OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

JUL - 8 2010

The Honorable Carl Levin
Chairman, Committee on Armed Services
United States Senate
Washington, DC 20510

Dear Mr. Chairman:

This letter provides the final report to Congress pursuant to Section 737 of the National Defense Authorization Act for Fiscal Year 2006. Section 737 requests the Secretary of Defense conduct a study of adverse health events that may be associated with the use of antimalarial drugs, including mefloquine, also known as Lariam. Earlier reports (February 2007 and March 2009) described studies of the Armed Forces Epidemiology Board and the Deployment Health Research Center concerning mefloquine use among Service members, as well as the Armed Forces Institute of Pathology (AFIP) study of suicides in deployed and recently deployed Service members.

Although a link between mefloquine use and suicides is not apparent, suicides continue to be a significant issue in which DoD is fully engaged to determine the cause and develop and implement preventive measures. The enclosed report describes some of the activities undertaken to help better understand and prevent suicides within DoD.

Thank you for your continued support of the Military Health System.

Sincerely,

Charles L. Rice, M.D.
President, Uniformed Services University of the Health Sciences
Performing the Duties of the Assistant Secretary of Defense (Health Affairs)

Enclosure:
As stated

cc:
The Honorable John McCain
Ranking Member

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

JUL - 8 2010

The Honorable Susan Davis
Chairwoman, Subcommittee on Military Personnel
Committee on Armed Services
U.S. House of Representatives
Washington, DC 20515

Dear Madam Chairwoman:

This letter provides the final report to Congress pursuant to Section 737 of the National Defense Authorization Act for Fiscal Year 2006. Section 737 requests the Secretary of Defense conduct a study of adverse health events that may be associated with the use of antimalarial drugs, including mefloquine, also known as Lariam. Earlier reports (February 2007 and March 2009) described studies of the Armed Forces Epidemiology Board and the Deployment Health Research Center concerning mefloquine use among Service members, as well as the Armed Forces Institute of Pathology (AFIP) study of suicides in deployed and recently deployed Service members.

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Charles L. Rice, M.D.
President, Uniformed Services University of the Health Sciences
Performing the Duties of the Assistant Secretary of Defense (Health Affairs)

Enclosure:
As stated

cc:
The Honorable Joe Wilson
Ranking Member

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

JUL - 8 2010

The Honorable Ike Skelton
Chairman, Committee on Armed Services
U.S. House of Representatives
Washington, DC 20515

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Enclosure:
As stated

cc:
The Honorable Howard P. "Buck" McKeon
Ranking Member

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

JUL - 8 2010

The Honorable James H. Webb
Chairman, Subcommittee on Personnel
Committee on Armed Services
United States Senate
Washington, DC 20510

Dear Mr. Chairman:

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Performing the Duties of the Assistant Secretary of Defense (Health Affairs)

Enclosure:
As stated

cc:
The Honorable Lindsey O. Graham
Ranking Member

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

JUL - 8 2010

The Honorable Daniel K. Inouye
Chairman, Subcommittee on Defense
Committee on Appropriations
United States Senate
Washington, DC 20510

Dear Mr. Chairman:

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Charles L. Rice, M.D.
President, Uniformed Services University of the Health Sciences
Performing the Duties of the Assistant Secretary of Defense (Health Affairs)

Enclosure:
As stated

cc:
The Honorable Thad Cochran
Ranking Member

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

JUL - 8 2010

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United States Senate
Washington, DC 20510

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cc:
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Ranking Member

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

JUL - 8 2010

The Honorable David R. Obey
Chairman, Committee on Appropriations
U.S. House of Representatives
Washington, DC 20515

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Enclosure:
As stated

cc:
The Honorable Jerry Lewis
Ranking Member

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

JUL - 8 2010

The Honorable Norm Dicks
Chairman, Subcommittee on Defense
Committee on Appropriations
U.S. House of Representatives
Washington, DC 20515

Dear Mr. Chairman:

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Enclosure:
As stated

cc:
The Honorable C. W. Bill Young
Ranking Member

Department of Defense
Final Report to Congress
Adverse Health Events Associated with Use of Anti-Malarial Drugs
October 2009

Background

H.R.1815, the National Defense Authorization Act (NDAA) for Fiscal Year (FY) 2006, Conference Report 109-360, Section 737, requires the Secretary of Defense to conduct a study of adverse health events that may be associated with the use of antimalarial drugs, including mefloquine, also known as Lariam. The study shall include a comparison of adverse health events (including mental health) that may be associated with antimalarial drugs including mefloquine.

