PARTNER MILITARY COMMANDS

IDCRP Program Coordination Center at USU
Walter Reed National Military Medical Center
Walter Reed Army Institute of Research
Military HIV Research Program
Naval Medical Research Center
US Army Medical Research Institute of Infectious Diseases
Armed Forces Health Surveillance Center

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VISION
To substantially reduce the impact of infectious diseases in the military population through collaborative clinical research.

MISSION
To conduct multicenter infectious diseases clinical research, focusing on high-impact cohort and interventional trials, to inform and improve care of the Warfighter.

THE INFECTIOUS DISEASE CLINICAL RESEARCH PROGRAM (IDCRP)
was founded in 2005 under an interagency agreement between the Uniformed Services University of the Health Sciences (USU) and the National Institute of Allergy and Infectious Diseases (NIAID). The work of the program, executed through a unique, adaptive and collaborative clinical research network, has a direct impact on force readiness by advancing clinical practice and informing health policy for military personnel.

In collaboration with partners from the Department of Defense (DoD), academia, government and industry, IDCRP supports a broad clinical research portfolio within the Military Health System. From observational, longitudinal cohort studies to field-based interventional trials to evaluation of long-term health outcomes, IDCRP conducts protocols that address critical knowledge gaps in the control and prevention of infectious disease in the military. What is learned from these studies has far-reaching implications for public health and disease prevention beyond military communities.
As we end 2015, the Infectious Disease Clinical Research Program (IDCRP) marks our 10th anniversary providing innovative leadership in military multi-center clinical research. The sustained success rests on the robust partnership among the Uniformed Services University (USU), our Department of Defense (DoD) colleagues, and the National Institute of Allergy and Infectious Diseases (NIAID). IDCRP has set a new standard for Military Health System (MHS) collaborative clinical research through detailed strategic plans assuring high impact military medical research, rigorous scientific and ethical review, and a streamlined and effective regulatory process. The IDCRP is poised to continue leading within the new Defense Health Agency. This past year has seen continued evolution and success across all seven research areas: trauma related infections, deployment and travel related infections, human immunodeficiency virus infections, acute respiratory infections, skin and soft tissue infections, sexually transmitted infections and emerging infectious diseases/antimicrobial resistance. The program continues to produce impactful publications in peer-reviewed journals, while also generating high quality evidence for senior military leaders. Many successes are outlined in the report that follows.

As this year ends we have successfully enacted all major recommendations from the 2014 external program review. The IDCRP is now officially chartered as a DoD research program, formalizing the program’s mission and aims as well as operational and executive oversight. In addition, a critical reappraisal and approval of the program’s Strategic Plan has been completed. The Plan strengthens the pivotal role the program is tasked in support of DoD goals, as well as emphasizing the DoD, NIAID, and VA partnerships required to fulfill the IDCRP Mission. The Plan further clarifies the critical importance of our USU home and a robust and vibrant DoD partner network.

I wish to thank our USU leadership, our Steering Committee, the long-standing partnership with NIAID, and the effective implementation of our plans through the Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc. I also want to thank our DoD funding partners through the Defense Health Program, the Military Infectious Diseases Research Program, the Navy Bureau of Medicine and Surgery, and the Armed Forces Health Surveillance Center. This year we bid farewell and express gratitude to our outgoing Director, COL Scott Miller. In early 2016 we are pleased to welcome back CAPT Tim Burgess as our incoming Director. Lastly, our accomplishments are borne out through the hard work of our active duty and civilian investigators, the dedicated team of research professionals across the network, and most importantly the military service members and beneficiaries who volunteer to participate as research subjects.

It is a privilege to serve with such a great team.

David R. Tribble, MD, DrPH
Acting Director
DEPARTMENT OF DEFENSE SITES

U.S. Military Hospitals and Clinics
- Brooke Army Medical Center, San Antonio, TX
- Landstuhl Regional Medical Center (LRMC), Germany
- Madigan Army Medical Center (MAMC), Joint Base, Lewis McChord, WA
- Martin Army Community Hospital (MACH), Ft Benning, GA
- Naval Medical Center Portsmouth (NMCPR), VA
- Naval Medical Center San Diego (NMCSD), CA
- SAMHS—San Antonio Military Health System, TX
- Soto Cano Air Base, Honduras (JTF-Bravo)
- TAMC—Tripler Army Medical Center
- Troup Medical Clinic, Fort Sam Houston, TX
- U.S. Naval Expeditionary Base, Camp Lemonnier, Djibouti
- Walter Reed National Military Medical Center (WRNNMC), Bethesda, MD
- Womack Army Medical Center (WAMC), Ft Bragg, NC

