The Infectious Disease Clinical Research Program (IDCRP) is headquartered at the Uniformed Services University (USU) in Bethesda, MD. 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. The IDCRP is currently comprised of the largest DoD centers including ten military hospitals and five military research facilities (as well as their subordinate units). IDCRP has 90 civilian employees who work closely with active duty investigators at each of these sites. Participating centers are partners in the IDCRP’s network Infectious Diseases Institutional Review Board (ID IRB) at USU developed to undertake multicentered investigations with only a single IRB review at USU and secondary review at the Pentagon by a TriService Panel at DoD Health Affairs. Currently there are over 70 active protocols in the IDCRP’s growing portfolio.
2009 was another year of robust development for the Infectious Disease Clinical Research Program at Uniformed Services University. The IDCRP network is larger, with numerous multicentered protocols and a substantial increase in funding from multiple sources outside the NIH. This 2nd Annual Report demonstrates the breadth and depth of the IDCRP network, research, finances, accomplishments and direction as we move into the next decade.

This has been the year for launching large multicenter studies. After a year of planning and negotiating, the Trauma Infectious Diseases Outcome Study (TIDOS) started following injured warriors from Iraq and Afghanistan to Germany and then on to CONUS MTFs and even to the VA. Meanwhile, testing of a promising pentavalent Staphylococcus aureus vaccine in Army and Navy trainees began in Portsmouth and San Antonio. The April discovery of a novel recombinant H1N1 influenza strain by the Naval Health Research Center demonstrated the adaptability of the IDCRP network to respond rapidly to novel threats with the creation of the Acute Respiratory Infection Consortium (ARIC). The team identified research gaps, clinical and laboratory strengths of network partners and formulated a multicentered protocol that went from concept to initiation in only four months. As the scientific team drafted the protocol, the IDCRP leadership mobilized to obtain NIAID, DoD GEIS and Navy BUMED funding for a respiratory program that will study respiratory disease threats to the DoD community now and in the future.

The HIV Working Group has continued to build on its successes. The HIV Natural History Study continues to generate high impact publications and is the source of some of the IDCRP’s most important academic affiliations. Host genetics research performed in the DoD cohort continues to critically advance knowledge of the pathogenesis of HIV-AIDS. Recognizing the gap in clinical research in Sexually Transmitted Infections (STI) the Working Group broadened its scope and transitioned to become the HIV/STI Working Group with a highly successful kick-off DoD STI Prevention Workshop. They brought together key DoD and NIAID teams to help re-establish the leading role in STI research that the DoD played in decades past.

Finally, as I reviewed IDCRP’s Vision and Mission, I was struck by how closely they aligned with critical elements developed last summer by a NIAID expert panel for successful ID research in the next decade:

**Administrative:**
- Utilize a Central IRB
- Define oversight and monitoring
- Simplify adverse event reporting
- Streamline multilevel, duplicative development and review processes

**Operational:**
- Multifunctionality of clinical sites
- Flexibility to address emerging ID threats
- Relevant expertise in diverse areas
- Broad-based participation
- Robust studies that can also address pathogenesis
- Adapt models to fit the science

**International:**
- Recognize strengths and weaknesses of domestic and international sites
- Align regional activities with local needs
- Ensure adequate administrative and managerial support
- Explore partnerships with other funding sources

The IDCRP Strategic Plan had already identified many of these elements as critical for the success of a DoD network and we are satisfied to see just how many have already been achieved or are active goals for the IDCRP.

2010 promises to be an even better year for the IDCRP as data are generated from our large new studies and the real impact of well designed, rigorously reviewed, multicentered protocols in the DoD is made.

CAPT Gregory J. Martin MC, USN
Program Director
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, 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 pharma. 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” a research project, 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, but 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 ID 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 but 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.

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.
The IDCRP...

As seen in the diagram below, the IDCRP is ultimately responsible 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 comprised 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 after WG discussion, is 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. With their approval, the concept undergoes development through the WG as its resource requirements are determined by IDCRP Ops 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 carefully review and score proposals. Through this process, protocols are honed and reviewed for regulatory compliance and statistical rigor prior to submission to the ID IRB at USU.

As the diagram suggests, the process of protocol development involves many supporting partners within and external to USU and IDCRP.
FY09 was another year of expansion for the IDCRP. While protocols and funding increased significantly, so did the need for additional staff at all levels of the program. Most importantly, the IDCRP Program Coordination Center (PCC) had the long awaited arrival of an Education Program Director and the addition of three deputies. Col (ret) Martin Ottolini, MC, USAF, a pediatric infectious diseases physician with a long history of mentoring DoD residents and fellows, arrived in late 2008 to lead the Education Program. Due to his experience in respiratory disease, Dr. Ottolini also spearheaded the IDCRP response to the novel H1N1 pandemic. COL Mark Kortepeter, MC, USA, previously the Deputy Commander of USAMRIID at Fort Detrick, became Deputy Program Director and Chair of the Scientific Review Board. Eugene Millar, PhD, from Johns Hopkins School of Public Health, was investigating use of pneumococcal vaccine in Native American communities prior to being named as Deputy of the General Infectious Diseases Working Group during its rapid growth and initiation of large multicentered protocols. As the HIV Working Group expanded its scope into sexually transmitted infections (STI) Grace Macalino, PhD who was Deputy Director of the Arthur Ashe Institute for Urban Health in Brooklyn, NY became Deputy Director of the new HIV/STI Working Group and immediately helped lead a very successful DoD STI Prevention Conference at USU.

There has been significant growth in the staffing at the clinical sites as some large studies have been initiated. The total IDCRP employed staff is now over 100 and ranges from regulatory and data personnel to research associates, PhD scientists and physicians. The distribution of staff is shown in the table below:

<table>
<thead>
<tr>
<th>Active Duty Medical Officer (part time, except PCC)</th>
<th>Physicians/Scientists (MD or PhD)</th>
<th>Clinical Research Staff (CRC, CIA)</th>
<th>Research Support (techs, programmers, etc)</th>
<th>Admin Support (Site Mgr, Reg Aff, IRB staff, etc)</th>
<th>Total (not counting part time active duty)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FY09</td>
<td>FY09</td>
<td>FY10 New staff</td>
<td>FY09</td>
<td>FY10 New staff</td>
<td>FY09</td>
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<tr>
<td>ICDRP-PCC</td>
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<td>5</td>
<td>1</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>USU (ID IRB &amp; SAG)</td>
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<td></td>
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<tr>
<td>Spec Proc Lab MHRP</td>
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<tr>
<td>Brooke AMC</td>
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<td>2</td>
<td>1</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Wilford Hall MC</td>
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<td></td>
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<tr>
<td>Walter Reed AMC</td>
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<tr>
<td>Keesler AFMC</td>
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<tr>
<td>Tripler AMC</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>49</td>
<td>11.8</td>
<td>3.7</td>
<td>28.5</td>
<td>14.5</td>
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</table>
Collaborative Partners

The USU ID IRB

Recognizing the impact and delays experienced in multi-center research, the IDCRP founders knew that a multicenter collaborative research network would not be effective unless it had a streamlined protocol review pathway; one in which the many institutional scientific and ethical reviews could be consolidated to one single pathway for all participating institutions.

To address this critical need, in January 2008, a Memorandum of Understanding (MOU) was established. This MOU was then signed by the Assistant Secretary of Defense (Health Affairs), the Surgeons General for each service, and the President of Uniformed Services University. With the MOU, the Infectious Disease Institutional Review Board (ID IRB) and a Triservice DOD Health Affairs Headquarters level panel enabled a single IDCRP protocol review pathway for multicenter research. Since the first convened meeting in June 2008, the USU ID IRB has reviewed over 27 domestic and international protocols.

