. In response to the Centers for Disease Control and Prevention (CDC) Public Health Action Plan to Combat Antimicrobial Resistance, Uniformed Services University, CDC, Ft. Benning, and United States Army Public Health Command (formerly USACHPPM) investigators proposed an evaluation of strategies to prevent methicillin-resistant Staphylococcus aureus (MRSA) skin and soft tissue infections in military trainees at Ft Benning, Georgia. Past DoD surveillance data of SSTI has shown Fort Benning to have the highest rates at Army facilities with nearly 1 in 10 trainees developing an infection. This proposal was selected for 3-year intramural funding through the CDC Office of Antimicrobial Resistance and the study began in May 2010.

The study employs a cluster-randomized trial design to investigate a multi-component hygiene-based intervention on the incidence of MRSA SSTIs. During the 20-month evaluation period, five cycles of platoons (approximately 14 weeks per cycle) will enter and exit training activities. In total, the study population will be comprised of approximately 36,000 trainees observed over a 20-month period yielding high quality evidence to evaluate the intervention as well as to inform DoD prevention policy. To date, the study has been ongoing for 5 months capturing data on SSTIs (over 400 cases assessed this past summer), risk factors, compliance
with interventions, colonization microbiology, and operational/training impact. The deployment of a field trial at this study site paves the way for additional investigations including point-of-care diagnostics, SSTI natural history and immune responses, and cost-effectiveness analysis for military-specific prevention strategies.

Prevention of CA-MRSA requires a multi-pronged strategy. As in many infectious diseases, vaccination is often a critical component of the overall control effort. Currently no licensed vaccine is available; however, there is strong supporting evidence for one vaccine candidate which has been under development by Nabi Biopharmaceuticals for several years, a pentavalent vaccine composed of both conjugated capsular polysaccharides and recombinant toxoids. In 2009, the IDCRP-USU, along with the Henry M. Jackson Foundation, entered into a Cooperative Research and Development Agreement (CRADA) with Nabi in order to conduct a series of clinical trials leading to a ‘proof of concept’ of the vaccine’s efficacy in the target population, military trainees. Later that year, Nabi Biopharmaceuticals announced the sale of their S. aureus vaccine candidate to GlaxoSmithKline PLC (GSK). IDCRP has now partnered with GSK to ensure an effective transition as GSK advances the clinical development of the vaccine with a continued focus on prevention of SSTI in military and civilian populations.

The Nabi PentaStaph™ product (Pentavalent S. aureus Vaccine) is a five-component vaccine. Three of the antigen components induce antibodies that target S. aureus capsular polysaccharides Types 5, 8 and the cell wall antigen Type 336, which enhance the immune system’s ability to clear bacteria from the host. Types 5 & 8 capsular polysaccharides are expressed in approximately 80 percent of S. aureus strains, including many of the known MRSA strains. Type 336 polysaccharide accounts for approximately 20 percent of S. aureus infections that do not form a polysaccharide capsule in the human bloodstream. Two additional antigen components induce antibodies that target two of the most predominant and virulent toxins produced by the bacteria, which can significantly debilitate the human immune system: Panton-Valentine Leukocidin found predominantly in community-acquired MRSA, and alpha toxin, produced by almost all S. aureus isolates. This multi-target approach, which enhances the immune system’s ability to eliminate a broad spectrum of S. aureus strains and neutralizes the bacterial defenses of the most virulent strains, has been demonstrated in pre-clinical models to provide optimal efficacy, which is hoped would translate into human efficacy.

The first clinical trial of pentavalent S. aureus vaccine (IDCRP-035) received funding in 2009 through the Department of Defense Deployment Related Medical Research Program (DRMRP) of the Office of the Congressionally Directed Medical Research Programs (CDMRP). This study, performed at two clinical sites – Brooke Army Medical Center in San Antonio, TX and Naval Medical Center in Portsmouth, VA, successfully completed all enrollment and vaccination across the complete planned dose-range. In addition, the study investigated both the monovalent products (the S. aureus toxoids, rAT and rLukS-PV), a bivalent combination across the dose-range, and a booster dose. Currently, the study is in the final post-vaccination follow-up phase with immunology testing underway. Results of this first-in-human investigation are anticipated in the first half of 2011 providing needed information for continued clinical vaccine development.

Focus Area 3: Acute respiratory infection epidemiology, prevention and management with focus on pandemic influenza, adenoviruses, and other respiratory pathogens which impact military populations

Acute respiratory infections (ARI) remain a significant threat and burden to the health of military forces worldwide. Conducting studies of the epidemiology, treatment and prevention of ARI has been a high priority mission of the IDCRP. The emergence in 2009 of a novel influenza A virus (H1N1), and its rapid ascension to pandemic status, highlighted the tremendous impact of ARI, particularly influenza, on military as well as on civilian populations. Moreover, the H1N1 pandemic
revealed major gaps in current knowledge of influenza epidemiology, and further underscored the importance of effective strategies for its prevention and control.

For IDCRP, the evolution and rise of pandemic H1N1 was a major catalyst in the formation of a multi-site, multi-disciplinary research effort, termed the Acute Respiratory Infection Consortium (ARIC). With support from the NIAID as well as the DoD-Global Emerging Infections Surveillance and Response System (DoD-GEIS) program, the ARIC established a clinical research core for ARI at five military treatment facilities across the US, and strengthened existing ties with IDCRP-collaborating institutions, particularly the Naval Health Research Center (NHRC). While a number of other DoD institutions (e.g., US Air Force School of Aerospace Medicine, Walter Reed Army Institute of Research, overseas laboratories) have long been engaged in ARI surveillance and prevention research, IDCRP provides a unique contribution to the DoD mission through a number of studies of ARI with epidemiologic, microbiologic and immunologic measures.

At the core of the ARIC is an observational, longitudinal Natural History Study (IDCRP-045) of acute respiratory infection among military members and their dependants. Subject recruitment (both adults and children) is ongoing in both inpatient and outpatient settings of five, geographically representative military treatment facilities in the continental US. In addition to the primary objectives – to determine the etiology and immunology of ARI in this population – this study will also provide a critical foundation of clinical knowledge onto which future, within-network ARI intervention and prevention trials can be based. Through this study, we continue to build a specimen repository for future clinical and laboratory investigation which will ultimately strengthen a rapidly responsive, multi-centered network for future research.

In addition to its support and execution of the core Natural History Study, the ARIC is utilizing innovative methods in ARI research. A major challenge in the evaluation of therapeutic interventions for influenza has been the lack of standardized measures to characterize disease severity. In collaboration with investigators from the NIAID, the consortium initiated a study of patient-reported outcomes for influenza (Flu-PRO; IDCRP-045-01), which aims to develop and validate disease severity measures using information garnered through patient interviews. Through this study, advances are also being made in the clinical microbiology setting. Key to the success of ARIC research in the epidemiology and clinical aspects of ARI is an ongoing collaboration with the NHRC, an institution widely recognized for their expertise in novel viral diagnostic methods.

