The American Society of Tropical Medicine and Hygiene (ASTMH)—the principal professional membership organization representing, educating, and supporting scientists, physicians, clinicians, researchers, epidemiologists, and other health professionals dedicated to the prevention and control of tropical diseases—appreciates the opportunity to submit written testimony to the House Committee on Appropriations Subcommittee on Defense. According to Lt Gen Patricia Horoho, “historically, infectious diseases are responsible for more U.S. casualties than enemy fire.” Emerging infectious diseases do not recognize borders and “deficiencies in international state preparedness to address them remain a threat. Continued progress to address these emerging threats requires ongoing commitment to funding, developing personnel with expertise in infectious diseases, and maintaining stateside and overseas laboratory infrastructure and overseas field sites for clinical studies and response to contingencies.”

ASTMH respectfully requests that the Subcommittee expand funding for the Department of Defense’s (DoD) longstanding efforts to develop new and more effective drugs, vaccines, and diagnostics designed to protect our forces from infectious diseases, including funding for the important research efforts at the Walter Reed Army Institute of Research (WRAIR) and the U.S. Naval Medical Research Center (NMRC).

Tropical Medicine and U.S. Military Operations
The term “tropical medicine” refers to the wide-ranging clinical, research, and educational efforts of physicians, scientists, and public health professionals with a focus on the diagnosis, prevention, and treatment of diseases prevalent in the areas of the world with a tropical climate (but are also increasingly seen with the populations fleeing civil conflict as well as leisure travelers exploring new locations). Tropical diseases have the ability to blind, disable, disfigure, and can lead to death. Most tropical diseases are located in sub-Saharan Africa, parts of Asia (including the Indian subcontinent), Central and South America, and parts of the Middle East. These are the same areas where military troops are often deployed. Since many of the world’s developing nations and economies are located in these areas, tropical medicine tends to focus on diseases that impact the world’s most impoverished individuals.

DoD Research Protects the U.S. Military and Civilians and Contributes to Global Health
DoD’s Global Emerging Infections Surveillance and Response Systems (GEIS) enhances force health protection and global health security by focused coordination and support of international civil and military health networks to prevent, detect, and respond to emerging and priority microbial threats through infectious diseases surveillance, laboratory harmonization, capacity building, and scientific studies. During Operation United Assistance, the response to the most recent Ebola outbreak, the DoD has leveraged global health and medical countermeasure programs already in place, to support efforts in Ebola vaccine and therapeutic development, diagnostics and laboratory support, and training to ensure the safety of care providers and patients. Looking forward, more enduring support for tropical medicine/global health in those areas affected is warranted. Biosurveillance and response measures for emerging pathogens must be in place prior to the next event and ensure a timely and efficient response.

1 Prepared Statement of Lieutenant General Patricia D. Horoho, The Surgeon General, United States Army before the U.S. Senate Appropriations Committee, Subcommittee on Defense.
A core component of the ASTMH membership works with and supports the work of the DoD, and we understand first-hand the important role that research and development play in protecting the warfighter from the threat of infectious diseases, as well as making meaningful contributions to civilian health. Specifically, DoD infectious disease research contributes to:

- The protection of U.S. troops deployed, or likely to be deployed, in many tropical and limited resource areas;
- The safety of U.S. citizens, working, traveling, participating in volunteer work, and vacationing overseas who are impacted by these same tropical diseases;
- Protecting the U.S. from agents responsible for these diseases, which could be introduced and become established in the U.S. (as was the case with West Nile virus), or might even be weaponized; and
- Positively impacting people around the world who suffer disability and death from many of these same tropical diseases.

**Walter Reed Army Institute of Research**

A large part of DoD investments in infectious disease research and development are facilitated through WRAIR. Some of WRAIR’s major accomplishments include:

- Conducted clinical trials of a *P. vivax* vaccine candidate, the first human subject challenge model to test vaccine efficacy;
- Developed the world’s only dedicated cutaneous leishmaniasis drug development program;
- First identified HIV-1 heterosexual transmission and showed efficacy of an HIV vaccine, through the Military HIV Research Program; and
- Developed new Japanese encephalitis and hepatitis A vaccines. ²

WRAIR has advanced its work through critical public private partnerships and collaborative efforts with entities such as

- GlaxoSmithKline and Sanofi;
- Non-profit organizations such as the Bill & Melinda Gates Foundation, Medicines for Malaria Venture, and PATH;
- Universities such as the University of Maryland and SUNY Upstate Medical University; and,
- Other U.S. agencies including the Centers for Disease Control and Prevention (CDC), USAID, and the National Institutes of Health (NIH).

