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Mr. Chairman, Members of the Committee, thank you for the opportunity to appear before you today to discuss medical research in the Military Health System (MHS) and, in particular, our research collaborations across government, academia, and industry.

The MHS is a complex system that weaves together health care delivery, medical education, public health, private sector partnerships and cutting edge medical research. Research in the MHS is the engine to integrate and embed emerging evidenced-based practices into a learning health care system in which the health care providers, scientists, systems, and patients participate in the generation of knowledge on trends in health and illness, the testing and identification of best practices, and the assessment of the impact of practice changes.

Research by the MHS has played a significant role in the performance of military trauma care over the last 13 years of war. As the war progressed, we improved survivability rates – although the severity of injuries increased. Today, we deliver the highest survivability rates in the history of warfare and that survivability is coupled with greater post-injury quality of life. These notable achievements reflect the return on investment by MHS research in combat casualty care, traumatic brain injury (TBI), psychological health and suicide, rehabilitation and regenerative medicine, military operational medicine, military infectious diseases, and medical training and simulation. I will highlight achievements in some of these areas as well as our collaborations across government, academia and industry.

Combat Casualty Care Research

Accomplishments in combat casualty care have led to the fielding of safe and effective tourniquets, improved hemostatic dressings, as well as numerous clinical practice guidelines to improve trauma care on the battlefield. A significant enabler in these accomplishments is the

Joint Trauma System or JTS which has developed into the Department of Defense's (DoD) "go-to" entity for real-time process improvement to optimize survival and recovery of the warfighter. The swift translation of evidence from military research through the JTS to the battlefield represents a first in military medical history. The JTS maintains the Department of Defense Trauma Registry (DoDTR) which is the largest repository of combat injury and trauma management information in history. In this capacity, the JTS and the process it supports serve as a fitting "bedside" to generate many of the clinical questions that need answers from military medical and trauma research.

Recently, MHS researchers collaborating with industry received Food and Drug Administration approval for a hemostatic device for the control of bleeding from junctional wounds in the groin or axilla not amenable to tourniquet application. In addition, the MHS is conducting advanced development efforts on a dried plasma product to help control hemorrhage on the battlefield. Other research efforts investigate genetic, genomic, and immunological responses to trauma and hemorrhage and finding improved means to reduce hypothermia.

Documenting and Sharing Lessons Learned

Advances in trauma care stemming from the military's learning health system have been accelerated by the unprecedented burden of injury resulting from the wars in Afghanistan and Iraq. While the more than 30 Clinical Practice Guidelines maintained by the JTS are evidence based, they are also responsive and practical. Reports on the translation of advances in military trauma care to the civilian community have become increasingly common. We are taking intentional steps to codify and garner the lessons within the military's learning health care

system and promote their translation to the civilian sector in partnership with the Institute of Medicine.

Vaccine Research

As a final step towards FDA licensure in the United States, a clinical trial of a third generation smallpox vaccine, already approved in Europe and Canada, is about to start in U.S. forces stationed in South Korea. The DoD is participating in the clinical trial with the vaccine manufacturer and has designated a staff member from the U.S. Army Research Institute of Infectious Diseases to serve as the DoD principal investigator. The new product is a modern smallpox vaccine that does not replicate in human cells and is expected to be a safe alternative for individuals who have certain contraindications to the current smallpox vaccine.

National Interagency Biodefense Campus

The National Interagency Biodefense Campus (NIBC) is a prime example of interagency collaboration and includes not only DoD, but the HHS' National Institute of Allergy and Infectious Diseases, the Centers for Disease Control and Prevention, and the Departments of Agriculture (USDA) and Homeland Security (DHS). Key DoD components of the NIBC are the U.S. Army Medical Research Institute of Infectious Diseases and the U.S. Navy Medical Research Center. The NIBC is leading in the development of medical counter measures as well as enhancing the US response to emerging threats and national emergencies and is one of the Nation's few laboratory centers with Biosafety level 3 and 4 laboratories conducting world class research against the world's most dangerous pathogens such as viral hemorrhagic fevers and plague. The

NIBC is a part of the larger interagency confederation known at the National Interagency for Biological Research (NICBR).