A multi-site network such as the ARIC can also be utilized for the execution of retrospective studies. The establishment of this large, geographically diverse clinical research network during an influenza pandemic afforded a unique opportunity to study the epidemiology and clinical characteristics of influenza A (H1N1) infection in a US population (IDCRP-058). One of the major objectives of this study is to determine host risk factors for severe (i.e., requiring hospitalization) influenza. Findings from this study may ultimately contribute to the development of treatment and prevention measures in the future.

Having a cadre of ARIC research personnel at various military treatment facilities has facilitated the consortium’s participation in multi-center protocols, specifically in the area of novel treatments for severe influenza. Investigators at the Naval Medical Research Center, working closely with a parallel effort at NIAID, launched a pilot study for collection of anti-Influenza A H1N1 (Swine Flu) hyperimmune plasma (IDCRP-046). A protocol investigating the efficacy of hyperimmune plasma (IDCRP-062) for the treatment of severe influenza infection is currently under regulatory review at participating clinical sites. In an era of increasing antiviral resistance, treatment options for patients with severe influenza are an ongoing concern. To this end, the consortium continues to explore the potential use of triple combination antiviral therapy through a
protocol initiated by Adamas Pharmaceuticals. Finally, as the consortium continues to evolve and grow, it is anticipated that additional treatment protocols will emerge, and the consortium will be well-positioned to participate in these interventional trials.

It is well known that immunocompromised individuals are at increased risk for morbidity and mortality from ARI. A study of the immunogenicity and effectiveness of H1N1 vaccine among immunocompetent vs. HIV infected subjects (*IDCRP-053*) was initiated in late 2009 and published in mid-2010. The accelerated timeline of this study and the publication of its findings highlights the strength and capability of this network and how it has already contributed to the advancements of knowledge of novel infectious pathogens, their treatment and prevention.

Lastly, the IDCRP has maintained an ongoing ARI research collaboration with the US Navy overseas laboratories. With support from the Centers for Disease Control and Prevention, the consortium executed a protocol entitled ‘Research and Public Health Practice on Influenza and other respiratory infectious diseases in the Middle East, Southeast Asia, and South American regions’. This large-scale effort will continue to broaden existing population-based investigations on influenza and other respiratory pathogens.

**Focus Area 4: Deployment/travel associated infections epidemiology, prevention and management/ Evidence-based support for DoD policy related to ID screening/surveillance**

Infectious disease threats to the military are often considered to be battle injury-related (*Focus Area 1*) or a component of ‘disease and non-battle injury’ or DNBI. The infections threatening the military occur while stationed in garrison in the continental US (CONUS) and frequently occur at levels far exceeding civilian counterparts (as in *Focus Area 2*, CA-MRSA or *Focus Area 3*, ARI) or, occur during overseas deployment. ID threats during military deployments have had dramatic effects throughout history and continue to impact modern militaries. These threats include extremely common ailments with predominantly short-term morbidity such as infectious diarrhea and acute respiratory infections, as well as less common but potentially fatal illnesses associated with fever such as malaria, dengue or rickettsial disease. The IDCRP’s CONUS-based tertiary care medical centers are frequently involved with the pre-deployment or pre-travel evaluation and management to prevent these infections as well as the evaluation and care of beneficiaries returning with infections acquired while abroad. This research focus area encourages investigator-initiated efforts to address investigations of priority infectious disease threats impacting military operations, particularly during or following deployment, generating necessary evidence for prevention and/or therapeutic strategies that support DoD policy.

The “Deployment and Travel Related Infectious Disease Risk Assessment, Outcomes, and Prevention Strategies among Department of Defense Beneficiaries (TRAVMIL)” (*IDCRP-037*) is a major new IDCRP initiative that started in December 2009 at the lead site, the Naval Medical Center Portsmouth, Portsmouth, VA. This multisite project is building a DoD Travel Medicine Research Consortium for the long-term study of traveland deployment-related infectious disease threats. TRAVMIL studies the epidemiology of these infections and evaluates current and new risk reduction and self-treatment strategies with regard to compliance, efficacy, cost-effectiveness, and side effect profile. A key component of the study will be assessing the utility of molecular diagnostics of stool, blood, and oropharyngeal samples, collected during travel by participants themselves, to determine the etiology of travel/deployment illness. Demonstrating the efficacy of testing in this manner will yield an important tool for assessing illness in forward deployed troops without access to advanced laboratories as well as develop a platform for prevention and treatment product testing in support of licensure. Ultimately, information gained from this study will be used to improve the quality of care given in DoD travel medicine clinics, to eliminate
ineffective interventions, and to provide region-specific infectious disease threat assessment for the DoD.

The study focuses on four key infectious diseases areas: traveler’s diarrhea, malaria, febrile illness, and influenza-like illness (ILI) using a combination of clinical data and laboratory testing. Clinical information will be obtained from participants using pre-travel surveys, travel diaries, a post-travel survey, and extended follow-up information. A retrospective component will allow investigators to enroll ill returning travelers who were not seen in travel clinics before travel or did not enroll in the cohort study. The study has drawn together an impressive collaboration including investigators at the Naval Medical Center Portsmouth (NMCP), Naval Medical Center San Diego (NMCSD), National Naval Medical Center (NNMC), Bethesda, MD, Naval Medical Research Center (NMRC), Naval Environmental and Preventive Medicine Unit-2 (NEPMU-2), Norfolk, VA, Brooke Army Medical Center in San Antonio, TX, and the Uniformed Services University. In addition to the four key infectious disease areas, the study creates a repository of clinical specimens linked to exposure and disease outcome for future studies of the development and validation of biomarkers, identification of novel pathogens, or performance of host genetic susceptibility to travel-related infectious diseases. Lastly, the study will provide a descriptive analysis of noninfectious health risks that affect travelers such as injuries due to driving accidents and recreational activities.

As of September 2010, approximately 180 travelers have been enrolled and the study has expanded to include NMCSD with NNMC coming onboard in 2011. Progress has been excellent with approximately 50% of individuals approached agreeing to enroll as well as high compliance rates for illness diaries and self collected stool cards. The study allows for both individual and group travel (i.e. shipboard deployments, humanitarian assistance missions, tropical medicine military students participating in overseas training, etc.). Procedural modifications have also enhanced potential for enrollment beyond the walls of the MTF travel clinic to permit involvement of greater numbers of deploying military personnel. The past year has also seen the development of a research lab with the NMCP Department of Clinical Investigation facilities directly to support the TravMil as well as the ARIC initiatives with multiplex PCR assay technology and enteric disease serology.