Focused on multicenter research and serving multiple sites, the USU ID IRB has been tailored to facilitate this goal. As the ID IRB consists of representatives from all three services, most of the participating research sites and USU and other federal institutions, the board is able to appropriately review protocols while providing unique local context to multicenter studies.

By consolidating the number of required reviews for multicenter research, the ID IRB has served an integral role in allowing the IDCRP to rapidly respond to infectious disease threats affecting military populations. To further streamline its processes, USU has recently adopted a fully electronic protocol submission and review system (IRBNet) to automate many of the previously paper-centric IRB procedures. The ID IRB and IDCRP staff continues to work collaboratively to advance multicenter, militarily-relevant infectious disease research.

IRB Composition:

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 RCHSPB of the NIAID

The Regulatory Compliance and Human Subjects Protection Branch (RCHSPB) of the NIAID works closely with the IDCRP in ensuring that protocols are appropriately reviewed prior to submission to the IRB. Protocols are reviewed by RCHSPB to ensure regulatory sufficiency, consistency throughout the documents, and development of protocol monitoring plans. Monitoring of prospective IDCRP protocols is performed by RCHSPB contracted staff to ensure the protection of human subjects; validate the integrity of the data collection and recording process; and to ensure compliance with all appropriate regulatory bodies and the ICH/GCP Guidelines. RCHSPB assists with the review of case report forms prior to implementation as well as operation manuals as needed. RCHSPB provides guidance on responsibilities for any FDA-regulated trials.

The DAC of the University of Minnesota

The Data Analysis Center (DAC), housed in the Division of Biostatistics, School of Public Health at the University of Minnesota, provides statistical and epidemiological collaborative support for IDCRP investigators. DAC personnel work closely with investigators throughout concept and protocol development; provide support, monitoring, and ongoing data summaries for prospective studies; direct and carry out statistical summaries and analyses of prospective and retrospective studies; and participate in the writing of abstracts and manuscripts. DAC personnel also provide statistical reviews during the working group review and scientific review of IDCRP protocols, as well as consultation on data collection practices, forms design, and grant writing. The DAC also offers support and mentoring for the IDCRP educational program and IDCRP junior investigators.

The DCAC

The Data Coordinating and Analysis Center (DCAC), in the Division of Retrovirology at the Walter Reed Army Institute of Research (WRAIR), 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.

The SPL

The Specimen Processing Laboratory (SPL), in the Division of Retrovirology at the WRAIR, functions as the IDCRP’s primary specimen processing and storage facility. SPL provides a full range of specimen support and is capable of processing and storing human, viral and bacterial materials.
The Education Program of the IDCRP expanded its agenda during the 2008 to 2009 fiscal year. These include two main initiatives:

**Development of Formal Education Courses:**

The IDCRP plays a critical role in supporting formal education in Clinical Research as part of the USU's Graduate Education program. The IDCRP has recently expanded the sequential research courses taught annually within the Department of Preventive Medicine and Biometrics with a 50% increase in course content and credit. A diverse group of students ranging from physician fellows to clinical research site managers have taken these courses, often as part of their MPH training. The first is our “Introduction to Clinical Trials” led by Col (ret) Martin Ottolini, and taught as a team effort by several of the expert staff at the Program Coordination Center (PCC) at USU and aided by our NIAID partners. This course gives future investigators a broad introduction into the process of developing new clinical research projects, as well as properly and ethically managing ongoing clinical research activities. The second course, “Clinical Trials Data and Analysis,” has been taught for several years by Dr. Ken Wilkins, statistician at the IDCRP PCC. This course gives students guidance in using their newly acquired research tools in the management and analysis of the data developed in their own research projects. These courses seek to “demystify” the complexities of the research enterprise and encourage the development of skills in support of a lifetime of discovery in support of our military research mission. We are engaged in discussions to expand this program to a larger regional community, and eventually long-distance learning.

The education team supported a short workshop entitled “Introduction to Clinical Research” at the 2009 Armed Forces Infectious Disease Society (AFIDS) Meeting in San Diego in April of 2009. This will be expanded to a day-long workshop for fellows and junior staff at the May, 2010 AFIDS Meeting.

**Mentorship of Fellows and Junior Staff Research Projects:**

The IDCRP is proud to have supported the development and approval of six new research protocols led by fellows or junior staff. This has occurred through the combined efforts of the excellent mentors at our MTF’s with the assistance of our PCC staff. New initiatives developed within the last year include:

- **IDCRP-021** Screening for Latent Tuberculosis Infection (LTBI) in US Army Recruits – by MAJ James Mancuso
- **IDCRP-039** Use of colistin serum concentrations to determine pharmacokinetic and pharmacodynamic relationships – by LT David Byers
- **IDCRP-040** The Epidemiology and Outcomes of Community-Acquired Pneumonia in the U.S. Military HIV Study Cohort – by MAJ Erica Johnson
- **IDCRP-042** Evaluation of host – pathogen response to gram-negative bacteremia using protein microarray technology – by CPT Kris Paolino
- **IDCRP-048** The association of serum vitamin D and testosterone levels with bone loss on DEXA testing in HIV infected participants – by CPT Jeff Sherwood
- **IDCRP-053** Immunogenicity of H1N1 Vaccination among HIV-Infected Compared to HIV Uninfected Persons – by LCDR Chris Duplessis

These are all in varying stages of development and execution and exemplify the IDCRP’s success in supporting the development of future researchers within our DoD community!
The IDCRP General Infectious Disease (GID) Working Group was officially constituted October 2006 at the Infectious Diseases Society of America conference. Expanding upon the ongoing research effort of the HIV Working Group, this group broadens the Program’s scope and research agenda to include several high priority infectious disease clinical concerns affecting the U.S. military, frequently with direct application to the civilian community. In the short span of three years, the GID Working Group has completed and/or initiated 20 active protocols with several others currently under review. The GID portfolio represents 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 approaches highlights the strengths of the IDCRP network and partners creating collaborations with Infectious Disease clinicians (adult and pediatric), Preventive Medicine physicians, Microbiologists, Trauma/Orthopedic Surgeons, Epidemiologists, and Statisticians. 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), Veteran’s Affairs medical centers, preventive medicine commands, recruit training commands, and the NIH.

The tremendous growth of the portfolio has been made possible by the expanding sponsorship and direct financial support of the projects through several sources, including the NIAID, CDC, US Navy Bureau of Medicine and Surgery (BUMED), and the US Army Medical Research Materiel Command (Deployment Related Medical Research Program). In addition, indirect support has been substantial as collaborators have leveraged significant resources in support of several projects, including the US Army Center for Health Promotion and Preventive Medicine (USACHPPM), US Army Institute for Surgical Research (USAISR), Brooke Army Medical Center (BAMC) Department of Clinical Investigation, and Nabi Biopharmaceuticals. The organization of the GID Working Group has also continued to evolve and strengthen to meet the needs of this effort. The addition of a new Deputy Director, Dr. Eugene Millar, an accomplished Infectious Disease Epidemiologist with multi-site clinical trials experience from Johns Hopkins Bloomberg School of Public Health, has brought new energy and perspectives to the group, further enhancing its capabilities and impact.

The GID portfolio includes a wide range of research designs, from retrospective cohort studies to FDA-regulated randomized controlled trials. The diversity of research approaches highlights the strengths of the IDCRP network and partners, including collaborations with Infectious Disease clinicians, Preventive Medicine physicians, Microbiologists, Trauma/Orthopedic Surgeons, Epidemiologists, and Statisticians.