U.S. Military Research Commands
- NMRC—Naval Medical Research Center
  - Enteric Diseases
  - Virology
  - Wound Infections
- NMRC—Subordinate Commands
  - Naval Health Research Center (NHRC), San Diego, CA
  - NAMRU-6—Naval Medical Research Unit No. 6 Lima, Peru
  - Naval Medical Research Center-Asia (NMRC-A), Singapore
  - Naval Medical Research Unit No. 3 (NAMRU-3), Cairo, Egypt
  - Naval Submarine Medical Research Laboratory (NSMRL)
- U.S. Army Institute of Surgical Research (USAIR)
- U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID)
- WRAIR—Walter Reed Army Institute of Research
  - Military HIV Research Program (MHRP)
  - Multidrug Resistant Network (MRSN)
  - Specimen Processing Lab (SPL)
  - Wound Infections
- WRAIR—OCONUS Laboratories
  - Armed Forces Research Institute of Medical Sciences (AFRIMS), Bangkok, Thailand
  - U.S. Army Medical Research Unit (USAMRU-K), Nairobi, Kenya
  - U.S. Army Medical Research Unit (USAMRU-G), Tbilisi, Georgia
  - U.S. Army Medical Materiel Development Activity (USAMMDA)

Other U.S. Military Commands/Programs
- Armed Forces Health Surveillance Branch (AFHSB)
- DoD Global Emerging Infection Surveillance (GEIS) Program
- Bureau of Medicine and Surgery, Department of Navy (BUMED)
- Navy Marine Corps Public Health Center (NMCPHC)
- Defense Health Agency (DHA)
  - Immunization Healthcare Branch—Military Vaccine Programs
  - Military Infectious Disease Research Program (MIDRP)
  - Congressional Defense Medical Research Program (CDMRP)

OTHER UNITED STATES OR FOREIGN GOVERNMENT AGENCIES
- National Institute of Allergy and Infectious Disease
  National Institutes of Health (NIAID/NIH)
  - Division of Clinical Research (DCR)
  - NIAID Flu Networks
  - Vaccine Research Center (VRC)
  - Division of AIDS (DAIDS)
- U.S. Department of Veterans Affairs
  - Atlanta Veterans Affairs Medical Center
  - South Texas Veterans Health Care System
  - St. Louis VA Medical Center
  - Veterans Aging Cohort Study
  - Veterans Affairs Connecticut Healthcare System
- Centers for Disease Control and Prevention (CDC)
- National Institutes of Health (NIH)—other collaborations
  - National Institutes of Mental Health (NIMH)
  - National Institute for Neurological Disease and Stroke (NINDS)
  - National Institute of Health Clinical Center (NINCC)
- United Kingdom Ministry of Defence
  - British Army Training Unit (BATUK), Nanyuki, Kenya
  - Camp Bastion, Afghanistan
  - Defence Statistics (Health) MOD Abbey Wood
  - Defence Medical Directorate, Birmingham
- Food and Drug Administration (FDA)

ACADEMIA
- Columbia University
- Harvard School of Public Health
- University of California Los Angeles
- University of Maryland—Baltimore
- University of Nebraska
- University of Pittsburgh
- University of Virginia
- University of Texas Health Science Center at San Antonio
- Vanderbilt University
- Emory University
- Johns Hopkins University
- University of California San Diego
- University of Minnesota
- University of Pennsylvania
- University of Vermont
- University of Washington
- University of Texas Medical Branch
- University of Texas San Antonio
- Yale University

RESEARCH ORGANIZATIONS AND INDUSTRY PARTNERSHIPS
- Leidos Inc.
- Scripps Research Institute
- NovaDigm Inc.
- Henry M. Jackson Foundation for the Advancement of Military Medicine
Acute respiratory infections (ARI) remain a major cause of disease among military personnel across the trainee, non-trainee, and deployed environments. In 2015, the ARI team continued the ARI natural history study conducted at five military medical treatment facilities across the U.S. with Fort Benning, GA added this past year focusing on military recruits. Working with NIAID collaborators, IDCRP developed and is validating Flu-PRO, a standardized measure of ARI symptoms and severity to apply to treatment/prevention trials and clinical practice. Dr. Mary Fairchok and colleagues found early use of antiviral therapy after influenza-like illness onset may reduce clinical severity compared to those who used the drug late, published in the *Journal of Clinical Virology*. A study funded by the MultiCare Institute for Research and Innovation and led by Dr. Fairchok, examined the association between Vitamin D concentration and ARI etiology and severity. The findings suggest that the use of Vitamin D supplementation during influenza-like illness onset may reduce symptom severity.

