2015 Fact Sheet
Mefloquine Exposure

BACKGROUND
The drug mefloquine hydrochloride (previously marketed as Lariam®) is an anti-malarial drug that was developed by the United States military during the 1970s at the Walter Reed Army Institute of Research (WRAIR) as a replacement for chloroquine. Since its introduction mefloquine has been widely provided to U.S. Special Forces and to hundreds of thousands of troops on large deployments including to Somalia, Iraq, and Afghanistan. Mefloquine has a long history of causing many disturbing side effects, the severity of which is only now becoming apparent.

As early as 1973 in the first human Phase I trials, researchers found that mefloquine was associated with transient dizziness. By 1981, vertigo accompanied by confusion had been noted in Phase II trials. By 1983, serious psychiatric effects including hallucinations, disorientation, and transient confusion were commonly reported. By the time of mefloquine’s U.S. licensure in 1989, the product insert emphasized the risk of, “dizziness, and disturbed sense of balance or neuropsychiatric reactions,” and warned, “If signs of unexplained anxiety, depression, restlessness or confusion are noticed, these may be considered prodromal to a more serious event.” By 1994, the U.S. product insert warned of risk of, “encephalopathy of unknown etiology,” and that dizziness and psychiatric effects could continue even after therapy. By 2008, following reports of persistent vertigo lasting as long as 12 months, the U.S. product insert was updated to warn that in, “a small number of patients, dizziness and loss of balance have been reported to continue months after mefloquine has been stopped.”

IMPORTANCE
Over the last ten years, it has become increasingly clear that the use of mefloquine is accompanied by a greatly increased risk of severe neurological damage. In 2012, at a Senate Appropriations, Subcommittee on Defense hearing, testimony was offered that toxicity of mefloquine was the “third signature injury” of modern war, alongside Post-Traumatic Stress Disorder (PTSD) and Traumatic Brain Injury (TBI). Additionally, military authors at the Center for Disease Control have stated that along with the problems the drug can directly cause, it can also, “confound the diagnosis and management of PTSD and TBI.” Recently, the dangers of mefloquine exposure has been further brought to light with the Department of Defense’s (DOD) decision on 13 April 2013 to revise and update the DOD Guidance on Medications for Prophylaxis of Malaria to sharply restrict the use of the drug and label it as a “last resort” drug. These concerns were further amplified by the FDA's decision on 29 July 2013 to require a black box label on mefloquine, warning of a risk of serious psychiatric and neurologic effects, some of which could be permanent. Fortunately, the last decade has seen the development of multiple safe and effective alternatives to mefloquine. In acknowledgement of the availability of safer drugs, on 13 September 2013 the U.S. Army’s Special Operations Command (USASOC) issued specific orders prohibiting the use of the drug outright. However the drug otherwise remains available for use across the military services, and few resources are available to help those suffering its long-term effects.

RECOMMENDATION
The Association of the United States Navy recommends ceasing the distribution of mefloquine to service members for the prevention of malaria, except in cases of declared national emergency where the distribution is absolutely necessary. Congress, with its oversight authority, should establish legislation requiring DOD to report on the availability of mefloquine alternatives, and the progress of all scientific studies on the drug’s toxicity and to estimate of the number of servicemembers previously exposed to the drug. Additionally, DOD should expand the mission of the Hearing Center of Excellence, the Vision Center of Excellence, and the Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury to include diagnosis and management of servicemembers suffering detrimental effects of mefloquine. Lastly, DOD should develop and implement policies to effectively evaluate military disability claims regarding adverse effects of mefloquine exposure.