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of Public Health, has provided further expertise to the GID team with immediate impact on the rapidly expanding clinical research effort in acute respiratory infection addressing the emergent threat of the pandemic novel swine-origin influenza A virus (H1N1). The GID Clinical Research Associates, at the Program Coordination Center, are instrumental in protocol development and project management as they coordinate with research staff across the network. This past year has also seen major advances in statistical support and coordinated data management through the efforts of Drs. Ken Wilkins (PCC) and Lynn Eberly (Data Analysis Center) and Tanya Antonille (GID Team lead, Data Coordinating and Analysis Center).

There are five current GID research focus areas:

- **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, Operations Iraqi Freedom (OIF) and Enduring Freedom (OEF), 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

  Current research efforts addressing these priority areas are detailed in the following sections. For additional information, please refer to the appendix at the back of this report.

- **Focus Area 2: 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.**

- **Focus Area 3: Deployment/travel associated infections epidemiology, prevention and management/ Evidence-based support for DoD policy related to ID screening/ surveillance/prophylaxis and treatment.**

- **Focus Area 4: 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).**

- **Focus Area 5: Rapid response to novel infectious diseases threats to public health, recently exemplified by the rapid development of an Acute Respiratory Infection research portfolio in response to pandemic novel H1N1 influenza threat.**
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 isolates, and applied laboratory studies of current surgical management approaches, and reconsideration of optimal use of older therapeutic agents as antimicrobial resistance narrows the available effective agents.

The “Departments of Defense and Veterans Affairs Multicenter 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 multi-site 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 of Surgical Research (USAISR), Walter Reed Army Institute of Research (WRAIR)], Veterans Affairs (St. Louis VAMC), and the Uniformed Services University. The US Navy Bureau of Medicine and Surgery (BUMED), through the Wounded Warrior Initiative, has provided sponsorship of this effort with expanded partnership currently in development with the Naval Health Research Center. This protocol seeks to systematically capture clinical, microbiology and risk factor data, and clinical bacterial isolates necessary to assess both short- and long-term outcomes in order to provide evidence-based recommendations for the prevention and management of these infections. Since TIDOS began June 2009, data collection has been undertaken on approximately 550 patients at Landstuhl Regional Medical Center with approximately half being transferred to one of the IDCRP participating CONUS military hospitals. At the time of publication, 137 patients have enrolled in the TIDOS cohort and 786 clinical isolates have been retained for the bacterial repository. Interim analyses and published reports will be conducted annually to address the study objectives to inform clinical practice and future studies. In addition to 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. Additionally, this is the first IDCRP study to initiate a research collaboration with the VA and is tackling many of the technical, administrative and regulatory issues that will make additional studies with the VA easier to initiate.

Infections due to gram-negative 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). Troops medevaced from combat areas have had extraordinarily high incidence of ABC infections that have been acquired during their initial management at facilities in theater. Furthermore, these wound infections have demonstrated serious problems with multidrug resistance. At BAMC, a highly productive study (IDCRP# 005) has focused on characterization of ABC antimicrobial susceptibility for a range of old and new therapeutic agents. The BAMC team is performing a critical investigation of assay interpretative criteria using established and new diagnostic methods, with future efforts to explore healthcare related topical biocidal susceptibility. 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.

WRAMC investigators also led a successful effort (IDCRP# 007) to better understand the natural history of gram-negative MDRO colonization. Hospitalized U.S. service member (transferred from Iraq or Afghanistan) colonization rates were compared to patients admitted from the Washington, DC community through an intensive serial surveillance of multiple anatomic sites. Study findings supported patient-to-patient transmission, long duration of colonization, and a high proportion
of colonized but uninfected subjects leading to modifications in DoD Infection Control policy through the implementation of active surveillance of gram negative MDRO colonization.

Retrospective analysis of existing Joint Theater Trauma Registry (JTTR) data (IDCRP # 006) has highlighted the major impact of infectious complications by demonstrating that approximately one third of trauma patients in the initial periods of OIF are affected. Commencing in 2010, DoD and VA investigators will utilize a multisite retrospective cohort study design to focus on a major concern of acute and long-term morbidity, trauma-associated osteomyelitis (IDCRP # 044). This large-scale effort is supported through 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 drug resistance in these injuries has become a major clinical problem that has required utilization of some older antibiotic regimens. Colistin is one of these older antibiotics that has been resurrected as an "antibiotic of last resort" in many MDRO infections, but is lacking important PK/PD data that can inform optimized management. To provide clinicians the information they need to most effectively use colistin, an important multisite study (IDCRP # 039) will start in 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.

**Focus Area 2: 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**

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 additional 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.
Investigators at the National Naval Medical Center and the Uniformed Services University in collaboration with the NIH Clinical Microbiology Department and the US Marine Corps Base Quantico evaluated whether 2% chlorhexidine-impregnated cloths (CHG) reduce SSTI rates and S. aureus colonization in Marine Corps Officer candidates during 6-10 weeks of training (IDCRP # 001). Platoons were cluster randomized (1562 subjects enrolled) to receive CHG or control cloths. CHG applied thrice-weekly did not reduce rates of SSTI in trainees which remained high (approximately 7-9% affected during 6-week period). S. aureus colonization also increased in both groups throughout the training period, although, to a lesser extent in those assigned CHG. S. aureus colonization was not a risk factor for SSTI. Based on this study, ongoing research is needed 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 Army Center for Health Promotion and Preventive Medicine (USACHPPM) investigators have proposed an evaluation of strategies to prevent methicillin-resistant Staphylococcus aureus (MRSA) skin and soft tissue infections in military trainees at Ft. Benning, Georgia. This proposal was selected for 3-year intramural funding through the CDC Office of Antimicrobial Resistance.

A cluster-randomized prospective design will investigate a multi-component hygiene-based intervention on the incidence of MRSA SSTIs. The proposed interventions used singly or in combination include enhanced training and education, periodic chlorhexidine showers, and a novel (microfiber) environmental cleaning device. 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 inform DoD prevention policy.

As stated previously, 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. It is a pentavalent vaccine composed of both conjugated capsular polysaccharides and recombinant toxoids. The IDCRP-USU, along with the Henry M. Jackson Foundation, entered into a Cooperative Research and Development Agreement (CRADA) with Nabi last year 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.

PentaStaph™ (Pentavalent S. aureus Vaccine) is a five-component vaccine. Three of the antigen components induce antibodies that target S. aureus capsular polysaccharides Types 5 and 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 hopefully will translate into efficacy in humans.

The first clinical trial (IDCRP# 035) received funding through the Department of Defense Deployment Related Medical Research Program (DRMRP) of the Office of the Congressionally Directed Medical Research Programs (CDMRP), and started enrollment in the Fall 2009. This initial study will investigate the safety and im-
During the 20-month evaluation period, five cycles of and a novel (microfiber) environmental cleaning device. Tions used singly or in combination include enhanced on the incidence of MRSA SSTIs. The proposed interven- gate a multi-component hygiene-based intervention A cluster-randomized prospective design will investi- intramural funding through the CDC Office of Antimi- Benning, Georgia. This proposal was selected for 3-year skin and soft tissue infections in military trainees at Ft. methicillin-resistant have proposed an evaluation of strategies to prevent and Preventive Medicine (USACHPPM) investigators CDC, Ft. Benning, and Army Center for Health Promotion and Prevention Medicine (USACHPPM) investigators CDC, Ft. Benning, and Army Center for Health Promotion

Focus Area 3: Deployment/travel associated infections epidemiology, prevention and management/ evidence-based support for DoD policy related to ID screening/ surveillance prophylaxis and treatment

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 (DNBI). The infections threatening the military occur while stationed in garrison in CONUS and frequently occur at levels far exceeding civilian counterparts (as in Focus Area 2, CA-MRSA), or occur during overseas deployment. ID threats during military deployments have had dramatic effects throughout history and continue to impact modern mili- taries. 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 benefici- aries returning with infections acquired while abroad. This research focus area encourages investigator-initiated efforts to address priority infectious disease threats impacting military operations, particularly during or fol- lowing deployment, generating necessary evidence for prevention and/or therapeutic strategies that support DoD policy.