WRAIR worked in collaboration with PATH Malaria Vaccine Initiative and GlaxoSmithKline to develop the malaria vaccine candidate, RTS,S, which recently underwent the first ever large-scale Phase 3 trial for a malaria vaccine. The vaccine candidate was shown to decrease clinical episodes of malaria in children in Africa and may protect them for up to 18 months. While we await the final RTS,S results and the promise that it brings for children living in malaria-endemic countries, RTS,S is not suitable as a vaccine for adults who have never experienced malaria during childhood, such as our military personnel. As a result, there remains a significant need for continued research funding in order to achieve more robust results.

WRAIR is headquartered in Silver Spring, Maryland, and has facilities around the globe including U.S. Army Medical Research Unit—Europe (USAMRU-E) in Heidelberg, Germany; U.S. Armed Forces Research Institute of Medical Sciences (AFRIMS) in Bangkok, Thailand; U.S. Army Medical Research Unit in Nairobi,

Kenya (USAMRU-K)\(^3\). This diversity in research capacity puts WRAIR in a unique leadership position in research and development for tropical diseases—research that aids our military men and women as well as people living in disease-endemic countries.

**United States Naval Medical Research Center**

NMRC and its affiliated labs conduct basic and applied research in infectious diseases. NMRC is an active participant in global health security efforts and focuses on mitigating the spread of antimicrobial resistance and malaria. The Infectious Disease Directorate (IDD) of NMRC focuses on malaria, enteric diseases, and viral and rickettsial diseases. IDD conducts research on infectious diseases that are considered to be a significant threat to our deployed sailors, marines, soldiers, and airmen.

The primary objective of the Navy Malaria Program is to develop a vaccine that kills the parasite during the first few days of development in the liver, before it breaks into the blood. The program is also investigating vaccines that would target blood-stage infection to limit the severity of symptoms associated with this stage. Both of these vaccines could alleviate much of the suffering caused by this parasite in tropical areas.

The research is enhanced by IDD’s close working relationship with the Navy’s three overseas medical research laboratories located in Peru, Egypt, and the Pacific region. These laboratories, like those of WRAIR, afford diplomatic advancement through the close working relationships they have developed with governments and citizens of those countries. ASTMH has heard first-hand accounts of the successful diplomatic impact that both the WRAIR and NMRC overseas laboratories have on the communities where they are guests. Many of the researchers and staff who work in the laboratories are local to the area and speak highly of the role and contributions of the U.S. military laboratories.

**Case Studies - The Importance of DoD’s Infectious Disease Research Efforts**

Malaria claimed 540,000 lives in 2013, according to the latest World Health Organization (WHO) estimates, and prevention remains a global health priority. *Malaria has resulted in the loss of more person-days among U.S. military personnel than to bullets during every military campaign fought in malaria-endemic regions during the 20th century.*

Because service members deployed by the U.S. military comprise a majority of the healthy adults traveling each year to malarial regions on behalf of the U.S. government, the U.S. military has understandably taken a primary role in the development of antimalarial drugs. Nearly all of the most effective and widely used antimalarials were developed in part by U.S. military researchers, which is a remarkable accomplishment. Drugs that now continue to save civilians throughout the world were originally developed by the U.S. military to protect troops serving in tropical regions during WWII, the Korean War, and the Vietnam War.

In recent years the broader international community has increased its efforts to reduce the impact of malaria in the developing world, particularly by reducing childhood malaria mortality, and the U.S. military plays an important role in this broad partnership. Nonetheless, military malaria researchers at NMRC and WRAIR are working practically alone in the area most directly related to U.S. national security: drugs and vaccines designed to protect or treat healthy adults with no developed resistance to malaria who travel to malaria-endemic regions. NMRC and WRAIR are working on the development of a malaria vaccine and on malaria diagnostics and other drugs to treat malaria—an especially essential investment as current malaria drugs face signs of drug resistance.

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\(^3\) WRAIR Website: http://wrair-www.army.mil/WRAIRSubordinateCommands.aspx
The latest generation of malaria medicines is increasingly facing drug-resistance, which heightens the threat to global health security. The most deadly variant of malaria parasite—*Plasmodium falciparum*—is believed by the World Health Organization to have become resistant to “nearly all antimalarials in current use.” The malaria parasite demonstrates a notorious and consistent ability to quickly develop resistance to new drugs. Malaria parasites in Southeast Asia have already shown resistance to the most recently developed anti-malarial drug, artemisinin, and the specter of truly untreatable malaria is a “real and present danger.”

Developing new antimalarials as quickly as the parasite becomes resistant to existing ones is an extraordinary challenge, and one that requires significant resources before resistance becomes widespread, especially as U.S. military operations in malaria-endemic countries of Africa and Asia increase. Without new antimalarials to replace existing drugs as they become obsolete, military operations could be halted in their tracks by malaria. The 2003 malaria outbreak affecting 80 of 220 Marines in Liberia is an ominous reminder of the impact of malaria on military operations. Service members returned to Liberia last October for Operation United Assistance, an operation supporting the U.S. Agency for International Development-led efforts to contain the Ebola virus outbreak in western Africa. However, the threat malaria was much greater than Ebola. At the time, an Army Captain was quoted as saying, “Right now, based on current statistics, someone who is unprotected from malaria has a 50 percent chance per month of getting malaria in Liberia. Mathematically, statistically, in every way you look at it, malaria is the biggest killer.”