Tuberculosis (TB) is an uncommon ID threat to the military; however, the acute and chronic implications of TB, as well as, military-specific considerations, such as shipboard exposure potential and humanitarian relief among populations with hyperendemic levels of TB, heighten the requirement for effective TB prevention strategies within the DoD. TB prevention in the DoD is grounded in exposure screening at two pivotal time points: accession and deployment-related. The foundation of the current strategy to prevent tuberculosis in the US military is universal skin testing for latent tuberculosis infection (LTBI), beginning at accession. Testing for LTBI in the US has shifted to targeted testing of only persons at high risk; however, the military’s policy of universal testing for LTBI has resulted in a large volume of testing (> 250,000 TB skin tests at accession with >20,000 treated each year with concerns of potentially high false positive tests in this predominantly low-risk population). A well-designed investigation is critically needed and was called for by the Armed Forces Epidemiological Board AFEB (now the Defense Health Board) to inform DoD policy and revise the military TB screening program. Uniformed Services University investigators (led by LTC James Mancuso as a major component of his doctoral thesis), in collaboration with investigators at Ft. Jackson, South Carolina completed a study (IDCRP-021) to specifically address this major concern.

This study received funding support through the US Army Public Health Command (formerly USACHPPM) leveraging IDCRP resources. The study successfully enrolled 2000 recruits in a span of three months. This effort represents one of the most comprehensive evaluations of a TB screening program, military or
civilian, by comparing skin tests, standard TB skin test and the Battey skin test (PPD-B) to assess sensitization to non-tuberculous mycobacteria (NTM), both commercially-available interferon gamma release assays (IGRAs), and risk factor questionnaires. The investigators concluded that targeted testing of a heterogeneous population (the DoD accession population) is feasible with acceptable sensitivity and specificity using the standard TB skin test or either IGRA assay. Cost-effectiveness analysis demonstrated that targeted testing in this population would significantly increase the efficiency of the DoD TB screening program and reduce false positives avoiding referrals for unnecessary treatment and potential for adverse medication reactions among low-risk individuals while still maintaining an acceptable level of effectiveness. The data from this study will provide the basis for a formal recommendation to inform a change in current Army policy.

Focus Area 5: Vaccines of military importance with focus on infections with high impact on military populations (such as S. aureus, respiratory infections, and infections with bioterrorism potential implications)

Vaccination is central to the control and prevention of infectious diseases in both military and civilian populations. The US Military Infectious Disease Research Program leads several critical research and development efforts within the DoD to address prevention strategies for many ID threats. The IDCRP has prioritized a role in partnering, when appropriate, with other DoD and NIAID vaccine clinical development efforts. As discussed in the preceding section, S. aureus clinical vaccine development is a scenario where there is no major research and development effort within the DoD despite a significant and recurrent impact from CA-MRSA SSTI. Under this circumstance, the IDCRP provides a major contribution to the overall DoD infectious disease research portfolio filling an unmet research need, as recognized by the funding support awarded by the Department of Defense Deployment Related Medical Research Program (DRMRP).

In addition to investigation of vaccines for endemic infections, the DoD and the NIAID Vaccine Research Center (VRC) actively investigates preventative measures for Category “A” Bioterrorism Agents, which are defined as: “...organisms that pose a risk to national security,” based on ease of dissemination, person-to-person transmission, high case fatality rates, and potential for major public health impact/public panic/social disruption with requirement for special public health preparedness action. Agents causing viral hemorrhagic fevers, including Ebola and Marburg viruses, fall under this classification and are prioritized for vaccine development. Ebola and Marburg infections are diseases of military importance related to possible projection of United States and allied forces into endemic areas. Hemorrhagic fevers have disrupted combat and training operations in the Balkans, Korea and the South Pacific. Hence, the DoD has actively supported research into preventative measures for Ebola and other Hemorrhagic fevers. At present, there is no effective treatment and no licensed vaccines for Ebola or Marburg.

Based upon the collaborative relationships developed between the VRC and military investigators, the opportunity arose to evaluate the safety and immunogenicity of an Ebola DNA and a Marburg DNA Vaccine in healthy adults in a Walter Reed Army Institute of Research (WRAIR) collaborative field site at Makerere University in Kampala, Uganda (IDCRP-022). This study successfully completed all enrollments and vaccination for both recombinant deoxyribonucleic acid (DNA) vaccines against Ebola virus and Marburg virus infections as well as the concomitant administration of both candidate vaccines in the past year. Longitudinal safety monitoring and immunological analysis are ongoing with initial results expected in the upcoming year.
The IDCRP was created to reproduce the success of the DoD investigators at the major Military Treatment Facilities (MTFs) studying HIV in the U.S. military since the early 1980’s. Formerly a long-standing component of the Military HIV Research Program (MHRP), the Working Group (WG) arose in the Division of Retrovirology at the Walter Reed Army Institute of Research, previous home to the U.S. Military HIV Natural History Study (HIV NHS, IDCRP-000) for twenty years following its inception in 1986. In 2002, a consortium was developed (Tri-service AIDS Clinical Consortium, TACC) through an interagency agreement between the Division of Clinical Research at NIAID and the military centers conducting the HIV NHS. In 2006 this consortium moved its headquarters to USU to help establish the IDCRP and became the IDCRP HIV/STI WG. In part, the purpose of this group was to provide a forum for DoD experts in clinical HIV care and research to prioritize efforts to improve the quality of clinical HIV research within the military and to act as long-term stewards of the valuable collection of samples and data represented in the HIV NHS. Since that time, the Working Group has grown and expanded its scope, becoming increasingly productive with a range of protocols including prospective and retrospective observational cohort studies, interventional studies and randomized controlled trials. The WG is widely collaborative with many academic researchers as well as several organizational partners including MHRP, the Armed Forces Health Surveillance Center (AFHSC), and the International Network for Strategic Initiatives in Global HIV Trials (INSIGHT).

2010 has been an exciting year for the HIV/STI Working Group with continued growth and productivity. The focus of the WG this year has been continuing to increase the impact of our work both within the DoD and in the scientific community. Three notable accomplishments this year include the use of data and analyses from our HIV NHS cohort in the Institute of Medicine report to the U.S. Social Security Administration regarding updating the HIV disability listings. The DoD HIV cohort was the only single cohort with mortality data cited in the report and our analyses clearly helped show that today HIV is not the same disease it was in the early 1990’s; however, low CD4 counts remain a serious concern, markedly affecting prognosis. This report will help shape outcomes at a U.S. national level regarding the benefits delivered to those with HIV infection. The WG has also impacted the DoD this year in collaboration with the AFHSC through a featured Medical Surveillance Monthly Report article on the epidemiology of sexually transmitted infections among active duty service members. This effort was requested by the DoD HIV/STI Prevention Working Group, a collaborative body originated and supported by the IDCRP HIV/STI WG, which includes over twenty DoD and federal organizations, and will serve as important baseline information for a number of HIV/STI surveillance and prevention efforts going forward. Finally, (IDCRP-056) a study comparing the efficacy of conjugate pneumococcal vaccine in HIV infected patients and the first prospective randomized clinical trial to be conducted by the IDCRP HIV/STI WG, was successfully published this year.
in *The Journal of Infectious Diseases* with two follow-on manuscripts submitted. This work demonstrated no benefit to using conjugate vaccine instead of standard polysaccharide vaccine to boost immunity to pneumococcal infection in HIV-infected patients, answering an important question and showing the need for improved immunization strategies.