Notable findings from the ARI studies demonstrated only moderate influenza vaccine effectiveness with variation by year and flu subtype as well as higher protection among individuals <18 years. Annual receipt of influenza vaccine may be of some benefit by lessening symptom severity among those who do get certain influenza strains as reported by Dr. Robert Deiss. In the setting of influenza outbreaks or military deployments, a mass vaccination strategy may be required possibly using self-administration of live attenuated influenza vaccine (SA-LAIV). An IDCRP trial, led by CAPT Tim Burgess, demonstrated comparable SA-LAIV immunogenicity using either health-care worker administered vaccine or self-administration (Burgess et al., 2015; *Vaccine*). Researchers also examined ARI caused by human rhinovirus (HRV), one of the most prevalent viral respiratory pathogens in both civilian and military settings. Information on development of strategies for prevention of HRV disease and transmission and improved clinical management of severe HRV infection was also investigated (Chen et al., 2015; *Journal of Clinical Virology*). Additional case series studies, collaboration between IDCRP and Diatherix, examining epidemiology of other viral respiratory pathogens were conducted for adenovirus, respiratory syncytial virus, coronavirus, human metapneumovirus, and coxsackievirus/echovirus.

Future efforts include study of the epidemiology, immunology, and clinical characteristics of emerging novel respiratory pathogens and ARI in the military recruit and hospitalized settings. The ongoing large-scale natural history study will target populations with increased relevance for the military servicemen. Further randomized controlled treatment trials of hyperimmune anti-influenza plasma are planned for the coming fiscal year, and data from an ongoing trial of vaccine self-administration are being further analyzed. Data from these studies are critical for the development of novel diagnostic and treatment methods, as well as for planning of future treatment and prevention trials in military settings.
SEXUALLY TRANSMITTED INFECTIONS

Given the age and socio-demographics of military personnel, sexually transmitted infection (STI) prevalence remains higher among military members compared to civilian counterparts. Recently, research interest in STIs and their relevance to the military has grown, particularly given the inclusion of Neisseria gonorrhoeae by the CDC as one of the top three drug resistant threats in the U.S.

In 2015, five new STI research concepts were approved: two protocols focused on broadening the scope of the Gonococcal (GC) Resistance study, led by Dr. Grace Macalino, to include evaluating extragenital site testing among HIV+ individuals and HIV-negative women, investigations of the impact of rapid STI diagnostics on the treatment of Trichomonas vaginalis, the impact of more rapid turnaround time with GC/CT test results on clinical practices, and a study evaluating social and sexual networks among military members and their association with STI risk behaviors. The first annual STI Investigators Meeting (March 2015) was very successful, leading to better engagement with existing collaborators and addition of new partners. Dr. Elisabeth Kostas-Polston, faculty member in the USU Graduate School of Nursing, successfully submitted a Congressionally Directed Medical Research Program grant on human papillomavirus vaccine uptake among active duty service women. Fort Sam Houston collaborators on the GC Resistance study connected us to their colleagues at the Lackland Air Force Base basic training clinic, while Dr. Kostas-Polston has expanded our reach to include Ob-Gyn colleagues and clinics at both Walter Reed National Military Medical Center (WRNMMC) and Fort Bragg.

In addition, sexual risk behavior data from HIV NHS participants allows for important socio-behavioral STI research. Building on the foundation of the GC Resistance study, we now have access to populations of high-risk HIV-negative active duty members and have expanded our presence into clinical settings where STIs are being treated. Study recruitment has expanded to include asymptomatic individuals with a suspected STI and the collection of clinical outcomes has been added. The DoD GC Resistance Repository and Reference Laboratory, led by Dr. Ann Jerse within USU Microbiology and Immunology Department, is fully functional and provides support for the entire GC Resistance study effort. Recent efforts have supported DoD clinical and research labs providing quality assurance support to develop standards related to GC sensitivity testing.

- Sexual risk behavior analysis data from HIV Natural History Study related to STIs completing in 2016
- GC Repository agreements with the outside of Continental U.S. laboratory are complete and we have begun receiving isolates
- GC Resistance Study enrollment expanded to include asymptomatic individuals significantly increasing subject numbers
HIV remains a global threat and, thus, continues to be a research priority for the U.S. military. The HIV Research Area is focused on longevity, health, and function of HIV+ active duty and beneficiaries. Each year approximately 350 new HIV infections are diagnosed in the DoD associated with an additional estimated $80 million–$140 million in lifetime healthcare costs to DoD and Veterans Affairs health systems. The HIV research area addresses gaps in understanding HIV in the military and specifically aims to assess clinical practices that improve survival, minimize the development of AIDS and non-AIDS comorbidities, and maximize function, including fitness for duty, among those who are infected. The HIV program has grown around the 30-year HIV Natural History Study (NHS), which has enrolled over 5,950 HIV infected active duty members and beneficiaries since 1986. This military cohort of racially diverse, healthy, young individuals is representative of a large portion of those in the U.S. with HIV, but is unique among study populations due to routine screening for HIV resulting in early HIV diagnosis and management.