U.S. Army Medical Research Institute of Chemical Defense

With your support the DoD has invested significantly in the U.S. Army Medical Research Institute of Chemical Defense (MRICD) with a recapitalization project. The MRICD is currently at the 95% stage of construction completion for a new Command and state of the art laboratory building. They are scheduled to occupy the new building in early January 2015. The MRICD is the Nation's Center of Excellence for medical chemical defense research. Their world renowned scientists conduct basic and applied research on the mechanisms of action of chemical warfare threat agents, toxic industrial chemicals, and toxins of biological origin. These hazardous chemicals and toxins endanger not only our deployed our military forces but also pose an extremely serious homeland security threat to our entire civilian population as recent events in the Middle East have shown. The MRICD operates on a whole of government approach by being the premier laboratory to research candidate pretreatment, prophylactic, and treatment compounds. These compounds establish a scientific and technical base from which to plan and formulate enhanced medical countermeasures for our entire population. Their efforts have produced many candidates for transition into the advance development arena. Their scientists are on point to investigate medical countermeasures for all non-traditional agents as well as any emerging chemical threat agent regardless of the source. The MRICD also provides consultative subject matter expertise on medical chemical defense issues. They educate and train the full spectrum of military / civilian first responders and medical professionals in the identification and management of chemical casualties. Many of our allied partners have recently sent personnel to be trained in their courses so they can treat chemical casualties no matter the circumstances.

Rehabilitation and Regenerative Medicine Research

Due to advances in combat casualty care, increasing numbers of Service members are surviving with extreme trauma to the extremities and head. Research by the MHS in rehabilitation and regenerative medicine focuses on definitive and rehabilitative care innovations required to reset Service members, both in terms of duty performance and quality of life. The program has multiple initiatives to achieve its goals, including improving prosthetic function, enhancing self-regenerative capacity, improving limb and organ transplant success, creating full functioning limbs and organs, repairing damaged eyes, treating visual dysfunction following injury, improving pain management, and enhancing rehabilitative care. Innovative reconstructive research supported by the MHS in partnership with Brigham and Women's Hospital has performed successful face transplants on patients with severe facial deformity to provide functional and aesthetic benefits. In addition, research supported by the MHS in partnership with Johns Hopkins Hospital performed a bi-lateral hand transplant on a Service member who lost all four limbs from a road side bomb in Iraq. Today that Service member has achieved significant function in both hands. Regenerative medicine technologies present many opportunities for the treatment of combat-related traumatic injury and the MHS is supporting the Armed Forces Institute of Regenerative Medicine-Warrior Restoration Consortium to position promising technologies and therapeutic/restorative practices for entrance into human clinical trials. The Warrior Restoration Consortium is a partnership with more than 30 academic institutions and industry partners to address five focus areas in: extremity regeneration; craniomaxillofacial regeneration; skin regeneration; genitourinary/lower abdomen

reconstruction; and composite tissue allotransplantation (i.e., organ transplant from a donor) and immunomodulation or modification of the immune response.

Research to Improve Mental Health for Service Members and Military Families: The National Research Action Plan

Although significant and continuing improvements in combat casualty care and personal protective equipment have limited fatal injuries, many Service members return with TBI, Post Traumatic Stress Disorder (PTSD), suicidal thoughts or behaviors, and comorbidities. These comorbidities include depression; substance abuse related to alcohol, tobacco, and other drugs, including the misuse and abuse of prescription drugs; and chronic pain, all of which can complicate the prevention and treatment of PTSD, TBI, and suicidal behaviors. Family members also are affected by the multiple stressors associated with deployment and reintegration. Overall, the need for mental health services for Service members and their family members is anticipated to increase in coming years.

To improve prevention, diagnosis, and treatment of mental health conditions affecting veterans, Service members, and military families, the President issued an Executive Order in 2012 directing Federal agencies to develop a coordinated National Research Action Plan (NRAP). The Departments of Defense, Veterans Affairs, Health and Human Services, and Education responded with a wide-reaching plan to improve scientific understanding; provide effective treatment; and reduce occurrences of PTSD, TBI, various co-occurring conditions, and suicide.

