Seroprevalence, seroincidence and immunologic response studies to inform recommendations for tick-borne encephalitis virus (TBEV) vaccination in U.S. Service Members serving in the EUCOM AOR

Tick-borne encephalitis virus (TBEV), one of six tick-borne flaviviruses that can cause disease in humans, is an emerging infectious pathogen of growing concern in Europe, Russia and the Far East. Mortality rates range between 0.5% and 35% and survivors often experience long-term neurologic sequelae. TBEV transmission is widespread within the USEUCOM AOR, and disease burden is among the highest in the world in areas where U.S. military personnel are currently operating. TBEV vaccines have been licensed and available in Europe for several decades, but until recently, were not approved in the US. In 2018, following a risk assessment released by the Armed Forces Medical Intelligence Center, the USEUCOM Surgeon made a direct request for the advancement of one or more of the EMA approved TBEV vaccines to approval by the FDA. This request was subsequently echoed in a memorandum from the USEUCOM and NATO Supreme Allied Commander to the Assistant Secretary of Defense for Health Affairs. An integrated product team was formed, with WRAIR Emerging Infectious Disease Branch providing expertise and consultation. A risk assessment and sampling framework was developed for two retrospective studies: 1) TBEV vaccine recipient study to describe the immunologic response in U.S. service members who received one or more doses of a European-approved TBEV vaccine; and 2) a seroprevalence and seroincidence study of U.S. military personnel stationed in TBEV-endemic regions of USEUCOM to define the post-exposure seroprevalence and risk of TBEV infection. As of February 2022, approximately 350 serum samples from U.S. Service Members were identified for the vaccine recipient study and 4,000 from U.S. Service Members who served in high incidence areas of Germany and the Baltic States (Lithuania, Latvia, Estonia) in the period between 2009 and 2019 for the seroprevalence and seroincidence study. The performance of commercially available screening antibody assays was evaluated on reposed sera from DoDSR for soldiers with known TBEV vaccine exposure (at least one dose). This identified a screening antibody performance gap that impacted the feasibility of the diagnostic plan proposed for the seroprevalence and seroincidence study. We identified a novel, highly sensitive and highly specific laboratory-developed screening antibody assay developed at the Bundeswehr that could be tech-transferred to WRAIR for use as screening assay. The research portfolio of vaccine recipients and seroprevalence studies will be presented to the Advisory Committee on Immunization Practices.