Led by Dr. Brian Agan, a recent focus of IDCRP HIV research has been non-AIDS comorbidities, as the population with HIV is aging to live near-normal lifespans, but appears to be experiencing cardiovascular disease, diabetes, and cancer at higher rates than those without HIV. A recently approved study of non-AIDS morbidities (DoD HIV Virtual Cohort) is designed to collect data of all HIV-infected active duty members and beneficiaries. This cohort will have a large HIV-negative control group for comparisons to determine risks for other diseases which could be attributable to HIV infection.

Four IDCRP sites are participating in the Strategic Timing of Antiretroviral Therapy (START) study, which evaluates the benefits of early HIV antiretroviral therapy. This study, conducted in collaboration with the multinational INSIGHT network, found that early initiation of antiretroviral therapy (at CD4 >500) results in decreased morbidity and mortality (Lundgren et al., 2015; New England Journal of Medicine). These findings have already impacted U.S. and international guidelines.

One comorbidity common among people with HIV is HIV associated neurocognitive disorder (HAND). Within the military, HAND is cited as a primary reason for limited duty status among infected service members, making the understanding and detection (screening tool) of HAND in the military setting essential. The ongoing DoD ALLHANDS study led by Dr. Agan aims to address these needs by conducting a longitudinal cohort study and validating a previously identified screening tool.
In 2016, work in sexually transmitted infection (STI) treatment and prevention among those with HIV is expected to expand with the addition of a social network questionnaire to the NHS. This will help identify risk factors for HIV and STI acquisition to inform future prevention studies. Currently, the first NHS risk behavior analyses are being finalized with preliminary results showing the proportion of subjects reporting men who have sex with men is higher compared to earlier DoD studies. While behavioral risk may have changed, this may also indicate a change in the military climate allowing individuals to feel more comfortable reporting the behavior.

Additionally, recent analyses have begun to shed light on the association between HIV and syphilis infection led by Dr. Anuradha Ganesan. Within the military as well as civilian populations, a large number of syphilis infections are occurring in people with HIV. Many of the syphilis cases, including in the NHS, are repeat infections, demonstrating an opportunity for preventive interventions.

Related to STI detection and surveillance, the NHS is being leveraged to conduct a new study led by Dr. Ganesan to examine: 1) prevalence of gonorrhea and chlamydia (GC/CT) infection and associated risk factors in people with HIV; 2) concordance between self- and provider-collected swabs for detecting GC/CT infection; 3) feasibility of performing self-administered rectal and pharyngeal swabs and oral rinses in HIV+ persons; and 4) performance of novel methods for identifying drug resistant Neisseria gonorrhoeae isolates. If self-testing is successful, this could increase testing and treatment rates and have widespread implications for HIV-infected service members in reducing the prevalence and potential transmission of these common STIs.
The Deployment and Travel Related Infections Research Area:
1) provides epidemiologic and clinical data including pathogen-specific estimates of disease incidence among deployed troops;
2) develops rapid, deployable diagnostic platforms for pathogen specific diagnoses; and 3) executes clinical trials and effectiveness studies to improve recommendations regarding primary prevention and treatment of infections during deployment.

In 2015, Madigan Army Medical Center and Landstuhl Regional Medical Center were added to the research area’s primary protocol investigating risk assessment, outcomes, and prevention of deployment and travel-related infections (TravMil) and have focused on the enrollment of active duty deployers. Efforts across all sites to maintain a majority of enrollees as active duty service members have been very successful (>70%).

Collaboration between IDCRP personnel from Madigan Army Medical Center and Naval Medical Center San Diego resulted in the enrollment of 50 service members deployed to Thailand as part of Operation Hanuman Guardian. Additionally, service members participating in the 2015 Pacific Partnership, whose deployment had a high risk of infectious disease threats, were enrolled. The first TravMil manuscript was published in the Journal of Travel Medicine (Lalani et al., 2015). Results from a pilot study evaluating detection limits of the Luminex PCR assay for enteropathogens were also published (Lalani et al., 2015; Diagnostic Microbiology and Infectious Diseases).

The Trial Evaluating Ambulatory Treatment of Travelers’ Diarrhea (TrEAT TD) study, led by CAPT Mark Riddle (Naval Medical Research Center; NMRC), continued enrollments at British Army Training Unit Kenya and Joint Task Force Bravo-Soto Cano Air Base. The acute watery diarrhea arm closed to enrollment in mid-2015. Enrollment for the dysentery/febrile arm will continue during the 2016 Cobra Gold exercise among deploying US military personnel in Thailand. DoD OCONUS laboratories, as well as the lab at Naval Medical Center Portsmouth, began preparations to screen for extended spectrum β-lactamase-producing isolates directly from initial and post-treatment stool along with archived Enterobacteriaceae isolates. The research team expects to analyze results starting in early 2016 and the investigative team will hold a TD management consensus symposium attended by military and civilian experts in April 2016.