In 2009, the research focus of the program was broadened from HIV alone to also include other sexually transmitted infections (STI). STI are a significant issue for active duty troops as well as beneficiaries and studying these within the military population presents a unique opportunity to advance science and clinical practice. This change also opened the door to Prevention, which has been brought into the research program as a Focus Area and also meets a NIAID Strategic Priority. With shared risks of transmission, efforts directed toward STI Prevention will benefit HIV Prevention and will be more visible due to the much higher numbers of people affected. Again, prevention-related investigation within the DoD builds on a unique opportunity, presenting the chance to enhance military public health and to add meaningfully to the broader scientific knowledge base.

While these changes are important to shape the HIV/STI Working Group for the future, it has been similarly important to maintain and strengthen the current highly productive research areas that have been the focus of the program over the past several years. For example, the HIV Natural History Study continues to develop and this year has been significantly improved through the addition of comprehensive pharmacy data electronically captured from the Tricare Management Authority for all subjects from 2001 to present and forward. Further, in just this past year the WG has produced 36 manuscripts (21 published, 4 accepted, and 11 more submitted) as well as 17 national/international meeting presentations. The list of journals publishing our research this year has included *Nature Medicine, Blood, Clinical Infectious Diseases, The Journal of Infectious Diseases, PLoS ONE, AIDS, JAIDS,* and many others. We continue to have a variety of prospective clinical trials and observational studies as well as a strong series of HIV NHS substudies demonstrating the value of the HIV Natural History Study. One measure of the importance and impact of these substudies is the large number of external collaborators participating as co-investigators (31 investigators from 19 institutions) as well as $1,396,687 contributed by these investigators (leveraged) toward the accomplishment of IDCRP HIV/STI science.

This year again promises to be productive for the Working Group as several studies will reach completion and many analyses and resultant manuscripts are already planned and ongoing. We will also continue to develop our STI research program including working collaboratively to develop an international network of sites to study the epidemiology and risk factors for sexually transmitted infections, to evaluate the rates and risk factors for antimicrobial resistance among these pathogens, to test point of care diagnostics both in garrison as well as in field settings, and to deploy and evaluate prevention-related interventions. The transition of data management and statistical capabilities from external to ‘in house’ may affect our operations in the short term, but should result in increased efficiency in coming years. The planned rebalancing of the IDCRP research portfolio as the GID side of the program grows is ongoing and continues to provide incentive to take our work to the next level in seeking external funding. Already, applications have been submitted to the Doris Duke Charitable Foundation and the National Institute of Mental Health (R01), with others to the National Institute of Allergy and Infectious Disease and the DoD Global Emerging Infections Surveillance and Response System planned for early 2011. In all of this, we will continue to seek new and expand existing research collaborations and to foster the career development of our active duty and civilian investigators.

What follows is a brief description of the IDCRP HIV/STI research portfolio by our five major focus areas.
Focus Area 1: Natural history of HIV infection in active duty, military beneficiaries, and other relevant populations

With nearly 25 years of longitudinal data and specimens from over 5000 HIV-infected DoD beneficiaries, the U.S. Military HIV Natural History Study (IDCRP-000) remains the cornerstone of HIV research and productivity within the Working Group. Benefiting from the unique racial/ancestral balance of the cohort (approx 45% European American, 45% African American, 8% Hispanic) as well as a setting with open access to healthcare, free medications, generally stable income, very low injection drug use, and a high level of education, this resource allows the program to address goals including 1) improving outcomes through understanding of factors associated with HIV infection and its treatment as well as complications of these, 2) understanding the safety and efficacy of non-HIV vaccine strategies important to the HIV-infected military and other relevant populations, and 3) understanding factors associated with HIV co-infections including STI and bidirectional effects on disease manifestations and progression. We are in the process of reviewing and revising the specific aims of this important protocol in order to maximize its relevance and long term value.

A number of studies are being conducted to provide a better understanding of HIV and its consequences in the military setting with early diagnosis and care as well as modern antiretroviral therapy. Some of these have investigated questions such as, is HIV becoming more virulent (IDCRP-000-12)? Others have described the population of HIV-infected subjects who are spontaneously able to control the HIV virus and/or who have long periods without progression of disease (IDCRP-000-05) as well as their response to treatment once it is needed. Further studies are underway to investigate host factors related to viral control and long term non-progression. A series of investigations to understand malignancies either directly or indirectly associated with HIV (IDCRP-014, -000-04, -000-09) have been very successful, showing that several cancers are more common among HIV seropositive individuals (prostate, anal, and Hodgkin’s disease) and that non-AIDS defining cancer rates (primarily skin cancers in European Americans) are rising in this group as well. Additional factors related to HIV progression are being studied including various co-infections (IDCRP-003, -000-07, -000-27, -000-29). Predictors and outcomes of highly active antiretroviral therapy (HAART) are likewise being carefully examined including trajectory of viral load decline after HAART initiation (IDCRP-000-03), CD4 and CD8 counts (IDCRP-000-14, -000-19), hepatitis B co-infection (IDCRP-000-28), adherence (in development), and others. In collaboration with the NIAID, an international study investigating the development of immune reconstitution inflammatory syndrome (IRIS), a serious complication associated with initiation of antiretroviral therapy, (IDCRP-008) in those starting HAART with CD4<100 is underway in Kenya with planned expansion this year to Thailand. Complications of HIV itself are also being aggressively studied including neurocognitive disorders (IDCRP-016), renal dysfunction (IDCRP-052 and -000-17), liver disease (IDCRP-050), and coronary artery disease (IDCRP-018).

Recent investigations have capitalized on the NHS to answer important questions about HIV and HAART outcomes without socioeconomic confounding faced by other observational cohorts. As an example, three IDCRP studies, two current and one prior, address an ongoing controversy about the effects of race/ethnicity on HIV treatment and outcomes—Factors Associated with Initiation of HAART in a Military HIV cohort (IDCRP-000-13), CD4+ Count at Initiation of HAART and Response to Therapy (IDCRP-000-14), and Effectiveness of Highly-Active Antiretroviral Therapy by Race (closed), convincingly demonstrating that HAART provision and outcomes are equivalent by race/ethnicity in the DoD care setting. Other ongoing work seeks to understand vaccine strategies to prevent HIV co-infections including pneumococcus as well as hepatitis B. An over-arching protocol entitled, The Clinical Effectiveness of Hepatitis B Vaccination in HIV Positive Patients (IDCRP-000-27), has included Predictors of Hepatitis B Vaccine Response and HBV Immunization Prior to
HIV diagnosis and Risk of Subsequent HBV Infection. These studies for the first time validated the use of surface antibody titer as a correlate of protection in HIV-infected individuals. In addition, these studies demonstrated that while HBV immunization before HIV infection is strongly protective, surprisingly, vaccination is not protective against hepatitis B overall if given after HIV infection. Optimization of factors associated with response including use of HAART, a CD4 count >350, and an undetectable viral load may allow development of protective immunity. It is concerning that failure to respond to hepatitis B vaccine given after HIV infection is associated with markedly increased risk of chronic hepatitis B infection. New national CDC guidelines are in draft and our findings are likely to be incorporated.