To meet the requirements of the NDAA for FY 2006, the Assistant Secretary of Defense for Health Affairs commissioned four scientific studies to examine adverse outcomes associated with the use of antimalarial medications. The purpose of these studies was to assess the comparative rates of adverse events resulting from the use of antimalarial medications in deployed Service members. These medications include Chloroquine, mefloquine, Doxycycline, and Malarone. This deliberative approach to the study ensured a sound scientific basis for the eventual study findings.

Armed Forces Epidemiological Board

In response to concerns within the Department of Defense (DoD) about the adverse effects of mefloquine, the Assistant Secretary named to the Armed Forces Epidemiological Board (AFEB), now the Defense Health Board, an expert panel of independent physicians, scientists, epidemiologists, and ethicists from highly respected civilian institutions and academia, to address this issue in 2004. Specifically, the Assistant Secretary requested that the AFEB provide guidance and make recommendations on the design of a study or studies to address the issue of adverse health effects, including neuropsychological outcomes and suicide, among deployed and recently deployed Service members who were taking mefloquine. A select AFEB subcommittee met initially on April 12, 2004. On May 12, 2004, the subcommittee presented their recommendations to the full AFEB body, which endorsed their recommendations.

The AFEB published the results of its study in a memorandum titled, "Armed Forces Epidemiological Board (AFEB) Select Subcommittee to Develop Mefloquine Study Options," dated May 21, 2004. This report is available from the AFEB web site (http://www.ha.osd.mil/afeb/2004/2004-06.pdf) and is attached to this report. Among the core recommendations were:

- [The Board recommends a] "careful and well-designed descriptive study of the health outcomes potentially related to mefloquine is a prerequisite to subsequent studies."

- "Because of the rare nature of suicide and the large number of variables that need to be assessed, the Board feels a case-control study design is most appropriate for studying factors associated with suicide, including mefloquine."

Department of Defense Center for Deployment Health Research

Based on these recommendations, the Assistant Secretary commissioned two studies. The Deployment Health Research Center at the Naval Health Research Center in San Diego led the first, which was tasked to look at the comparative rates of adverse events (including neuropsychiatric) associated with antimalarial drug use. This study has been completed, and a final report was provided on March 3, 2005. The findings were published in the *American Journal of Tropical Medicine and Hygiene* (Wells T, Smith TC, Smith B, Wang LZ, Hansen CJ, Reed RJ, Goldfinger W, Corbeil TE, Spooner CN, Ryan MAK, "Mefloquine Use and Hospitalizations Among U.S. Service Members, 2002-2004," May 2006). The results suggest that there was no association between the use of mefloquine and severe health effects, as measured by hospitalizations, across a wide range of health outcomes. Specifically, the study found "little evidence that mefloquine-prescribed active-duty Service members were at increased risk for hospitalizations over a broad range of outcomes, including mental disorders, and diseases of the nervous system." A copy of the published findings is attached to this report.

Armed Forces Institute of Pathology

The Assistant Secretary commissioned the second study to the Armed Forces Institute of Pathology (AFIP) to address questions concerning suicide in deployed and recently deployed Service members. However, before AFIP could proceed with this descriptive study, it needed to develop a standardized method of determining DoD suicide rates (a uniform definition of how to count suicides and how to calculate and present suicide rates). At that point, each Service calculated suicide rates differently. The AFIP worked with the DoD Suicide Prevention and Risk Reduction Committee (SPARRC) to develop recommendations to standardize suicide rate calculations in military populations. AFIP also assisted with the development of a standardized post-suicide data collection instrument to uniformly assess risk factors. Both the standardized rate methodology and DoD-Suicide Event Report have now been adopted across all Services. This effort has allowed for a direct comparison of the suicide rates among the military Services for the first time. These efforts also permit comparisons with the civilian population. Counts for each Service are now formally reported quarterly, and rates annually through the SPARRC.