The NRAP, released in August 2013, is a strategic blueprint for interagency research to identify and develop more effective diagnostic and treatment methodologies to improve

outcomes for TBI, PTSD, and related conditions as well as develop and test suicide risk assessments and suicide prevention and treatment interventions. These efforts include collaborative research on biomarkers to detect disorders early and accurately; safe and effective treatments to improve function and quality of life; and developing a more precise definition of mTBI. The NRAP includes clear timelines and goals to achieve the same level of urgency, specificity of deliverables, as well as accountability, as expressed in the Executive Order. It is important to note that improving mental health outcomes for Service members and Veterans and the NRAP are included in the newly-established Cross-Agency Priority Goal framework overseen by the Office of Management and Budget and the Performance Improvement Council. The Cross-Agency Priority Goal, *Improving Mental Health Outcomes for Service members and Veterans*, was announced on March 10, 2014, and will continue over a three year period. Leadership will report quarterly to the Office of Management and Budget on their progress under the Goal.

Critical to the implementation of the NRAP is a continuing understanding of the agency-specific activities and assuring a collaborative and integrated research strategy to meet the requirements in the NRAP. This collaboration and integration is provided in an annual Joint Review and Analysis meeting on research related to PTSD, TBI, suicide prevention, and substance abuse. Agency representation at the meeting included DoD, the Department of Veterans Affairs (VA), the Department of Education (represented by the National Institute on Disability and Rehabilitation Research [NIDRR]), and Health and Human Services (represented by the National Institute of Neurological Disorders and Stroke, the National Institute of Mental Health, and the National Institute on Drug Abuse).

MHS researchers are attempting to answer questions across the research continuum. However, fundamental gaps in scientific knowledge remain, such as: the lack of a clinically-useful definition for mild TBI (mTBI)/concussion makes it difficult to adequately diagnose this condition. Note mTBI and concussion are used interchangeably herein. For mTBI, improved techniques are needed to determine if symptoms are attributable to the traumatic event. Prevention and treatment interventions are needed that address the comorbidities that often occur with PTSD. Evidence-based approaches are limited for reducing suicide risk, and the relationships between PTSD, TBI, suicide, and co-occurring conditions are not well understood.

Activities are underway in support of inter-agency collaboration, including the DoD's Systems Biology Program and the Millennium Cohort and Family Cohort Studies, the VA's Million Veteran Program, the National Institutes of Health (NIH) biomarker research program, and research dedicated to advancing prevention and treatment interventions. The DoD and the Centers for Disease Control are partnering with the Brain Trauma Foundation to develop a clinically useful definition of mTBI/concussion. Suicide prevention research includes the DoD's Military Suicide Research Consortium and the National Institute of Mental Health and DoD Army Study to Assess Risk and Resilience in Service members (Army STARRS) program.

Data-sharing efforts include the DoD/NIH Federal TBI Research Informatics System for TBI clinical research (a central repository for new TBI-related data that links to existing databases to facilitate sharing of information), the VA computing infrastructure, and NIDRR's TBI Model Systems National Database, which contains retrospective data on the clinical progress and outcomes of individuals with moderate to severe TBI.

Recently initiated activities include two new joint funded DoD and VA research consortium efforts with academia to support PTSD and TBI biomarker studies. The Consortium

to Alleviate PTSD is a new research effort focused on biomarker discovery and development with the aim of identifying biomarkers for subacute and chronic PTSD that can be used for therapeutic and outcome assessment. This represents a major investment to advance knowledge related to biomarkers and clinical utility. The Chronic Effects of Neurotrauma Consortium will establish the association of the chronic effects of mTBI and common comorbidities; determine whether there is a causative effect of chronic mTBI/concussion on neurodegenerative disease and other comorbidities; identify diagnostic and prognostic indicators of neurodegenerative disease and other comorbidities associated with mTBI/concussion; and develop and advance methods to treat and rehabilitate chronic neurodegenerative disease and comorbid effects of mTBI/concussion.

The MHS is funding a wide variety of studies relevant to military family members, including research focused on: understanding risk and resilience factors of military families and communities; suicide bereavement in Service members and their families; interventions to enhance resilience, address and prevent relationship problems, and support families during deployment; the effectiveness of web-enhanced support tools for military families; and the effects of military deployment of parents on adolescent mental health

Conclusion

Scientific progress is incremental and takes time, but Service members and their family members need more effective prevention strategies and treatments, so our research mission is urgent. I am both pleased and proud to be here with you today to represent the men and women who perform the research mission of the MHS, and I look forward to answering your questions.