Focus Area 2: HIV/STI prevention in the DoD: understanding HIV/STI risks and how to target prevention interventions in military settings and operational environments

The IDCRP HIV/STI Working Group expanded its portfolio in 2009 to include a focus on Prevention, meeting both a NIAID strategic priority and a call by the CDC for increased attention to prevention, given that proven prevention efforts exist and HIV/STI incidence continues to remain unchanged. The IDCRP organized and has continued to support the DoD HIV/STI Prevention Working Group which includes representation from twenty organizations in three military services as well as Health Affairs and NIAID; multiple disciplines such as preventive medicine, public health and infectious diseases; and perspectives including surveillance, clinical care, research, programs, and policy. This Working Group continues to meet quarterly and has a number of developing initiatives.

The IDCRP goal within this focus area is to inform and positively impact DoD HIV/STI prevention policy and programs through research, data, and communication of these to DoD leadership. While prevention efforts already exist in the DoD, HIV and STI surveillance, prevention and treatment efforts have often been addressed in different silos, despite similarities in risk behaviors. Bridging this gap can result in more robust collaborations and more powerful research studies with broader impact.

One research objective is to understand the prevalence, incidence, and risk factors for incident HIV/STI and changes of these over time, using existing DoD databases and surveillance data. The 20 year epidemiology of Hepatitis B in the U.S. Military HIV Natural History Study (IDCRP-000-27) has already been described and published, and we are currently in the process of submitting a manuscript describing the epidemiology of syphilis in the same cohort (IDCRP-000-30). Similar analyses are in process related to Chlamydia and Gonorrhea. These analyses will be consolidated within the broader protocol (Sexually transmitted infections (STIs) in the HIV Natural History Study, an RV168 substudy, IDCRP-000-26) to support and inform strategies to identify and target individuals at risk for incident HIV/STI.

Another objective is focused on assessing behavioral, environmental, and other currently unmeasured risk factors for incident HIV/STI in active duty members and beneficiaries, since it is challenging to accurately target prevention interventions in the DoD setting due to a lack of information about behavioral risk factors for incident STI/HIV.

Finally, new well-targeted prevention programs are needed. The Working Group has submitted its first NIH R01 application in this area which seeks to meet the Navy requirement of successfully implementing proven STI prevention measures among HIV-infected service members. If funded,
work carried out under this grant will broadly inform implementation of such proven measures across a variety of domains and settings within the DoD. Future protocols are planned to include conducting HIV/STI prevention trials with both HIV seropositive and at-risk individuals, and studying the effectiveness of current DoD HIV/STI prevention programs.

Focus Area 3: Understanding immunopathogenesis, host (e.g. genetic), and pathogen-related factors and host-pathogen interactions affecting military clinical care and outcomes of HIV and STI infections

Because of the nature of the DoD population, including racial balance, relatively stable income, high level of education, minimal drug abuse, and open access to healthcare with free medications, many of the socioeconomic confounders that have plagued genetic association and other host factor studies in other cohorts are minimized in this setting.

This uniqueness has been effectively utilized by our investigators to develop collaborations with leading investigators in the areas of genetics, pharmacogenetics, and host immunity from groups including the Center for HIV/AIDS Vaccine Initiatives, the University of Texas Health Sciences Center, Vanderbilt University, the Harvard Broad Institute and many others to address the goal of improving HIV outcomes through understanding host factors associated with HIV infection and treatment as well as complications of these. Ongoing studies are answering important questions related to host genetic determinants of HIV acquisition and progression (IDCRP-054, -000-05, -000-08), HAART response and outcomes (IDCRP-000-18), and the development of cancers as a complication of HIV infection (IDCRP-000-09). Others are studying immune aspects of HIV including assessment of T-cell subsets and their association with progression (IDCRP-000-02), vaccine response in relationship to HIV outcomes (IDCRP-000-27), as well as neutralizing antibody responses in long-term nonprogressors (in development). The ultimate goal of all of these studies is to use the unique setting and strengths of the military to translate basic science research into clinical findings and to incorporate this into the care of individual patients and preventive measures to benefit population health.

Focus Area 4: Improving outcomes of DoD beneficiaries through evidence-based medicine for HIV/STI prevention, diagnosis, care and treatment emphasizing the use of data from Focus Areas 1, 2, and 3

The formation of the IDCRP allowed expansion of the scope of the HIV Working Group to include sexually transmitted infections (STI) and from running an observational HIV cohort study to also conducting randomized treatment and other interventional trials. Our goals within this area include 1) improving the ability to detect and diagnose HIV and STI in the clinical setting 2) optimizing the safety and efficacy of non-HIV vaccine strategies, 3) testing, validating, and optimizing the safety and efficacy of STI-preventive vaccine strategies, 4) testing approved and novel agents and strategies that modify the effects of HIV infection, and 5) testing approved and novel agents and strategies to prevent the development of AIDS-defining and serious non-AIDS defining conditions.
The first IDCRP HIV randomized clinical trial, *An Open-Label Randomized Study of Pneumococcal Conjugate Vaccination in HIV in Comparison to Polysaccharide Vaccine Boosting in Previously Vaccinated Patients (IDCRP-056)*, has been successfully published this year. Importantly, this investigation demonstrated that boosting of immunity to *Streptococcus pneumoniae* through re-vaccination remains challenging and that the new conjugate vaccine (Prevnar) offered no benefit over the previous polysaccharide vaccine (Pneumovax). Further investigation of the correlates of protection and strategies to elicit protection are ongoing with a manuscript recently accepted.

In an effort to describe and mitigate the consequences of co-infection with HIV and *Staphylococcus aureus*, another WG protocol being conducted at four sites, *Staphylococcus Aureus Infections and a Randomized Double-Blind Study on Decolonization Procedures for Prevention of MRSA Infections Among HIV-Infected Persons (IDCRP-003)*, has completed enrollment of the observational cohort (n=550) and is nearing full enrollment of the randomized trial.

With the emergence of H1N1 influenza worldwide, the IDCRP rapidly responded with several protocols conducted through the General Infectious Disease (GID) Working Group. In a joint effort to understand the response to and protection from the H1N1 vaccine, the GID and HIV/STI WG combined to support the development, approval, execution, and completion of a new study (IDCRP-053) in less than four months comparing the response to H1N1 vaccine in HIV-infected versus uninfected individuals and outcomes of this. Data from this investigation were rapidly compiled and analyzed and resulted in acceptance of the primary manuscript for publication in *Clinical Infectious Disease* just ten months after the study was first conceived.

Another collaborative HIV-related trial includes, *A study to assess the practicality and potential utility of the RDI’s computational modeling as an aid to antiretroviral treatment selection in clinical practice (IDCRP-000-15)*, a collaboration with the NIAID and the Resistance Database Initiative (RDI) evaluating the acceptance and impact of a computerized, neural network model to help predict the best HAART regimen in the setting of viral resistance. With the primary manuscript from this effort recently accepted to JAIDS the RDI has released the newest version of its publicly available software (www.hivrdi.org).