The study titled “Deployment and Travel Related Infectious Disease Risk Assessment, Outcomes, and Prevention Strategies among Department of Defense Benefi- ciaries (TRAVMIL)” (IDCRP# 037) is a major new IDCRP initiative that started in late 2009. This multisite project will build a DoD Travel Medicine Research Consortium for the long-term study of travel- and deployment-re- lated infectious disease threats. TRAVMIL will study the epidemiology of these infections and evaluate 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, self-collected by participants while they are traveling, to determine the etiology of travel/deployment-related illness. Demon- strating 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 developing a platform for pre-licensure evaluation of prevention and treatment products. 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 assessment of infectious disease threats for the DoD.

The study will focus on 4 key infectious diseases areas: traveler’s diarrhea, malaria, febrile illness, and influenza-like illness (ILI), while using a combination of clinical data and laboratory testing. Clinical information will be ob- tained from participants using pre-travel surveys, travel diaries, a post-travel survey, and extended follow-up information. A retrospective component will allow in- vestigators 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 impres- sive collaboration including investigators at the Naval Medical Center Portsmouth (NMCP), Naval Medical Cen- ter 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, Naval Medical Research Unit-2 Jakarta, Indonesia (NAMRU-2) and the Uniformed Services University. In addition to the 4 key infectious disease areas, the study will create a repository of clini-
cal specimens linked to exposure and disease outcome for future studies of the development and validation of biomarkers, identification of novel pathogens, and performance of host genetic susceptibility to travel-related infectious diseases. Lastly, the study will also provide a descriptive analysis of noninfectious health risks that affect travelers such as injuries due to driving accidents and recreational activities.

Tuberculosis (TB) is an uncommon infectious disease 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 efforts 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 to inform DoD policy and revise the military TB screening program. USU investigators, in collaboration with investigators at Ft. Jackson, South Carolina have undertaken a study (IDCRP# 021) to specifically address this major concern. The study received funding support through the US Army Center for Health Promotion and Preventive Medicine (USACHPPM), and it successfully enrolled >2000 recruits in a span of 3 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. Analysis is currently underway; however, preliminary findings support targeted testing to screen military populations and will form the basis of a formal recommendation to inform a change in current Army policy.

Focus Area 4: Vaccines of military importance with focus on infections with high impact on military populations

Vaccine-based prevention is a central approach to control 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 effort will advance development of the NIAID VRC candidate vaccines with enrollment beginning in the Fall 2009.

**Focus Area 5: Rapid response to novel infectious disease threats to public health**

A critical aspect of the IDCRP mission is to provide an effective rapid response addressing clinical research priorities in the event of a novel infectious disease threat to the US military and/or to the public health in general. The ability to be poised to respond to such an urgent research mission requires an infrastructure that supports rapid high quality protocol development, timely and critical scientific review, coordinated and responsive human subjects and regulatory review, a distributed clinical research infrastructure with central oversight, effective and timely resource management with the capacity to receive and process funding, and a dedicated core of knowledgeable health researchers and allied staff. This is a tall order for any organization and has been a central tenet of the IDCRP in the past three years of growth.

As anticipated with infectious diseases, the waiting period for a novel threat to arise is brief. When the current public health threat came in the form of the novel swine-origin influenza A virus (H1N1), the IDCRP rapidly responded. Acute respiratory infections (ARI) have been a significant source of disease and non-battle injury (DNBI) among military forces for centuries; therefore, ARI clinical research within the IDCRP is a focus area that was already under discussion and preliminary investigations were being considered prior to the current pandemic. Several groups within the DoD, such as the DoD-Global Emerging Infection Surveillance (DoD-GEIS) program with their various partners including the Naval Health Research Center (NHRC), the US Air School of Aerospace Medicine (USAFSAM), overseas DoD laboratories, and Walter Reed Army Institute of Research (WRAIR) already invest significant effort yielding world class research in ARI surveillance and prevention strategies. As it has done in trauma-related infections, HIV, and other areas, the IDCRP brings a unique contribution to the existing DoD efforts by engaging investigators across the military treatment facilities and forging effective collaborations with DoD and NIAID research laboratories. In addition, the IDCRP in collaboration with the US Navy OCONUS laboratories were awarded a 5-year grant from the Centers for Disease Control and Prevention (NCIRD/CDC) funding opportunity ‘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 further broaden existing efforts investigating population-based epidemiological studies on influenza and other respiratory pathogens based at the Naval Medical Research Unit-3 (NAMRU-3) in Cairo, Egypt, the Naval Medical Research Unit-2 (NAMRU-2), in Jakarta, Indonesia, and the Naval Medical Research Center Detachment (NMRC-Peru) in Lima, Peru.

The Acute Respiratory Infection Consortium (ARIC) study (IDCRP# 045) was expeditiously developed to address this need. This study marks the beginning of a multi-site, multi-disciplinary research collaboration to investigate the natural history, host response, and potential therapy of acute respiratory infection in military members and their families. Subject recruitment will take place in both inpatient and outpatient settings of military treatment facilities in the continental US. In less than 4 months, this project has successfully done the following: 1) protocol development through a collaborative effort bringing the combined strengths of several pediatric and adult infectious disease clinical researchers, laboratory-based influenza experts within the DoD (NHRC, NMRC, and WRAIR)
and NIH, epidemiologists, and statisticians, 2) obtained scientific and IRB approval for implementation across multiple sites, 3) received supplementary funding from NIAID and DoD-GEIS with the development of a resource plan to accommodate the extensive expansion of site infrastructure, and the 4) addition of two new clinical sites, Madigan Army Medical Center and Keesler Air Force Medical Center. The success of this effort highlights the tremendous capacity of the IDCRP to respond to novel infectious disease threats with rapidly developed and instituted multicentered research protocols.

The ARIC Natural History Study and the established consortium provides a solid foundation for additional research efforts related to diagnostics, transmission, prevention, and therapy. A substudy of the ARIC project will investigate the dynamics of influenza transmission within families, a particular concern for novel viral strains. The need for a validated surrogate measure to assess the severity of ILI has been a shortcoming of much influenza research and NIAID-IDCRP have spearheaded an investigation of potential surrogates as part of the ARIC study. An additional important objective of the ARIC project is the establishment of a specimen repository for future clinical and laboratory investigation, and a rapidly responsive multi-centered network for future ARI research. Immunocompromised individuals are at particular risk of greater morbidity and mortality from ARI. In a combined effort with the IDCRP HIV/STI Working Group, a study of the H1N1 vaccine in immunocompetent vs. HIV infected subjects (IDCRP# 053) was initiated in October 2009. This observational study will describe the immunogenicity of the H1N1 vaccine among HIV seropositive versus HIV seronegative military beneficiaries receiving immunization as part of routine clinical care. Data will also be collected on the clinical efficacy of the vaccine (number of ILI and documented influenza events) as well as any adverse reactions temporally associated with vaccination between the two groups including any effects on the CD4 count and HIV RNA levels among HIV-infected persons.