Humanitarian missions also place Americans at risk of malaria, as evidenced by several Americans contracting malaria while supporting Haitian earthquake relief efforts.

Leishmaniasis is a vector-borne disease that comes in several forms, the most serious of which is visceral leishmaniasis (VL), which affects internal organs and is deadly if left untreated. According to the WHO, there are 1.3 million new cases of leishmaniasis annually and it kills between 20,000 and 30,000 people. VL has between 200,000 and 400,000 new cases annually. Co-infection of leishmaniasis and HIV is becoming increasingly common, and WHO notes that because of a weakened immune system, leishmaniasis can lead to an accelerated onset of AIDS in HIV-positive patients.

Because of leishmaniasis’ prevalence in Iraq and Afghanistan, DoD has spent time and resources on the development of new diagnostics and new drugs for the treatment of cutaneous leishmaniasis. As more troops return from Iraq and Afghanistan, it is likely DoD and the Department of Veterans Affairs will see an increase in leishmaniasis cases in our soldiers. WRAIR discovered and developed a topical treatment for cutaneous leishmaniasis that, once FDA approved, will be the world’s first topical treatment for this chronic and disfiguring disease. While essential for the safety of our servicemen and women abroad, these types of innovations will also be extremely beneficial to at-risk populations worldwide living in leishmaniasis-endemic countries.

Dengue fever (“breakbone fever”), according to the WHO, is the most common of all mosquito-borne viral infections. About 2.5 billion people live in places where dengue infection can be transmitted by mosquitoes, and last year we saw cases that were transmitted by local mosquitoes in the U.S. There are four different viruses that can cause dengue infections. While infection from one of the four viruses will'

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6 World Health Organization: http://www.who.int/mediacentre/factsheets/fs375/en/
leave persons immune to that strain of the virus, it does not prevent them from contracting the other three, and subsequent infections can often be more serious. The DoD has seen about 28 cases of dengue in soldiers per year. While none of these cases resulted in the death of a soldier, hospitalization time is lengthy. As troops rebalance to the Pacific, they will deploy to areas plagued with dengue. Experts predict that infectious diseases will be the primary cause of hospitalization of U.S. military in the Asia-Pacific region. Currently, there are several research and development efforts under way within the DoD both for treatments and vaccines for dengue.

**U.S. Government Action is needed for Mission Readiness**

Recent events only strengthen the case for increased investments in research and development that will protect our troops, prepare us for the foremost health security threats, and enable us to prevent and control the spread of infectious diseases and respond to the potential challenge of drug resistance. A more interconnected world is increasing opportunities for infectious diseases to emerge and spread globally, as demonstrated with last year’s Ebola outbreak. Considered to be the worst in history, the outbreak impacted nine countries including the U.S. More than 25,000 people were infected and over 10,000 people died worldwide. The outbreak underscored the need for a robust U.S. investment in R&D that will enable us to have the necessary tools at the ready for the next infectious disease global health challenge.

The role of infectious diseases in the success or failure of military operations is often overlooked. Even a cursory review of U.S. and world military history, however, underscores that the need to keep military personnel safe from infectious diseases is critical to mission success. Ensuring the safety of those men and women in future conflicts and deployments will require research to develop new tools. Additional funds and a greater commitment from the federal government are necessary to make progress in tropical diseases prevention, treatment, and control.

Although several promising new infectious disease drugs are in development at WRAIR and NMRC, the U.S. government’s funding level for these programs has been anemic for several years. There are indications that the current budget process may decrease or not keep up with medical research inflation, let alone increase in real dollars, despite burgeoning evidence that many of our military’s current drugs are rapidly approaching obsolescence.

Fortunately, a relatively small amount of increased funding for this program would restore the levels of research and development investment required to produce the drugs that will safeguard U.S. troops. In relation to the overall DoD budget, funding for infectious diseases research programs is very small. While we understand there are tough choices to make in this fiscal environment, cutting funding for this program would deal a major blow to the military’s efforts to reduce the impact of these diseases on soldiers and civilians alike, thereby undercutting both the safety of troops deployed to tropical climates and the health of civilians in those regions.

ASTMH feels strongly that increased support for efforts to reduce this threat is warranted and we look forward to collaborating with the Subcommittee on efforts to maximize the health and safety of all military troops. A more substantial investment will not only help to protect American soldiers, but potentially save the lives of millions of individuals around the world. We thank you for your leadership and appreciate the opportunity to share our views in our testimony. Please be assured that ASTMH stands ready to serve as a resource on this and any other tropical diseases policy matter.