Collaborators at the University of Virginia have completed development of a customized TaqMan Array for determining TD pathogen etiology. The next phase will involve validating assay
performance on stool samples and stool smears, using samples from DoD repositories, ongoing clinical trials and observational studies.

The Knowledge, Attitude, Practice and Outcomes Study (KAPOS) protocol, led by LTC(p) Patrick Hickey, is under review and will commence in 2016. A randomized, placebo-controlled rifaximin traveler’s diarrhea prevention study (Prevent TD), led by CDR Ramiro Gutierrez, was approved this year at three sites across the IDCRP network, which are gearing up to begin enrollment. Prevent TD will continue the successful collaboration with the UK military as done in TrEAT TD. In 2016, the research area will expand on this year’s successes with the initiation of new multicenter randomized trials, new enrollment sites emphasizing operational military locations, and a wealth of new data from both the high quality observational cohort study and interventional trials coupled with initial assessment and validation studies of the self-collected stool filter card and enteropathogen diagnostic panel. The first of many future IDCRP sponsored policy/guideline development efforts this coming year highlights the critical impact to inform and improve the care of the Warfighter.
Infectious complications of battlefield wounds are one of the major causes of death, morbidity, and disability during wartime. The Trauma Related Infections Research Area addresses knowledge gaps in prevention and clinical management. The Trauma Infectious Disease Outcomes Study (TIDOS), led by Dr. David Tribble, began in June 2009 and systematically collects medical management and clinical outcomes data from all levels of care on DoD personnel injured during deployment. Eligible subjects were given the opportunity to enroll in a longitudinal study, which follows them for a minimum of five years after initial hospital discharge. This study is being conducted in collaboration with Dr. Jay MacDonald and colleagues at the St. Louis Veterans Affairs Medical Center (VA), who collect medical information from enrolled subjects who register for care at the VA after leaving active military service.

With the cessation of combat operations in Afghanistan, enrollment in the TIDOS cohort concluded in January 2015 (total of 1,359 enrollees) with follow-up ongoing in the 1,300+ participants. During the past year, TIDOS researchers continued to conduct a comprehensive effort to capture wound-specific outcomes (i.e., timing of wound closure), as well as improve characterization of injuries that will ultimately impact clinical practice guidance recommendations. The first analysis of TIDOS enrollees who entered VA care was presented at the ID Week conference in San Diego this past year. This analysis highlighted the significant ongoing risk for new and recurrent infectious complications following cohort participants up to two years beyond initial hospitalization for traumatic injury.

Approval of data-sharing and ethical reviews was successfully completed by both the US DoD and the United Kingdom Ministry of Defence this past year. The first comparative analysis of TIDOS and the Wound Infection Surveillance Programme is moving forward and will investigate US and UK invasive fungal wound infection (IFI) rates and patient outcomes. Many surgical and medical practices are approached similarly; however, there are differences including Medevac/patient movement, damage control orthopedic surgery, and other trauma-related factors.

TIDOS HIGHLIGHTS

- Infection rate of 34% and 28% in personnel wounded in Afghanistan and Iraq, respectively.
- Compliance with Joint Trauma System antimicrobial prophylaxis recommendations with open fractures improved from 2009 to 2014.
- Open tibia case-control osteomyelitis risk factor analysis complete (highest risk of osteomyelitis with below knee amputations).
- IFI molecular diagnostics pilot study successful with 95% concordance between PCR-based results and histopathology.

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TIDOS TIMELINE

- 2004: Joint Theater Trauma Registry (JTTR) established.
- 2005: Joint Theater Trauma System established.
- OCT: Meeting to set priorities for IDCRP general infectious disease section—combat trauma infections and multidrug-resistant organisms (MDROs) a top concern.
- MAR–SEPT: Meetings held with clinical groups to develop collaborations.
- DEC: Discussions with USAISR to establish collaboration and development of a JTTR supplemental infectious disease (ID) module.
- JAN–JUN: Protocol and ID module development leading to SRB submission.
- SEPT: Memorandum of Understanding between USU and USAISR establishing ID module and DoDTR (formerly JTTR) (data-sharing).
- NOV: USU Scientific Review Board approval.
- FEB–APR: USU ID Institutional Review Board review and approval.
- MAY: Clinical site approval from WRAMC, NNMRC, BAMC, and LRMC.
- JUNE 01: TIDOS start date.
- TIDOS ID module data collection begins.
- TIDOS microbiological specimen repository established.
- TIDOS cohort enrollment begins.
- SEPT: Navy BUMED Wounded, Ill, and Injured (WII) funding support for TIDOS.
- MAY–JUN: Completion of 3-month interim analysis of inpatient and cohort data.
- JUN: VA Institutional Review Board approval for TIDOS-VA collaborations.
- JUL: TIDOS presents data at plenary Advanced Technology Applications for Combat Casualty Care (ATACCC) meeting.
wound care (e.g., negative pressure wound therapy; NPWT), and post-injury antibiotic prophylaxis selection. Given the commonalities of the combat trauma populations, there is a great opportunity to compare wound infection epidemiology and clinical outcomes in an effort to investigate best practices in surveillance, prevention, and treatment, to inform future guidance in other military engagements.