Treatment research is also under development within the IDCRP. Investigators at the Naval Medical Research Center, working closely with a parallel effort at NIAID, are instituting a pilot study for collection of anti-Influenza A H1N1 (Swine Flu) hyperimmune plasma (IDCRP # 46). Cir- culating novel H1N1 isolates are resistant to amantadine and rimantadine, and there is concern this virus may also acquire high level resistance to oseltamivir that is seen in circulating seasonal H1N1 virus. The future course of this epidemic is not clear. Due to potential concerns with future treatment options for influenza, additional H1N1 therapeutics are warranted justifying initial efforts to collect hyperimmune plasma in support of potential future clinical trials.

Similar concerns regarding optimal antiviral therapy, particularly for severely ill patients with H1N1 has led IDCRP investigators at the NHRC, NMCSD, and USU to enter into discussions with Adamas Pharmaceuticals which is proposing a double-blind, randomized, placebo-controlled study comparing the efficacy, safety, and tolerability of oral administration of triple combination antiviral drug (IDCRP #047) therapy with amantadine, ribavirin, and oseltamivir versus oseltamivir monotherapy for severely ill and/or immunocompromised patients at risk for complications with influenza A. These and other efforts investigating ARI risks and management strategies will continue focusing on this current pandemic as well as other respiratory pathogen threats of importance for the DoD.
HIV/Sexually Transmitted Infections (STI) Working Group

The IDCRP was created to reproduce the success of the DoD investigators at the major Military Treatment Facilities (MTFs) studying HIV in the US military since the early 1980’s. As the IDCRP was initiated at USU in 2006, the IDCRP HIV/STI Working Group (WG) was formed to continue HIV studies in the unique cohort of DoD active duty and beneficiaries.

A long-standing component of the U.S. Military HIV Research Program, the WG arose in the Division of Retrovirology at the Walter Reed Army Institute of Research, former home to the DoD HIV Natural History Study (NHS, IDCRP-000) for twenty years following its inception in 1986. In 2002, a consortium of the Division of Clinical Research at NIAID and the military centers conducting the NHS was developed through an Interagency Agreement (IAA), thus forming the Tri-service AIDS Clinical Consortium (TACC). The purpose of this group was to provide a forum for DoD experts in clinical HIV care and research to prioritize the efforts to improve the quality of clinical HIV research within the military and to act as long-term stewards for the valuable collection of samples and data represented in the NHS. In mid-2006, the TACC moved to USU to help establish the IDCRP and became the IDCRP HIV Working Group. 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 the U.S. Military HIV Research Program and the International Network for Strategic Initiatives in Global HIV Trials.

2009 has been an exciting year for the Working Group with many changes and continued growth and productivity. Most notably, in February the Director, Colonel Scott Wegner, retired from the U.S. Air Force and left the IDCRP to return to clinical oncology. His participation in the HIV research program over the past fifteen years and his leadership for the past eleven years was instrumental in many ways, including fostering the transfer of primary program funding from the Army to NIAID, movement of the program from WRAIR to USU to help found the IDCRP, and expansion of the research to include new collaborators and areas of focus. Col Wegner saw the HIV Natural History Study through two rewrites and helped to create a model of single IRB oversight of multi center investigation that has been incorporated as a cardinal feature and strength of the IDCRP. His long-time interest in HIV antiretroviral drug resistance led Col Wegner to conduct the sentinel Clinical Efficacy of Resistance
Testing (CERT) trial, showing that routine access to viral resistance testing could improve clinical outcomes and decrease treatment failure. This effort was recognized through incorporation into clinical practice guidelines as well as by his invitation to participate in and serve on resistance boards, symposia, and NIH study sections firmly establishing the IDCRP as a participant in some of the key national and international HIV research groups.

The HIV/STI program is now directed by Brian Agan, MD, the prior Deputy Director, an infectious diseases physician and former Air Force (AF) officer who trained and worked in San Antonio at Wilford Hall (WHMC) and later at Brooke Army Medical Center (BAMC). While on active duty, Dr. Agan served as the WHMC/BAMC site PI for the HIV Natural History Study. He later separated from the AF to work directly for the research program, led the effort to draft the current version of the NHS protocol, and served as HIV Program Deputy Director since 2006. With his promotion, there has been a new and important addition to the organization, Grace Macalino, PhD, MPH, who was hired as the new Deputy Director in July 2009. She brings a wealth of experience including completing two master’s degrees, a PhD in epidemiology at Johns Hopkins, serving as faculty at Brown University Medical School, the Director of the Center for Health Disparities Research Institute for Clinical Research and Health Policy Studies at Tufts New England Medical Center and most recently as Deputy Director of the Arthur Ashe Institute for Urban Health in Brooklyn, New York. Dr. Macalino has been very successful as an independently-funded principal investigator of grants in HIV prevention with a focus on communities and prison populations and was responsible for program funding for the Arthur Ashe Institute.

The focus of the Working Group this year has been toward increasing the impact of our work both within the DoD and in the scientific community. With this, the research focus of the program was broadened from HIV 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 opens the door to Prevention, which has been brought into the research program as a new 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 add meaningfully to the broader scientific knowledge base. To kick off this new effort, the IDCRP hosted a highly successful DoD-wide HIV/STI Prevention workshop in September. A series of protocols are in development laying the groundwork for investigation of the epidemiology of STIs and risk factors for STI (including behavior). Testing prevention interventions will include a comparative trial.

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. In just this past year, the WG has produced 39 manuscripts (25 published, 10 accepted, and four submitted) as well as 18 meeting presentations. The list of journals publishing our research this year has included Nature Medicine, Clinical Infectious Diseases, The Journal of Infectious Diseases, Annals of Internal Medicine, Archives of Internal Medicine, PLoS ONE, AIDS, JAIDS, Vaccine, and many others. We continue to have a variety of prospective clinical trials and observational studies as well as a strong series of NHS substudies demonstrating the value of the HIV Natural History Study. This engine of productivity has been enhanced this year through electronic capture of laboratory data at five (soon to be six) of seven participating centers which not only provides improved completeness and fidelity of data, but also removes this burden from research staff. As the result of this and other cost-saving efforts, the NHS has come in under budget this year and is calculated to require fewer resources in 2010 than it did in 2009. Also of note, (IDCRP-056) a study comparing the efficacy of conjugate pneumococcal vaccine in HIV infected patients, was the first prospective randomized clinical trial to be conducted by the IDCRP HIV/STI WG and was completed successfully this year. 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.

With the change in Working Group leadership and looking toward the coming year and beyond, we have undertaken a critical reassessment of the research program including focus areas, goals and objectives, open protocols, funding, and collaborations. There are several strong lines of investigation within the program that will be continued and enhanced and new areas that will be added. In a number of cases, we have identified opportunities to consolidate work in order to foster collaboration, integration of efforts, and to maximize effectiveness. The WG has many external collaborators including leaders in a number of fields and in this past year our protocols have leveraged over $2.2 million in outside funding to conduct research. In FY10 and beyond, the WG will expand existing research collaborations while supporting and assisting IDCRP investigators as they seek their own extramural research funding support. In time, this will not only enhance the IDCRP and the HIV/STI Working Group, but will 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. Benefitting 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.

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. Future studies are planned 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 of and outcomes of highly active antiretroviral therapy (HAART) are likewise being carefully examined including age (IDCRP-000-01), 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. 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 in Kenya opened this year and has already submitted its first abstract findings to
the Conference on Retroviruses and Opportunistic Infections (CROI) meeting. 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), coronary artery disease (IDCRP-018), and endocrine complications (IDCRP-000-06, -000-22).

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 have 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 guidelines are in draft and these findings are likely to be incorporated.