Next, AFIP completed a descriptive epidemiologic study characterizing Active Duty suicides to include those among Regular, Reserve, and National Guard personnel. However, due to staffing losses, that data could not be verified and submission for publication was abandoned. Another report conducted by the U.S. Army Center for Health Promotion and Preventive Medicine found for the period of 1980 through 2004, suicide rates among military recruits were lower than those of comparably aged U.S. civilians (Military Medicine; October 2007, Vol. 172 Issue 10, p1024-1031). From the same period a study titled "The physical and mental health of a large military cohort: baseline functional health status of the Millennium Cohort" (*BMC Public Health.* November 26, 2007; 7:340) found that the baseline health status of this military cohort was better than that of the U.S. general population of the same age and sex distribution over the same period. The final phase of the AFIP study was to be a case-control epidemiologic study. Due to staff reductions associated with the Defense Base Realignment and Closure Act, AFIP lost the necessary staff and expertise and was unable to complete this phase.

Other Activities

Data taken from the U.S. Army Center for Health Promotion and Preventive Medicine "Analyses of Army Suicides," January 1, 2003, to July 31, 2009, demonstrate that Army suicide rates in 2006 were 15.3 per 100,000 soldiers, which then rose to 16.8 and 20.2 respectively in 2007 and 2008. In contrast, during the same period, antimalarial medications were no longer routinely required in Iraq and when an antimalarial drug is indicated in Afghanistan, mefloquine is chosen only half the time. Numerous prevention programs and resiliency-building initiatives are in place to address risk factors associated with suicides in Service members. The primary demographics and risk factors for suicide among military members are similar to that of the general population. Some of the demographics include male gender, younger age, and lower pay grades, while risk factors include social isolation, relationship problems, and excessive use of alcohol. The Services are aware of these risk factors and have developed prevention strategies as well as resilience-building interventions to promote protective factors. Some of these measures include reducing barriers to obtaining mental health care services, fostering unit support, and strengthening military communities. Examples of initiatives include the Mental Health Self-Assessment Program, which is a comprehensive mental health education program for Service members and their families. This program is designed to raise awareness about mental health and facilitate the linkage between those in need of care and mental health resources. Another program is the Signs of Suicide Program, which is a school based program for military families proven to reduce suicide attempts in the high school population. The Transition Support Program provides a bridge of support for Service members while they are transitioning between health care systems or providers. The DoD SPARRC includes representatives from the Services to share lessons learned and develop best practices. The responsibilities of this committee were transferred to the Defense Centers of Excellence for Psychological Health and Traumatic

Brain Injury in October 2008. Each Service also has programs. One such program includes a $50 million, multi-year study initiated by the Department of the Army. This study examines suicides and suicidal behavior among soldiers across all phases of the Army. This endeavor is in conjunction with the National Institute of Mental Health (NIMH). The intent is to mitigate causes of suicide, assess the effectiveness of suicide prevention programs and provide recommendations to senior leadership. More recently, in accordance with Section 733 of the Duncan Hunter National Defense Authorization Act for Fiscal Year 2009, DoD established a task force on the prevention of suicide by members of the Armed Forces. This task force is charged with a number of tasks that include:

- Identifying trends and common causal factors in suicides by members of the Armed Forces;
- Assessing, and updating suicide education and prevention programs of each military department;
- Determining the appropriate type, method, and personnel to investigate the causes and factors surrounding suicides by members of the Armed Forces and how to use that data;
- Determining the appropriate reporting requirements following a suicide investigation; and
- Determining methods for protecting confidentiality of information contained in reports of investigation of suicide by members of the Armed Forces.

Although a link between mefloquine use and suicides is not apparent, suicides continue to be a significant issue in which DoD is fully engaged to determine the cause and develop and implement preventive measures.