Multidrug-Resistant and Virulent Organisms (MDR/VO) initiative, a substudy of the TIDOS project led by Dr. Katrin Mende, received funding this past year and is anticipating a series of analyses of laboratory results this coming year. The MDR/VO project is a collaborative effort involving USU and multiple DoD clinical laboratories, maximizing understanding of complex polytrauma wounds such as bacterial antagonism, resistance impact, biofilm, and exploration of the complex polymicrobial combat wound.

Leveraging TIDOS data, an IFI molecular diagnostic retrospective study on archived tissue specimens led by Dr. Anuradha Ganesan is being performed to evaluate the use of multiplex polymerase chain reaction (PCR)-based methods in identifying molds in patients at risk for IFI. Collaboration with the DoD Joint Pathology Center is underway, which will allow critical assessment of diagnostic techniques with eventual translation of validated improved methods for future clinical use. Another trauma-related protocol focused on combat trauma-associated osteomyelitis led by Dr. Tribble completed a case-control risk factor analysis related to open tibial fractures. Other osteomyelitis analyses related to open fractures of the femur and arm long bones are expected to be completed during 2016. A collaboration with the VA has also been established this past year and will extend the follow-up period as well as investigating impact on other health conditions, healthcare utilization and cost impact. The research area continues a robust agenda emphasizing the critical need to sustain peacetime efforts to improve understanding, prevention, and management of battlefield trauma infectious complications to provide DoD with best practice guidance for future conflicts.
Skin and soft tissue infections (SSTI) impose significant health and operational burdens on military personnel. *Staphylococcus aureus* is a major cause of SSTI, and an increasing proportion of community-acquired *S. aureus* infections are caused by methicillin-resistant *S. aureus* (MRSA) strains that have been associated with complicated infections. Prevention of SSTI remains a major priority for the military medical community, particularly in recruit settings.

The objective of the SSTI program is to determine effective strategies for SSTI prevention and control among military populations. The current research area portfolio includes studies of the epidemiology, clinical characteristics, immunology and microbiome of SSTI in military settings. With respect to *S. aureus*/MRSA, there are laboratory-based investigations to elucidate mechanisms of disease pathogenesis and to better understand the evolution and divergence of disease-causing strains. These data will strengthen the overall foundation of knowledge regarding SSTI risk and yield new insights for the development of future SSTI treatment and prevention strategies.

In 2015, the investigative team, led by LTC Michael Ellis, completed a SSTI case-control study enrolling >3,000 military trainees at Fort Benning, GA. In addition to the conventional epidemiologic methods, this multi-disciplinary effort also included several aims to study the molecular epidemiology, immunology and microbiome-related aspects of SSTI. This protocol has advanced the current understanding of the molecular relatedness of clinical and colonizing strains of *S. aureus*, immune responses, and features of the host microbiome which may impact susceptibility to *S. aureus* acquisition and disease. The team also launched an observational, longitudinal cohort study to capture: (1) events of acquisition and colonization that typically precede individual SSTI episodes, and (2) temporal/spatial dynamics of *S. aureus* transmission and SSTI in the exposure setting of the military training environment. In 2016, the investigative team will begin an evaluation of *S. aureus* colonization and SSTI among submarine crews embarking on extended deployments.

Vaccination for *S. aureus* remains the optimal strategy for the prevention of infection. In 2015, the investigative team partnered with NovaDigm Therapeutics, Inc. to propose a field-based, Phase 2 trial evaluating the safety, immunogenicity and efficacy against nasal acquisition of a novel vaccine candidate, NDV-3A. Should funding support be secured, this trial will be executed in 2017 with participation from the Fort Benning training population.
Establishing rapid response capacity to combat emerging infectious diseases is critical to maintaining health for the Warfighter over time. Recent experience of Ebola virus disease (EVD) in West Africa and the consequent military response demonstrated that any outbreak worldwide can pose a threat to military forces. Additionally, the continuing outbreak of chikungunya virus and its spread from the Caribbean to South America puts our deploying forces at risk. The Emerging Infectious Diseases and Antimicrobial Resistance (EIDAR) research area has implemented clinical research protocols to evaluate the etiology, epidemiology, clinical presentations and outcomes of such infections.

