**Component:** DHA  
**Topic #:** DHA201-001  
**Title:** Diagnostic Platform for Rapid Identification of Pathogens in Infected Wounds that is Useable in a Battlefield Environment  
**Technology Areas:** Bio Medical  
**Acquisition Program:** Office of the Principal Assistant for Acquisition- USAMRDC

**OBJECTIVE:** Develop state-of-the-art diagnostic technology for rapid identification of pathogens in infected wounds that can be used to triage injured warfighters and guide clinical decisions in a modern battlefield environment.

**DESCRIPTION:** U.S. military service members who are medically evacuated from theatre due to combat-related injuries have sustained high impact insults such as explosions, gunshot wounds and motor vehicle accidents, leading to significant skin and soft tissue injuries that may be frequently contaminated. A large proportion of these service members are at increased risk for infectious complications of their traumatic injuries, and the most common infections involve skin and soft tissue, wound infections, and osteomyelitis and sepsis if not treated in a timely manner. Acinetobacter baumannii has been identified as one of the most frequently associated organisms with skin and soft tissue infections among wounded warriors, occurring in 35% of wound infections. Within this 35%, up to 90% of the culture isolates were assessed to be antimicrobial resistant (AMR) [1]. Community-acquired methicillin-resistant Staphylococcus aureus (CA-MRSA) is a well-recognized cause of skin and soft tissue infections (SSTI) in US military hospitals with a reported prevalence of 68% to 70% in selected military hospital emergency rooms [2]. High rates of MRSA skin and soft tissue infections have been observed among soldiers in training [3,4]. In addition to skin and soft tissue infection, MRSA is the most frequently isolated organism late in infection in traumatically injured service members [5]. Late infection in this population often results in limb salvaging amputation [6]. Pseudomonas aeruginosa and Klebsiella pneumoniae are responsible for significant morbidity and mortality among both civilian and military populations, often colonizing mucosal surfaces, wounds, and foreign devices such as catheters and endotracheal tubes with biofilms that are highly resistant to antibiotic penetration and clearance by the immune system. In civilian and veteran populations these same types of infections frequently occur in individuals that have skin and soft tissue and prosthetic joint infections [4,5]. In a patient infected with multi-drug resistant organisms, the treatment choices often become limited due to waning approvals of new antibiotics [6]. Frequently, these patients are hospitalized for prolonged periods of time and subsequently experience multiple episodes of hospital readmissions related to infectious complications of their wound or orthopedic implants. In addition to increased patient morbidity, provision of medical care for service members with infected traumatic wounds can be very costly and lead to intense resource utilization.

Early diagnosis of infection in injured warfighters could provide early guidance to caregivers. Treatment of chronic infections are less successful, so the goal is to improve early detection and rapid intervention before the infection is established and progressing. Current diagnostic systems are complex with often multiple steps from sample processing to interpretation, are often restricted to fixed laboratories, require cold chain for reagents, and not available to front line users. This effort seeks to support development of novel approaches to detect infected wounds at the bedside or in the field to rapidly inform medics and early caregivers on best approaches to wound and infection management.

**PHASE I:** Selected contractor determines the feasibility of the concept by developing a prototype diagnostic assay that has the potential to meet the broad needs discussed in this topic description. Currently there are no FDA-cleared, field-capable assays that can be used to rapidly identify the most common bacterial pathogens causing wound and sepsis infections as described in references 1-6 (to include but not limited to the ESKAPE group of pathogens: Enterococcus spp., Staphylococcus aureus, Klebsiella pneumonia, Acinetobacter baumannii, Pseudomonas aeruginosa, Enterobacter spp, and Escherichia coli), as well as an ability to determine the respective antibiotic susceptibility of the detected pathogen to guide treatment decisions for wound infections in injured warfighters. Development of an assay for the detection of bacterial infections with MDR bacteria is therefore a high priority. In some infections, a possibility of multiple pathogens and bacterial strains can be present within a single sample, so the assay must be sensitive and specific enough to identify each pathogen.

**PHASE II:** Based on the results from Phase I, the selected contractor provides up to 3 Initial lots of 250 prototype assays each to the COR. These initial lots will be evaluated for sensitivity and specificity using a diversity set of bacterial strains for evaluation in vitro, then if efficacious for analysis of samples (blood and tissue, or directly) from preclinical animal infection studies. Can coordinate with
WRAIR/NMRC for assistance with preclinical evaluation if needed. Feedback regarding the sensitivity/specificity of each lot of prototype assays will be provided to the contractor. This data will then be used to optimize each subsequent lot of assays. The goal in Phase II is the development of a prototype assay that provides 85% sensitivity and 85% specificity when compared to current bacterial culture and antibiotic susceptibility testing methods. Once sensitivity and specificity requirements have been met in preclinical tests, the selected contractor will confirm the performance characteristics of the assay (sensitivity, specificity, positive and negative predictive value, accuracy and reliability) using clinical specimens. The regulatory strategy for using different types of clinical specimen should be clearly described in the Phase II proposal. Human use protocols for using clinical specimen should be approved by Institutional Review Board (IRB) of all participating institutes. The elected contractor will require a Federal-Wide Assurance of Compliance before government funds can be provided for any effort that requires human testing or uses of clinical samples. The selected contractor will also conduct stability testing of the prototype device in Phase II. Stability testing will follow both real-time and accelerated (attempt to force the product to fail under a broad range of temperature and humidity conditions and extremes) testing in accordance with FDA requirements. The assay must be rapid (<30 min), soldier-friendly (i.e., easy to operate), inexpensive, portable, and stable (no requirement of refrigeration). The assay should be at least 85% as sensitive and specific as current (non-deployable, non-FDA cleared) assays and sera, plasma, whole blood, or other types of specimen can be used without sample processing. The data package plan required for application to the U.S. Food and Drug Administration will be prepared at the end of phase II.

PHASE III DUAL-USE APPLICATIONS: During this phase the performance of the assay should be evaluated in a variety of field studies that will conclusively demonstrate that the assay meets the requirements of this topic. The contractor may coordinate with WRAIR/NMRC to set up field testing sites. The selected contractor shall make this product available to potential military and non-military users throughout the world. Military applications: MDR bacterial infections occur worldwide. The diagnosis of these wound infections and sepsis cases are often delayed, because the currently available tests, mostly reliant on bacterial culture or high-complexity nucleic acid amplification, are not field-capable, not rapid, and can vary considerably among different laboratories even when using the same procedure or method. With the availability of an easy and rapid assay developed under this topic, wounded and ill soldiers can be treated in a timely manner in any military medical organization (such as a Battalion Aid Station, a Combat Support Hospital, Forward operation base, or a fixed medical facility). The contractor should coordinate with WRAIR/NMRC to establish a National Stock Number (NSN) for potential inclusion in into appropriate "Sets, Kits and Outfits" that are used by deployed medical forces. Civilian applications: MDR bacterial infections occur in communities and hospitals, in wounds, skin and soft tissue infections, pneumonia, and blood stream infections. We envision that the contractor that develops the rapid diagnostic assay and will be able to sell and/or market this assay to a variety of civilian medical organizations, and that this market will be adequate to sustain the continued production of this device.

REFERENCES:


KEYWORDS: Wound Infections, ESKAPE, AMR, Diagnostic