Future directions within this focus area will include testing the value of combining genetic, immune, and other factors to predict an individual’s risk of adverse outcomes and the application of strategies to prevent these; seeking opportunities to contribute to STI point of care diagnostics; and vaccine development through clinical trials.

**Focus Area 5: Informing and positively impacting DoD HIV/STI policy and programs through research, data, and communication of these to leadership**

The ultimate goal of research conducted in the IDCRP HIV/STI Working Group is not only to help individual patients, but to have a broader DoD public health impact by producing needed and useful data that inform leadership, are incorporated into policy, and result in program benefits through the spectrum of prevention, care, and treatment. This focus is carried throughout the work described above. Additionally, we are pursuing specific goals including to 1) promote a positive environment and culture change through increased leadership awareness and understanding of the importance of HIV/STI in the DoD and 2) understand the effects of changes in HIV/STI-related policies and programs on rates of HIV/STI infections and outcomes. One initiative that could impact policies is a planned survey of military clinicians related to their attitudes, facilitators and barriers to existing military sexual health related policies and the potential impact on clinician practices if policies were to change. Findings from this study could provide justification for additional training and support for clinicians. Another protocol that has immediate policy implications is the recently submitted NIH R-01 application, "HIV Prevention in the Military: An Implementation Study for HIV+ Individuals". In addition to identifying factors associated with successful implementation of an intervention for HIV seropositive active duty members, one of the specific aims is to generalize our findings into the development of evidence-based implementation guidelines for interventions within military clinic settings. One of the outcomes of this proposal will be to submit the evidence-based implementation guidelines to the Clinical Proponency Steering Committee, a DoD body that makes tri-service policy recommendations across disease issues.
## IDCRP Protocols

<table>
<thead>
<tr>
<th>IDCRP #</th>
<th>Protocol Title</th>
<th>PI</th>
<th>IDCRP Sites</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>IDCRP-000</td>
<td>Natural History Study of HIV (RV168)</td>
<td>Agan</td>
<td>NMCP, NMCSD, NNMC, SAMMC, TAMC, WRAMC</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-001</td>
<td>MRSA Chlorhexidine RCT at MCB Quantico</td>
<td>Whitman</td>
<td>Marine Corps Base Quantico</td>
<td>Fully Enrolled</td>
</tr>
<tr>
<td>IDCRP-003</td>
<td>MRSA Skin Infections in HIV (RV210)</td>
<td>Crum-Cianflone/ Bavaro</td>
<td>NMCP, NMCSD, WRAMC, SAMMC</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-004</td>
<td>Antifungals PK in Burn Patients</td>
<td>Hospenthal</td>
<td>SAMMC</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-005</td>
<td>Drug Resistant Acinetobacter Antibiotic Susceptibility</td>
<td>Akers</td>
<td>SAMMC</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-006</td>
<td>Non-Extremity Infections in Combat (retrospective cohort)</td>
<td>Murray</td>
<td>SAMMC</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-007</td>
<td>GNR MDRO Colonization Natural History in Hospitalized Patients</td>
<td>Wortmann</td>
<td>WRAMC</td>
<td>Fully Enrolled</td>
</tr>
<tr>
<td>IDCRP-008</td>
<td>Obs. Study of Immune Reconstitution Inflammatory Syndrome (IRIS) in HIV</td>
<td>Shaffer/ Sawe/ Sereti</td>
<td>NIAID, USAMRU-K</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-010</td>
<td>Multinational Acinetobacter Bacteremia (retrospective analysis)</td>
<td>Waterman</td>
<td>WRAMC</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-011</td>
<td>Colistin Beads in Orthopedic Injuries</td>
<td>Waterman</td>
<td>WRAMC</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-013</td>
<td>Ventilator Associated Pneumonia (VAP) (retrospective study)</td>
<td>Brett-Major</td>
<td>NNMC, WRAMC</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-015</td>
<td>Atorvastatin effects on VL and Immune Activation in HIV</td>
<td>Ganesan</td>
<td>NMCSD, NNMC, NIAID</td>
<td>Fully Enrolled</td>
</tr>
<tr>
<td>IDCRP-016</td>
<td>Neurocognitive Changes in HIV</td>
<td>Hale/ Crum-Cianflone</td>
<td>NMCSD, NNMC, SAMMC, WRAMC</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-018</td>
<td>Cardiac disease and liver steatosis in HIV</td>
<td>Crum-Cianflone/ Bavaro</td>
<td>NMCSD</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-021</td>
<td>Latent TB Screening in the DoD</td>
<td>Mancuso</td>
<td>Ft. Jackson</td>
<td>Fully Enrolled</td>
</tr>
<tr>
<td>IDCRP-022</td>
<td>Ebola/Marburg Vaccine Phase II Study in Uganda</td>
<td>Ledgerwood</td>
<td>MUWRP, USMHRP, NIAID</td>
<td>Fully Enrolled</td>
</tr>
<tr>
<td>IDCRP-023</td>
<td>MRSA Predisposition in HIV (MRSA 2)</td>
<td>Crum-Cianflone/ Lederman</td>
<td>NMCSD, WRAMC</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-024</td>
<td>TIDOS-Trauma Infectious Disease Outcome Study</td>
<td>Tribble</td>
<td>NNMC, SAMMC, WRAMC, LRMC</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-025</td>
<td>Laser Microdissection Fungal Infection in Burn Patients</td>
<td>Hospenthal</td>
<td>SAMMC, USAISR, UTH-SCSA, UTSA</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-026</td>
<td>Pre-existing immunity, antigen expression, and vaccinia</td>
<td>Ngauy</td>
<td>WRAIR</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-027</td>
<td>Arbekacin susceptibility in Acinetobacter</td>
<td>Zapor</td>
<td>WRAMC</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-032</td>
<td>Leptospira Antibiotic Susceptibility</td>
<td>Hospenthal</td>
<td>SAMMC</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-035</td>
<td>Phase I/II <em>Staphylococcus aureus</em> Toxoids Vaccine Trial</td>
<td>Landrum</td>
<td>NMCP, SAMMC</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-037</td>
<td>TRAVMIL – Infections in DoD Travelers</td>
<td>Maguire</td>
<td>NMCP, NMCSD, NNMC</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-038</td>
<td>Strategic Timing of AntiRetroviral Treatment (START)</td>
<td>Agan</td>
<td>NMCP, NMCSD, NNMC, SAMMC</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-039</td>
<td>Pharmacokinetics of Colistin</td>
<td>Byers</td>
<td>NNMC, SAMMC, WRAMC</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-041</td>
<td>Phase I/II study of CD4-Zeta gene Modified T-cell administration</td>
<td>Aronson</td>
<td>WRAMC</td>
<td>Active</td>
</tr>
</tbody>
</table>
### Sub-studies of IDCRP Protocols:

<table>
<thead>
<tr>
<th>IDCRP #</th>
<th>Sub-study Title</th>
<th>PI</th>
<th>IDCRP Sites</th>
<th>Project status</th>
</tr>
</thead>
<tbody>
<tr>
<td>IDCRP-000-xx</td>
<td>HIV Natural History Sub-studies (RV168)</td>
<td>Agan</td>
<td>NMCP, NMCSD, NNMC, SAMMC, TAMC, WRAMC</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-000-01</td>
<td>Age and HIV outcomes</td>
<td>Weintrob</td>
<td>All IDCRP-000 Sites</td>
<td>Complete</td>
</tr>
<tr>
<td>IDCRP-000-02</td>
<td>Central memory T-cells (Tcm) (RV168B)</td>
<td>Ganesan</td>
<td>All IDCRP-000 Sites</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-000-03</td>
<td>Modeling VL response to HAART (RV168C)</td>
<td>Okulicz</td>
<td>All IDCRP-000 Sites</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-000-04</td>
<td>Cancers among HIV-Infected Persons (RV168D)</td>
<td>Crum-Cianflone</td>
<td>All IDCRP-000 Sites</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-000-05</td>
<td>Elite Controllers (RV168E)</td>
<td>Okulicz</td>
<td>All IDCRP-000 Sites</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-000-06</td>
<td>Weight Changes in HIV (RV168F)</td>
<td>Crum-Cianflone</td>
<td>All IDCRP-000 Sites</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-000-08</td>
<td>African American Setpoint WGAS (RV168H)</td>
<td>Weintrob</td>
<td>All IDCRP-000 Sites</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-000-09</td>
<td>HIV Cancer Genetics (RV168I)</td>
<td>Crum-Cianflone</td>
<td>All IDCRP-000 Sites</td>
<td>Active</td>
</tr>
<tr>
<td>Study ID</td>
<td>Title</td>
<td>Lead Investigator(s)</td>
<td>Sites</td>
<td>Status</td>
</tr>
<tr>
<td>----------</td>
<td>-------</td>
<td>----------------------</td>
<td>-------</td>
<td>--------</td>
</tr>
<tr>
<td>IDCRP-000-10</td>
<td>MMR Vaccine Response in HIV (RV168J)</td>
<td>Landrum</td>
<td>All IDCRP-000 Sites</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-000-11</td>
<td>Hepatitis A Vaccine Response in HIV (RV168K)</td>
<td>Crum-Cianflone</td>
<td>All IDCRP-000 Sites</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-000-12</td>
<td>Prevalence and Predictors of HIV Progression (RV168L)</td>
<td>Crum-Cianflone</td>
<td>All IDCRP-000 Sites</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-000-13</td>
<td>Factors associated with HAART initiation (RV168M)</td>
<td>Johnson/Agan</td>
<td>All IDCRP-000 Sites</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-000-14</td>
<td>CD4 Count at HAART and HIV outcome (RV168N)</td>
<td>Lifson</td>
<td>All IDCRP-000 Sites</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-000-15</td>
<td>Obtaining data for “Resistance Database Initiative” acceptance study (RV168O)</td>
<td>Agan</td>
<td>All IDCRP-000 Sites, NIAID, RDI</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-000-16</td>
<td>Causes of hospitalization in HIV (RV168P)</td>
<td>Crum-Cianflone</td>
<td>NMCD</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-000-17</td>
<td>Chronic Kidney Disease in HIV (RV168Q)</td>
<td>Ganesan</td>
<td>All IDCRP-000 Sites</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-000-18</td>
<td>Pharmacogenomics of protease-inhibitor Response in HIV(RV168R)</td>
<td>Weintrob</td>
<td>All IDCRP-000 Sites</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-000-19</td>
<td>Correlation of CD8+ cells and HAART Failure (RV168S)</td>
<td>Hale</td>
<td>All IDCRP-000 Sites</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-000-20</td>
<td>Pneumonia in HIV (RV168T)</td>
<td>Johnson</td>
<td>All IDCRP-000 Sites</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-000-21</td>
<td>Hepatitis E infections in HIV (RV168U)</td>
<td>Crum-Cianflone</td>
<td>All IDCRP-000 Sites</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-000-22</td>
<td>Vitamin D, Testosterone, DEXA and Osteoporosis in HIV(RV168V)</td>
<td>Sherwood/Aronson</td>
<td>WRAMC</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-000-23</td>
<td>Extreme Phenotype Genetics (RV168W)</td>
<td>Michael</td>
<td>All IDCRP-000 Sites</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-000-24</td>
<td>HIV Care Cost Effectiveness Analysis</td>
<td>Wortmann/Weintrob</td>
<td>All IDCRP-000 Sites</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-000-25</td>
<td>Hepatitis B vaccine Host Response</td>
<td>Landrum</td>
<td>All IDCRP-000 Sites</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-000-26</td>
<td>Sexually Transmitted Infections (STI) in HIV</td>
<td>Macalino</td>
<td>All IDCRP-000 Sites</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-000-27</td>
<td>Hepatitis B vaccine response in HIV (RV198)</td>
<td>Landrum</td>
<td>All IDCRP-000 Sites</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-000-28</td>
<td>Hepatitis B and HAART outcomes (RV200)</td>
<td>Chun</td>
<td>NMCP, NMCSD, NNMC, SAMMC, WRAMC</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-000-29</td>
<td>Hepatitis B and HIV progression (RV201)</td>
<td>Chun</td>
<td>NMCP, NMCSD, NNMC, SAMMC, WRAMC</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-000-30</td>
<td>20 Year Epidemiology of Syphilis in HIV (RV207)</td>
<td>Agan</td>
<td>NMCP, NMCSD, NNMC, SAMMC, WRAMC</td>
<td>Active</td>
</tr>
<tr>
<td>IDCRP-000-31</td>
<td>Pulmonary hypertension In HIV</td>
<td>Decker</td>
<td>All IDCRP-000 Sites</td>
<td>Active</td>
</tr>
</tbody>
</table>

**Key**
- **Active**: Studies enrolling or working toward enrollment.
- **Fully Enrolled**: Studies no longer enrolling, in analysis and/or manuscript production.
- **Complete**: Studies that are completed.
The IDCRP funds awarded to USU for research in the IDCRP network for FY11 are $15.1M. With the addition of leveraged resources from collaborators this will reach $19.2M in FY11.