In 2015, EIDAR established the capacity for DoD to participate in a multi-site clinical trial with a large consortium to test EVD treatment at MTFs. A contingency protocol (Epidemiology, Immunology and Clinical Characteristics of Emerging Infectious Diseases with Pandemic Potential [EpiCC]) was approved, allowing the collection of data and samples in a natural history study of both viral hemorrhagic fevers and severe acute respiratory infections in the Military Health System. A protocol was also approved to compare the immune response between those vaccinated against anthrax versus those with natural infection utilizing banked sera at the US Army Medical Research Institute for Infectious Diseases.

In collaboration with the Trauma Infectious Disease Outcomes Study, the Multidrug-Resistant and Virulent Organisms Initiative, a collaborative effort across DoD laboratories led by Dr. Katrin Mende, was established to expand our understanding of the complex microbiology inherent within combat wounds in order to lead to novel countermeasures. Furthermore, a carbapenem-resistant Enterobacteriaceae (CRE) study has been established to evaluate the incidence, prevalence, transmission patterns and antimicrobial resistance mechanisms of CREs. Collaborations are also planned between EIDAR and Deployment and Travel Related Infections research area to include new sub-studies from TravMil (Lt Col Heather Yun) and TrEAT TD (CAPT Mark Riddle) protocols, examining antibiotics for traveler’s diarrhea and multidrug-resistant organisms.

In 2016, the EpiCC contingency protocol will be expanded to other DoD partner clinical sites. A virtual cohort, led by Dr. Julie Pavlin, will also be established to determine the natural history of chikungunya infection with studies to determine risk factors for long-term sequelae with funding support from the Military Infectious Disease Research Program. In addition, EIDAR is planning new research concepts to evaluate emerging pathogens that may impact service members, including the Southwest/Western US endemic fungal infection, Coccidiomycosis, and a newly emergent tickborne pathogen, *Borrelia miyamotoi*. The EIDAR research area continues to evolve and remain responsive to emergent infection concerns impacting the military.
DATA COORDINATION CENTER AND BIOSTATISTICS

The Data Coordination Center (DCC), data hub for IDCPR research, is staffed by a team of talented data system designers, data managers, data entry staff, and SAS and Oracle programmers led by Mr. Ed Parmelee. The DCC provides expertise to principal investigators for the conceptualization, design, collection, management and cleaning, analysis, and publication of research study data.

The DCC utilizes multiple systems to receive data in either paper or electronic format; these include traditional desktop/laptop based electronic data capture (EDC), tablet-based EDC, web-based survey tools, and form scanning. Use of these myriad systems allows the IDCPR to enroll and collect data from subjects at medical treatment facilities and other collaboration sites around the world. The DCC continues to explore new methodologies to collect and manage data.

In 2015, the DCC worked with investigators to establish several process improvements including such critical needs as standardized case report forms and a framework for a standardized data dictionary. The DCC has also led efforts, through Defense Health Agency data-sharing agreements, to acquire Military Health System Data Repository (MDR) data in support of major IDCPR studies, the HIV Natural History Study and the Trauma Infection Disease Outcomes Study. This initiative will be increasingly important for all IDCPR research areas.

In the upcoming year, the DCC plans to continue to develop capabilities for managing data for FDA-regulated studies, execute data dictionary framework, select and install a new EDC system, improve data querying processes, expand the use of MDR as a data source to additional studies, including virtual cohort studies, explore use of MDR data to confirm or replace data collection at sites, and develop requirements to replace the current subject registry.

REGULATORY AFFAIRS, CLINICAL OPERATIONS, SCIENTIFIC REVIEW AND MONITORING

The IDCPR Regulatory Affairs team consists of staff at the network MTFs and IDCPR Program Coordination Center (PCC) coordinated by Mr. John Morais. Under the direction of the PCC Regulatory Affairs Coordinator, program personnel perform essential duties that include protocol development, rigorous pre-review of planned Institutional Review Board (IRB) submissions, consulting with investigators during the IRB review process, coordinating with IRB staff to address concerns, conducting on-site quality assurance and auditing, tracking study milestones, and maintaining regulatory documents for the program. Site staff ensures all local implementation requirements are met, and communicated regularly to the PCC.

The USU Infectious Disease (ID) IRB, established in 2008 via a Memorandum of Understanding (MOU), created a single review pathway for multi-center ID research within the military health system, and eliminated the need for multiple and repetitive scientific, ethical, and second level reviews at the medical treatment facilities. The ID IRB is composed of representatives of military treatment and research facilities participating in the IDCPR network and members who provide representation and/or advocacy for particular subgroups. With these resources and the unique military perspective behind them, the ID IRB fulfills its duty to safeguard the rights and welfare of human subjects. They are supported by a dedicated team in the Human Research Program Protections Office at USU. The IDCPR leadership is working closely with the USU Human Protections leadership to provide a renewal of the MOU incorporating the Defense Health Agency this coming year.