**Focus Area 2: HIV/STI prevention incorporating unique features of the DoD and its setting**

The IDCRP HIV/STI Working Group has expanded its portfolio this year to include a focus on Prevention, meeting both a NIAID strategic priority and a recent call by the CDC for increased attention to prevention, given that proven prevention efforts exist and HIV/STI incidence continues to remain constant. To kick off this new effort, the IDCRP hosted a DoD-wide HIV/STI Prevention workshop in September that was well attended with representation from twenty organizations in three military services as well as DoD 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. At the end of the day-long meeting, the group agreed to continue collaborating on the development of prevention efforts including research with IDCRP serving a central role. There is an effort underway to create a formal charter and during the workshop, the group created a list of gaps and needs in DoD HIV/STI Prevention, identifying research as well as policy and program targets for new work.
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 description of the epidemiology of syphilis in the same cohort (IDCRP-000-30). Similar analyses are in process related to Chlamydia and herpes simplex virus (HSV). These analyses will be consolidated within the broader protocol Predictive Modeling of STI Acquisition on the NHS cohort (in development) to support and inform this strategy 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. Risk factors, including behavior, for incident STI in the U.S. military is a protocol in development that will include both HIV seropositive and HIV seronegative active duty members to answer this important question.

Finally, new well-targeted prevention programs are needed. Future protocols will 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 clinical outcomes of HIV/STI infection

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 translate basic science research into clinical findings and to incorporate this into the care of individual patients.

Focus Area 4: Improving outcomes through evidence-based medicine for HIV/STI diagnosis, care and treatment

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-
Randomized Study of Pneumococcal Conjugate Vaccination in HIV in Comparison to Polysaccharide Vaccine Boosting in Previously Vaccinated Patients (IDCRP-056), has been successfully completed this year, being stopped early by the DSMB due to a lack of difference noted between arms. Importantly, this investigation demonstrates that boosting of immunity to Streptococcus pneumoniae through re-vaccination remains challenging and that the new conjugate vaccine (Prevnar) offers no benefit over the previous polysaccharide vaccine (Pneumovax). Further investigation of the correlates of protection and strategies to elicit protection are under consideration.

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), is nearing completion of enrollment.

A RCT pilot in collaboration with the NIH/NIAID Vaccine Research Center, A randomized placebo controlled trial of Atorvastatin in HIV positive patients not on antiretroviral medications with the specific aims of studying the effects of Atorvastatin on HIV viral load and immune activation markers (IDCRP-015), was also successfully completed this year. While we found no effect of atorvastatin on HIV viral load, we did note a significant decrease in immune activation. These results have sparked interest and a follow-up trial is in development. We are hoping that the long term impact of this work is to investigate how statin therapy might impact HIV pathogenesis and in turn, potentially impact HIV outcomes.

With the emergence of H1N1 influenza worldwide, the IDCRP has 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 have combined to support the development, approval, and activation of a new study (IDCRP-053) in less than two months, comparing the response to H1N1 vaccine in HIV-infected versus uninfected individuals and outcomes of this. This study is complete and will quickly provide needed data to inform influenza prevention efforts in HIV-infected individuals and will provide data for later study regarding vaccine-induced immunity.

Other ongoing HIV-related trials include, 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. 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 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.
## IDCRP Protocol History

<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>
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<tr>
<td>IDCRP-003</td>
<td>MRSA Skin Infections in HIV (RV210)</td>
<td>Crum-Cianflone/ Bavaro</td>
<td>NMCP, NMCSD, WRAMC</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>
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<tr>
<td>IDCRP-005</td>
<td>Drug Resistant Acinetobacter Antibiotic Susceptibility</td>
<td>Akers</td>
<td>SAMMC</td>
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<tr>
<td>IDCRP-006</td>
<td>Non-Extremity Infections in Combat (retrospective cohort)</td>
<td>Murray</td>
<td>SAMMC</td>
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<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>
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<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>
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<tr>
<td>IDCRP-010</td>
<td>Multinational Acinetobacter Bacteremia (retrospective analysis)</td>
<td>Waterman</td>
<td>WRAMC</td>
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<tr>
<td>IDCRP-011</td>
<td>Colistin Beads in Orthopedic Injuries</td>
<td>Waterman</td>
<td>WRAMC</td>
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<td>IDCRP-013</td>
<td>Ventilator Associated Pneumonia (VAP) (retrospective study)</td>
<td>Brett-Major</td>
<td>NNMC, WRAMC</td>
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<tr>
<td>IDCRP-014</td>
<td>Oral KSHV Complications in HIV</td>
<td>Marconi</td>
<td>SAMMC, San Antonio VA, UTHSCSA</td>
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<tr>
<td>IDCRP-015</td>
<td>Atorvastatin effects on VL and Immune Activation in HIV</td>
<td>Ganesan</td>
<td>NMCSO, NNMC, NIAID</td>
<td>Fully Enrolled</td>
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<tr>
<td>IDCRP-016</td>
<td>Neurocognitive Changes in HIV</td>
<td>Hale/ Crum-Cianflone</td>
<td>NMCSO, NNMC, SAMMC, WRAMC</td>
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<td>IDCRP-018</td>
<td>Cardiac disease and liver steatosis in HIV</td>
<td>Crum-Cianflone/ Bavaro</td>
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<td>IDCRP-021</td>
<td>Latent TB Screening in the DoD</td>
<td>Mancuso</td>
<td>Ft. Jackson</td>
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<td>IDCRP-022</td>
<td>Ebola/Marburg Vaccine Phase II Study in Uganda</td>
<td>Ledgerwood</td>
<td>MUWRP, USMHRP, NIAID</td>
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<td>IDCRP-023</td>
<td>MRSA Predisposition in HIV (MRSA 2)</td>
<td>Crum-Cianflone/ Lederman</td>
<td>NMCSO, WRAMC</td>
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<tr>
<td>IDCRP-024</td>
<td>TIDOS-Trauma Infectious Disease Outcome Study</td>
<td>Tribble</td>
<td>NNMC, SAMMC, WRAMC, LRMC</td>
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<tr>
<td>IDCRP-025</td>
<td>Laser Microdissection Fungal Infection in Burn Patients</td>
<td>D'Avignon</td>
<td>SAMMC, USAISR, UTHSCSA, UTSA</td>
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<tr>
<td>IDCRP-026</td>
<td>Pre-existing immunity, antigen expression, and vaccinia</td>
<td>Ngauy</td>
<td>WRAIR</td>
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<tr>
<td>IDCRP-027</td>
<td>Arbekacin susceptibility in Acinetobacter</td>
<td>Zapor</td>
<td>WRAMC</td>
<td>Active</td>
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<tr>
<td>IDCRP-032</td>
<td>Leptospira Antibiotic Susceptibility</td>
<td>Hospenthal</td>
<td>SAMMC</td>
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<tr>
<td>IDCRP-035</td>
<td>Phase I/II <em>Staphylococcus aureus</em> Toxoids Vaccine Trial</td>
<td>Landrum</td>
<td>NMCP, SAMMC</td>
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<tr>
<td>IDCRP-037</td>
<td>TRAVMIL – Infections in DoD Travelers</td>
<td>Maguire</td>
<td>NMCP, NMCSD, NNMC</td>
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<tr>
<td>IDCRP-038</td>
<td>Strategic Timing of AntiRetroviral Treatment (START)</td>
<td>Agan</td>
<td>NMCP, NMCSD, NNMC, SAMMC</td>
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<tr>
<td>IDCRP-039</td>
<td>Pharmacokinetics of Colistin</td>
<td>Byers</td>
<td>NNMC, SAMMC, WRAMC</td>
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<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>
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<tr>
<td>IDCRP-042</td>
<td>Host immune response to Gram negative bacteremia (protein microarray)</td>
<td>Paolino</td>
<td>NNMC, WRAMC</td>
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<tr>
<td>IDCRP-044</td>
<td>Case Control Study of Osteomyelitis Risk Factors in Orthopedic Injury (OIF/OEF)</td>
<td>Tribble</td>
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<td>IDCRP-045</td>
<td>ARIC- Acute Respiratory Infection Consortium of the DoD</td>
<td>Arnold</td>
<td>NMCSD, SAMMC, WRAMC, NMCP</td>
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<tr>
<td>IDCRP-046</td>
<td>H1N1 Antibody Plasmapheresis</td>
<td>Luke</td>
<td>NMCSD, NNMC</td>
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<td>IDCRP-047</td>
<td>Triple Combo Antiviral Drugs for Flu</td>
<td>Faix</td>
<td>NMCSD, NNMC, SAMMC, NHRC</td>
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<td>IDCRP-049</td>
<td>MRSA Infections in HIV</td>
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<td>IDCRP-050</td>
<td>Liver Dysfunction and NAFLD in HIV</td>
<td>Crum-Cianflone</td>
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<td>IDCRP-051</td>
<td>Dermatologic Conditions in HIV</td>
<td>Crum-Cianflone</td>
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<td>IDCRP-052</td>
<td>Renal Disease in HIV</td>
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<td>IDCRP-053</td>
<td>H1N1 Vaccine Response in HIV vs Non-HIV</td>
<td>Duplessis/ Crum-Cianflone</td>
<td>NMCP, NMCSD, SAMMC</td>
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<td>IDCRP-055</td>
<td>Ft Benning SSTI Prevention Strategies Study</td>
<td>Ellis</td>
<td>Ft. Benning</td>
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<td>IDCRP-056</td>
<td>Prevnar vs Pneumovax to Boost Immunity in HIV (RV150)</td>
<td>Hale/ Crum-Cianflone</td>
<td>NMCP, NMCSD, NNMC, SAMMC, WRAMC</td>
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Sub-studies of IDCRP Protocols:

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<tr>
<th>IDCRP #</th>
<th>Sub-study Title</th>
<th>PI</th>
<th>IDCRP Sites</th>
<th>Project status</th>
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<tr>
<td>IDCRP-000-xx</td>
<td>HIV Natural History Sub-studies (RV168)</td>
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<td>NMCP, NMCSD, NNMC, SAMMC, TAMC, WRAMC</td>
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<tr>
<td>IDCRP-000-01</td>
<td>Age and HIV outcomes</td>
<td>Weintrob</td>
<td>All IDCRP-000 Sites</td>
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<td>IDCRP-000-02</td>
<td>Central memory T-cells (Tcm) (RV168B)</td>
<td>Ganesan</td>
<td>All IDCRP-000 Sites</td>
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<td>IDCRP-000-03</td>
<td>Modeling VL response to HAART (RV168C)</td>
<td>Okulicz</td>
<td>All IDCRP-000 Sites</td>
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<td>IDCRP-000-04</td>
<td>Cancers among HIV-Infected Persons (RV168D)</td>
<td>Ganesan</td>
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<td>IDCRP-000-05</td>
<td>Elite Controllers (RV168E)</td>
<td>Okulicz</td>
<td>All IDCRP-000 Sites</td>
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<td>IDCRP-000-06</td>
<td>Weight Changes in HIV (RV168F)</td>
<td>Crum-Cianflone</td>
<td>All IDCRP-000 Sites</td>
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<td>IDCRP-000-07</td>
<td>Syphilis and AIDS Progression (RV168G)</td>
<td>Weintrob</td>
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<td>IDCRP-000-08</td>
<td>African American Setpoint WGAS (RV168H)</td>
<td>Weintrob</td>
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<td>IDCRP-000-09</td>
<td>HIV Cancer Genetics (RV168I)</td>
<td>Crum-Cianflone</td>
<td>All IDCRP-000 Sites</td>
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<td>IDCRP-000-10</td>
<td>MMR Vaccine Response in HIV (RV168J)</td>
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<td>IDCRP-000-11</td>
<td>Hepatitis A Vaccine Response in HIV (RV168K)</td>
<td>Crum-Cianflone</td>
<td>All IDCRP-000 Sites</td>
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<tr>
<td>IDCRP-000-12</td>
<td>Prevalence and Predictors of HIV Progression (RV168L)</td>
<td>Crum-Cianflone</td>
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<td>IDCRP-000-13</td>
<td>Factors associated with HAART initiation (RV168M)</td>
<td>Johnson/Agan</td>
<td>All IDCRP-000 Sites</td>
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<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>
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<tr>
<td>IDCRP-000-15</td>
<td>Obtaining data for “Resistance Database Initiative” acceptance study (RV168O)</td>
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<td>IDCRP-000-16</td>
<td>Causes of hospitalization in HIV (RV168P)</td>
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<td>IDCRP-000-17</td>
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<td>IDCRP-000-18</td>
<td>Pharmacogenomics of protease-inhibitor Response in HIV (RV168R)</td>
<td>Weintrob</td>
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<td>IDCRP-000-19</td>
<td>Correlation of CD8+ cells and HAART Failure (RV168S)</td>
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<td>IDCRP-000-20</td>
<td>Pneumonia in HIV (RV168T)</td>
<td>Johnson</td>
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<td>IDCRP-000-21</td>
<td>Hepatitis E infections in HIV (RV168U)</td>
<td>Crum-Cianflone</td>
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<td>IDCRP-000-22</td>
<td>Vitamin D, Testosterone, DEXA and Osteoporosis in HIV (RV168V)</td>
<td>Sherwood/Aronson</td>
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<tr>
<td>IDCRP-000-23</td>
<td>Extreme Phenotype Genetics (RV168W)</td>
<td>Michael</td>
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<td>IDCRP-000-27</td>
<td>Hepatitis B vaccine response in HIV (RV198)</td>
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<td>IDCRP-000-28</td>
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<td>IDCRP-000-29</td>
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<td>20 Year Epidemiology of Syphilis in HIV (RV207)</td>
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<td>IDCRP-000-31</td>
<td>Atazanavir</td>
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</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. |
IDCRP Finances

The IDCRP funds awarded to USU for research in the IDCRP network for FY10 are $17.9M. With the addition of leveraged resources from collaborators this will reach $21.5M in FY10.

Funding Sources for IDCRP in FY 2010

The majority of IDCRP funding has historically been through the InterAgency Agreement between USU and the NIAID.

In FY10 a total of $6.21M in outside funds and $3.66M in leveraged funds were added.

FY10 outside funding is further broken down in the table to the left.

Leveraged funds are the resources, primarily laboratory testing that are delivered by collaborating investigators in IDCRP protocols.

DRMRP – Deployment Related Medical Research Program

CDC – Centers for Disease Control and Prevention

BUMED – Navy Bureau of Medicine and Surgery

TIDOS – Trauma Infectious Diseases Outcome Study

GEIS – DoD Global Emerging Infections Surveillance System

ARIC – Acute Respiratory Infection Consortium

NIAID – National Institute of Allergy and Infectious Diseases
A seen in the figure above, the majority of IDCRP expenses are spent on personnel to staff the network clinical sites and Program Coordinating Center at USU. The expenses for the largest studies are broken down in the table below. At the initiation of the IDCRP in 2006 RV-168 was 100% of the protocol expense, with expansion of the General Infectious Diseases Working Group this has diminished to less than 50% for the first time in FY09.
IDCRP Publications

Cumulative IDCRP Presentations and Publications

- Presentations
- Publications
GID Related 2009 Publications and Presentations:

Research-related publications (reverse chronological order)


Published Case Reports, Reviews, Letters, and other publications


Submitted Research-Related Manuscripts


2009 Infectious Disease Society of America meeting, Philadelphia, PA

1. Poster #214: PAIGE WATERMAN, GLENN WORTMANN, MICHAEL P. KOZAR. “Colistin Concentration from Antibiotic-Impregnated Orthopedic Beads.”