### Funding Over Time

**Funding Sources for Research in the IDCRP Network**

<table>
<thead>
<tr>
<th>Funding Source</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>NIAID IAA: National Institute of Allergy and Infectious Diseases Interagency Agreement</td>
<td>$10,000,000</td>
<td>$10,000,000</td>
<td>$10,000,000</td>
</tr>
<tr>
<td>NIAID-ARIC: Funds earmarked for the Acute Respiratory Infection Consortium (ARIC), IDCRP-045</td>
<td></td>
<td>$1,644,009</td>
<td></td>
</tr>
<tr>
<td>DoD GEIS-ARIC: Global Emerging Infections Surveillance and Response System Funds earmarked for ARIC</td>
<td></td>
<td>$2,259,000</td>
<td>$500,000</td>
</tr>
<tr>
<td>BUMED TIDOS: Navy Bureau of Medicine and Surgery funds earmarked for the Trauma Infectious Diseases Outcomes Study, IDCRP-024</td>
<td></td>
<td>$976,932</td>
<td>$3,233,573</td>
</tr>
<tr>
<td>BUMED-Case Control Osteo: BUMED funds earmarked for Case Control Study of Osteomyelitis Risks in Orthopedic War Injuries, IDCRP-044</td>
<td></td>
<td>$271,255</td>
<td>$1,009,409</td>
</tr>
<tr>
<td>CDC Ft Benning: Centers for Disease Control funds earmarked for the Ft Benning SSTI Preventions Strategies study, IDCRP-055</td>
<td></td>
<td>$56,000</td>
<td>$299,068</td>
</tr>
<tr>
<td>CDC OCONUS Resp DZ: CDC funds earmarked for enhanced surveillance and host nation capacity building for influenza research, IDCRP-059, 060, 061</td>
<td></td>
<td></td>
<td>$1,931,000</td>
</tr>
<tr>
<td>DRMRP StaphVax: Deployment Related Medical Research Program (DRMRP) funds earmarked for the StaphVax Phase I/II Trial, IDCRP-035</td>
<td></td>
<td>$440,703</td>
<td></td>
</tr>
<tr>
<td>DRMRP-Colistin: DRMRP funds earmarked for the Study on the Pharmacokinetics of Colistin, IDCRP-039</td>
<td></td>
<td>$45,622</td>
<td>$45,622</td>
</tr>
<tr>
<td>NIH Clinical Center Rifaximin: Grant earned to study Rifaximin in HIV</td>
<td></td>
<td></td>
<td>$50,000</td>
</tr>
<tr>
<td>Leveraged Funds: Value of resources provided by collaborators for IDCRP Protocols</td>
<td>$2,253,460</td>
<td>$2,566,687</td>
<td>$4,084,342</td>
</tr>
</tbody>
</table>

**Annual Report 2010, IDCRP**

**Tom Dang**
**Director, Operations and Finance**

**Joel Curtin**
**Deputy Director, Operations and Finance**
As seen in the figure above, the majority of IDCRP expenses are spent on personnel to staff the network clinical sites and Program Coordination Center at USU. The expenses for the largest studies are broken down in the table below. At the initiation of the IDCRP in 2006, IDCRP-000 HIV NHS (RV-168) was 100% of the protocol expense. As the General Infectious Diseases Working Group (GID) has expanded its research portfolio, the GID and HIV/STI portions of funds have balanced out.

**FY2010 Protocol Expense Distribution**

[Diagram showing distribution of expenses with specific percentages and amounts for each project.]

*Includes DCAC & SPL expenses
**Does not include DCAC & SPL expenses
Research-related publications (reverse chronological order)


**Accepted Research-Related Manuscripts**


**Submitted Research-Related Manuscripts**


Research Related Presentations

2009 Infectious Disease Society of America meeting, Philadelphia, PA

1. Poster #214: Waterman P, Wortmann G, Kozar MP. **Colistin Concentration from Antibiotic-Impregnated Orthopedic Beads.**


3. Poster #216: Zapor M, Barber M, Summers A, Miller G, Feeney L, Eberly LE, Wortmann G. **In Vitro Activity of the Aminoglycoside Antibiotic Arbekacin against Acinetobacter baumannii-calcoaceticus Isolated from War Wounded at Walter Reed Army Medical Center.**

4. Poster #320: Johnson E, Roediger M, Landrum M, Ganesan A, Crum-Cianflone NF, Weintrob A, Barthel RV, Agan B. **Factors associated with HAART initiation in an open access cohort.**


7. Poster #365: Byers DK, Gibbs BT, Blaylock JM, Nayak G, Ferguson M, Tribble DR, Porter CK, Decker CF. **Longitudinal Assessment of Pulmonary Arterial Hypertension in Asymptomatic HIV-Infected Patients.**

8. Poster #369: Blaylock JM, Gibbs BT, Byers DK, Nayak G, Ferguson M, Tribble DR, Porter CK, Decker CF. **Longitudinal Assessment of Cardiac Diastolic Function in HIV-Infected Patients.**


2010 American Society of Tropical Medicine and Hygiene, Washington, DC


2010 International Conference on Health Policy Statistics, Washington, DC

20. Wilkins KJ, Macalino GE, Agan BK, Tribble DR, Martin GJ, Ottolini MG. Informing the design of host-pathogen interaction studies when infectious disease clinical research participants consent to use of their clinical specimens and electronic health records.

2010 Conference on Retroviruses and Opportunistic Infections (CROI), San Francisco, CA


26. Okulicz with SPARTAC/SMART. A Comparison of HIV Viral Rebound Following ART Cessation in Primary (SPARTAC) and Chronic (SMART) HIV Infection.


Decennial International Conference on Healthcare-Associated Infections, Atlanta, GA

1st Annual Frontiers of Translational Science Research Day, San Antonio, TX


NATO Human Factors & Medicine Panel Symposium on Use of Advanced Technologies and New Procedures in Medical Field Operations, Essen, Germany


2010 International AIDS Society, Vienna, Austria


2010 International Workshop on HIV Observational Databases, Sitges, Spain


2010 International Symposium on Pneumococci and Pneumococcal Diseases, Tel Aviv, Israel


2010 Advanced Technology Applications for Combat Casualty Care (ATACCC), St. Pete Beach, FL


The Joint Statistical Meetings, Washington, DC

37. Wilkins K, Tribble DR, Agan B, McDonald K, Martin GJ. *Appealing to assumptions of marginal structural models for time-to-event outcomes by using electronic health records.*
IDCRP at a Glance:

What we are:

We were established as an ongoing collaboration between the National Institute of Allergy and Infectious Diseases (NIAID) and Uniformed Services University (USU) to foster partnerships on clinical infectious disease research that is relevant to the Military and the NIAID.

Mission:

The IDCRP will design, conduct and publish collaborative clinical Infectious Disease research of importance to the DoD and NIAID through an effective research network that rapidly responds to evolving Infectious Disease threats.

Vision:

Reduce the impact of infectious diseases on the military population.

Who we are:

Program Director: COL Mark Kortepeter, MC, USA
A clinical research network made up of over 100 full-time equivalent personnel.

Where we are:

The Program Coordination Center at USU in Bethesda, MD.

10 Military Hospitals: WRAMC, NNMC, NMCP, NMCSD, SAMMC, MAMC, TAMC, Ft. Benning, Keesler AFB, LRMC
10 other collaborative Military Research Sites: NHRC, WRAIR, NMRC, USAMRIID, MUWRP, KEMRI, NMRCDC-Peru, NAMRU-2, NAMRU-3, USAISR

Number of currently active protocols: 74

How to reach us:

Infectious Disease Clinical Research Program
4301 Jones Bridge Road, Building 28, Room 201
Bethesda, MD 20814

Phone (301) 295-1465
Fax (301) 295-1812
Email idcrp@idcrp.org
www.idcrp.org
The IDCRP Worldwide