The IDCPR Regulatory Affairs staff, NIAID Office of Clinical Research Policy and Regulatory Operations monitors, and USU ID IRB staff continue to work collaboratively to advance ethical, multicenter, militarily-relevant infectious disease research within the University and DoD.
STATE OF THE ART SPECIMEN REPOSITORIES

The program maintains study-specific repositories of host (e.g., blood), diagnostic (e.g., nasal wash) and/or pathogen (e.g., bacterial culture) specimens. IDCRP partners in the maintenance and application of these collections with groups such as the Military HIV Research Program, USU Department of Microbiology and Immunology, and the San Antonio Military Medical Center. This vast collection of human and microbiologic specimens is invaluable for studies of disease pathogenesis, the host immune response, and the development and evaluation of novel diagnostic methods.

EDUCATION AND MENTORSHIP

IDCRP has an education and mentorship program designed to foster growth of the next generation of clinical researchers in infectious diseases and related public health disciplines in the armed forces. The program assists in the development of a clinical research capstone curriculum and projects for medical students specializing in infectious diseases. IDCRP also creates and coordinates opportunities for medical and graduate students, residents and clinical fellows to conduct mentored research within the IDCRP community. In addition, the program provides support to IDCRP mentors and trainees to facilitate successful research experiences. The education program also supports the Armed Forces Infectious Disease Society (AFIDS) and Continuing Medical Education activities at WRNMMC.

CURRENT PROGRAM AND 2015 TOTALS AT A GLANCE

30 Trainees

- 21 trainees involved in active projects
  - Infectious Diseases—7 fellows from all 3 Department of Defense programs
  - Internal Medicine—6 residents in 5 programs
  - Pathology—1 resident
  - Surgery—3 residents (2 Orthopedics, 1 General Surgery)
  - Preventive Medicine—2 residents
  - Graduate Program at USUHS—11 DrPH, 1 PhD
  - Graduate Program at Baylor University—1 MS (Nutrition Sciences)

- 11 trainees participated in TrEAT TD rotations in Honduras
  - Infectious Diseases—1 fellow
  - Internal Medicine—8 residents in 5 programs
  - Preventive Medicine—1 resident
  - Graduate Program at USUHS—1 MTM&H

Presentations

15 trainee presentations at national conferences

Publications

7 trainee papers accepted by peer-reviewed journals

Awards

- ID Week Scholarship Grant (IDCRP)—C. Berjohn
- Emma L. Bockman Memorial Award (USU)—R. Johnson
- Norman T. Kirk Award (Society of Military Orthopedic Surgeons)—L. Lewandowski
Executive Steering Committee (ESC)

- Chief, Division of Clinical Research (DCR), National Institute of Allergy and Infectious Diseases (NIAID)
- Dean, School of Medicine, Uniformed Services University of the Health Sciences (USU)
- Director, Research, Development and Acquisition, Defense Health Agency

Operational Steering Committee (OSC)

- Surgeon General Infectious Disease Consultants—Army, Navy, Air Force
- Director, Armed Forces Health Surveillance Center
- Director, Military Infectious Diseases Research Program, MRMC
- Chief, Collaborative Clinical Research Branch, DCR, NIAID
- Chair, Department of Preventive Medicine and Biometrics, USU
- VA Representative (non-voting)
- HJF Representative (non-voting)

Program Coordination Center (PCC)

Scientific Directorate
- Science Director
- Science Deputy Director
- Research areas
  - Research area directors and lead clinical research managers
- Data Coordination Center
  - Data configuration
  - Data management
  - SAS programming
  - Oracle programming
- Education

NIAID Liaison
- Chair, Scientific Review Board

Deputy Director
- Research Administration
- Regulatory Affairs

Partnering Networks

- Military Hospitals
- Military Research and Development Commands
- Military Public Health Commands
- Non-DoD Partners
FY15 Protocol Expenses by Research Area
- 39% Human Immunodeficiency Virus
- 20% Trauma Related Infections
- 17% Deployment and Travel Related Infections
- 12% Acute Respiratory Infections
- 7% Skin and Soft Tissue Infections
- 4% Sexually Transmitted Infections
- 1% Emerging Infectious Disease and Antimicrobial Resistance

FY15 Expenses by Sponsor
- 13% US Navy Bureau of Medicine and Surgery
- <1% Center for Disease Control
- 15% Defense Health Program
- 2% Defense Medical Research and Development Program
- 3% Global Emerging Infections Surveillance and Response System
- <1% International Network for Strategic Initiatives in Global HIV Trials, NIAID Division of AIDS
- 1% Military Infectious Diseases Research Program
- 64% National Institute of Allergy and Infectious Disease
- <1% US Army Medical Material Development Activity
- 2% Uniformed Services University of the Health Sciences