3. Poster #216: MICHAEL J. ZAPOR, MELISSA BARBER, AMY SUMMERS, GEORGE MILLER, LEE A. FEENEY, LYNN E. EBERLY, GLENN WORTMANN. “In Vitro Activity of the Aminoglycoside Antibiotic Arbekacin against Acinetobacter baumannii-calcoaceticus Isolated from War Wounded at Walter Reed Army Medical Center.”


7. Poster #840: JULIE AKE, GLENN WORTMANN, PAUL SCOTT, MIKELJON NIKOLICH, ZHINING WANG, XIAOZHE HUANG, AMY WEINTROB, MELISSA BARBER, DAVID VAN ECHO, EMIL LESHO. “Host Nation Patient MDRO Colonization/Infection is Linked to Environmental Contamination in a Military Field Hospital.”

8. Poster #841: AMY C. WEINTROB, MELISSA BARBER, AMY M. SUMMERS, MOLLIE P. ROEDIGER, XIAOZHE HUANG, MIKELJON P. NIKOLICH, GLENN W. WORTMANN. “Incident Colonization with Gram Negative Multidrug Resistant Organisms (MDRO).”


10. Poster #881: MARK D. JOHNSON, CAREY SCHLETT, GREG A. GRANDITS, KATRIN MENDE, TIMOTHY J. WHITMAN,


12. Poster #LB-1: NANCY F. CRUM-CIANFLONE, PATRICK BLAIR, DENNIS FAIX, JOHN ARNOLD, SARA ECHOLS, STERLING SHERMAN, JOHN TUELLER, TYLER WARKENTIEN, GABRIELA SANGUINETI, MARY BAVARO, BRADEN HALE. “Epidemiologic Characteristics of the Novel H1N1 Influenza A Virus: Investigation of an Early Outbreak among U.S. Military Beneficiaries.”

12th Annual Force Health Protection Conference


2. Dr. David Tribble and LTC Michael Ellis. “Combating Skin and Soft Tissue Infections Associated with Community-Associated Methicillin-Resistant Staphylococcus aureus in Military Personnel.”

HIV/STI Related 2009 Publications and Presentations:

Research-related publications (reverse chronological order)


11. Crum-Cianflone, Nancy; Dilay, Angelica; Collins, Gary; Asher, Dean; Campin, Richard; Medina, Sheila; Goodman, Zach; Parker, Robin; Lifson, Alan; Capozza, Thomas; Bavaro, Mary; Hale, Braden; Hames, Charles. Nonalcoholic Fatty Liver Disease Among HIV-Infected Persons. *JAIDS* 50(5):464-73, 2009Apr 15.


in the incidence of cancers among HIV-infected persons and the impact of antiretroviral therapy: a 20-year cohort


Clark RA, Dolan MJ, Ahuja SK. HIV-1 disease-influencing effects associated with ZNRD1, HCP5 and HLA-C alleles are
attributable mainly to either HLA-A10 or HLA-B*57 allelic loss. *PLoS ONE* 3(11):e3636, 4 Nov 2008.

on monocytes and T cells by HIV via type I interferon: restricted expression of type I interferon receptor by CCR5-

19. Weintrob AC, Fieberg AM, Agan BK, Ganesan A, Crum-Cianflone NF, Marconi VC, Roediger M, Fraser SL, Wegner SA,
Wortmann GW. Increasing Age at HIV Seroconversion From 18 to 40 years is associated with favorable virologic


**Published Case Reports, Reviews, Letters, and other publications**


22. Walley NM, Julg B, Dickson SP, Fellay J, Ge D, Walker BD, Carrington M, Cohen MS, de Bakker PI, Goldstein DB,
Shianna KV, Haynes BF, Letvin NL, McMichael AJ, Michael NL, Weintrob AC. The Duffy antigen receptor for chemo-

Monitoring of Antimycobacterial Drugs in Patients with Both Tuberculosis and Advanced Human Immunodefi-


25. Crum-Cianflone NF, Weekes J, Bavaro M. Review: thromboses among HIV-infected patients during the highly

**Accepted Research-Related Manuscripts**

26. Amy C, Weintrob, Greg A. Grandits, Brian K. Agan, Anuradha Ganesan, Michael L. Landrum, Nancy F. Crum-
Cianflone, Erica N. Johnson, Claudia E. Ordóñez, Glenn W. Wortmann, Vincent C. Marconi, and the IDCRP HIV
Working Group. Virologic Response Differences between African Americans and European Americans Initiating
Highly Active Antiretroviral Therapy with Equal Access to Care. Accepted JAIDS.

27. Anuradha Ganesan, Pratip K. Chattopadhyay, Tess M. Brodie, Jing Qin, Wenjuan Gu, John R. Mascola, Nelson L.
Michael, Dean A. Follmann, Mario Roederer and the IDCRP HIV WG. Immunological and Virological Events in Early HIV Infection Predict Subsequent Disease progression. Accepted *J Infect Dis.*


Submitted Research-Related Manuscripts


2009 Infectious Disease Society of America meeting, Philadelphia, PA

1. **Poster #320:** ERICA JOHNSON, MOLLIE ROEDIGER, MICHAEL LANDRUM, ANURADHA GANESAN, NANCY CRUM-CIANFLONE, AMY WEINTROB, R. VINCENT BARTHEL, BRIAN AGAN. “Factors associated with HAART initiation in an open access cohort.”

2. **Poster #323:** NANCY F. CRUM-CIANFLONE, GREG GRANDITS, ANURADHA GANESAN, AMY WEINTROB, MICHAEL LANDRUM, ROBERT V. BARTHEL, BRIAN AGAN, and the Infectious Disease Clinical Research Program. “Trends in Hospitalizations among HIV-Infected Persons during the Late HAART Era: What are the Impact of HAART Use and CD4 Counts?”

3. **Poster #342:** NANCY F. CRUM-CIANFLONE, MOLLIE ROEDIGER, LYNN E. EBERLY, ANURADHA GANESAN, AMY WEINTROB, MICHAEL LANDRUM, ROBERT V. BARTHEL, KURT VYAS, BRIAN AGAN, and the Infectious Disease Clinical Research Program. “Obesity among HIV-Infected Persons: Impact of Weight on CD4 Cell Counts.”

4. **Poster #356:** DAVID K. BYERS, BARNETT T. GIBBS, JASON M. BLAYLOCK, GAUTAM NAYAK, MICHAEL FERGUSON, DAVID R. TRIBBLE, CHAD K. PORTER, CATHERINE F. DECKER. “Longitudinal Assessment of Pulmonary Arterial Hypertension in Asymptomatic HIV-Infected Patients.”

5. **Poster #369:** JASON M. BLAYLOCK, BARNETT T. GIBBS, DAVID K. BYERS, GAUTAM NAYAK, MICHAEL FERGUSON, DAVID R. TRIBBLE, CHAD K. PORTER, CATHERINE F. DECKER. “Longitudinal Assessment of Cardiac Diastolic Function in HIV-Infected Patients.”

2009 International AIDS Society, Cape Town, South Africa


International Workshop on HIV Observational Databases (HIV Cohorts Meeting), Lisbon, Portugal


2009 CROI - Montreal, Canada - IDCRP Poster Presentations


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