

DEPARTMENT OF VETERANS AFFAIRS

Determination of Presumption of Service Connection Concerning Illnesses Discussed in National Academy of Sciences Report on Gulf War and Health: Volume 5: Infectious Diseases

AGENCY: Department of Veterans Affairs.

ACTION: Notice.

SUMMARY: As required by law, the Department of Veterans Affairs (VA) hereby gives notice that the Secretary of Veterans Affairs, under the authority granted by the Persian Gulf War Veterans Act of 1998, Public Law 105–277, title XVI, 112 Stat. 2681–742 through 2681–749 (codified in part at 38 U.S.C. 1118), has determined that there is no basis to establish a presumption of service connection for Al Eskan disease, idiopathic acute eosinophilic pneumonia, wound and nosocomial infection, mycoplasmas, as discussed in the October 2006 report of the National Academy of Sciences, titled “Gulf War and Health Volume 5: Infectious Diseases”, or for any illness based on exposure to biologic-warfare agents during service in the Persian Gulf during the Persian Gulf War.

FOR FURTHER INFORMATION CONTACT: Thomas Kniffen, Chief, Regulations Staff (211D), Compensation and Pension Service, Veterans Benefits Administration, Department of Veterans Affairs, 810 Vermont Avenue, NW., Washington, DC 20420, (202) 461–9725.

SUPPLEMENTARY INFORMATION:

I. Statutory Requirements

The Persian Gulf War Veterans Act of 1998, Public Law 105–277, title XVI, 112 Stat. 2681–742 through 2681–749 (codified at 38 U.S.C. 1118), and the Veterans Programs Enhancement Act of 1998, Public Law 105–368, 112 Stat. 3315, directed the Secretary to seek to enter into an agreement with the National Academy of Sciences (NAS) to review and evaluate the available scientific evidence regarding associations between illnesses and exposure to toxic agents, environmental or wartime hazards, or preventive medicines or vaccines to which service members may have been exposed during service in the Persian Gulf during the Persian Gulf War. Congress directed the NAS to identify agents, hazards, medicines, and vaccines to which service members may have been exposed during service in the Persian Gulf during the Persian Gulf War.

Congress mandated that the NAS determine, to the extent possible: (1)

Whether there is a statistical association between exposure to the agent, hazard, medicine, or vaccine and the illness, taking into account the strength of the scientific evidence and the appropriateness of the scientific methodology used to detect the association; (2) the increased risk of illness among individuals exposed to the agent, hazard, medicine, or vaccine; and (3) whether a plausible biological mechanism or other evidence of a causal relationship exists between exposure to the agent, hazard, medicine, or vaccine and the illness.

Section 1118 of Title 38 of the United States Code provides that whenever the Secretary determines, based on sound medical and scientific evidence, that a positive association (*i.e.*, the credible evidence for the association is equal to or outweighs the credible evidence against the association) exists between exposure of humans or animals to a biological, chemical, or other toxic agent, environmental or wartime hazard, or preventive medicine or vaccine known or presumed to be associated with service in the Southwest Asia theater of operations during the Persian Gulf War and the occurrence of a diagnosed or undiagnosed illness in humans or animals, the Secretary will publish regulations establishing presumptive service connection for that illness. If the Secretary determines that a presumption of service connection is not warranted, he is to publish a notice of that determination, including an explanation of the scientific basis for that determination. The Secretary’s determination must be based on consideration of the NAS reports and all other sound medical and scientific information and analysis available to the Secretary.

Although section 1118 does not define “credible evidence,” it does instruct the Secretary to consider whether the results (of any report, information, or analysis) are statistically significant, are capable of replication, and withstand peer review. *See* 38 U.S.C. 1118(b)(2)(B). Simply comparing the number of studies that report a significantly increased relative risk to the number of studies that report a relative risk that is not significantly increased is not a valid method for determining whether the weight of evidence overall supports a finding that there is or is not a positive association between exposure to an agent, hazard, medicine, or vaccine and the subsequent development of the particular illness. Because of differences in statistical significance, confidence levels, control for confounding factors, and other pertinent characteristics,

some studies are clearly more credible than others, and the Secretary gives the more credible studies more weight in evaluating the overall weight of the evidence concerning specific illnesses.

II. Prior National Academy of Sciences Reports

The NAS issued its initial report titled, *Gulf War and Health, Volume 1: “Depleted Uranium, Sarin, Pyridostigmine Bromide, Vaccines,”* on January 1, 2000. In that report, NAS limited its analysis to the health effects of depleted uranium, the chemical warfare agent, sarin, vaccinations against botulism toxin and anthrax, and pyridostigmine bromide, which was used in the Persian Gulf War as a pretreatment for possible exposure to nerve agents. On July 6, 2001, VA published a notice in the **Federal Register** announcing the Secretary’s determination that the available evidence did not warrant a presumption of service connection for any disease discussed in that report. *See* 66 FR 35702 (2001).

The NAS issued its second report titled, *“Gulf War and Health, Volume 2: Insecticides and Solvents,”* on February 18, 2003. In that report, the NAS focused on the health effects of insecticides and solvents that were shipped to the Persian Gulf during the Persian Gulf War. The pesticides considered by the NAS were organophosphorous compounds (Malathion, diazinon, chlorpyrifos, dichlorvos, and azamethiphos), carbamates (carbaryl, propoxur, and methomyl), pyrethrins and pyrethroids (permethrin and d-phenothrin), lindane, and *N,N*-diethyl-3-methylbenzamide (DEET). The NAS considered 53 solvents in eight groups: aromatic hydrocarbons (including benzene), halogenated hydrocarbons (including tetrachloroethylene and dry-cleaning solvents), alcohols, glycols, glycol esters, esters, ketones, and petroleum distillates. On August 24, 2007, VA published a notice in the **Federal Register** announcing the Secretary’s determination that the available evidence did not warrant a presumption of service connection for any disease discussed in that report. 72 FR 48734 (2007).

The NAS issued an update on sarin in a report titled *“Gulf War and Health: Updated Literature Review of Sarin,”* on August 20, 2004. In that report, the NAS focused on the long-term health effects from exposure to the nerve agent, sarin. VA published a **Federal Register** Notice announcing the Secretary’s determination that it was not necessary to establish new presumptions of

service connection for any diseases based on the updated findings on long-term health effects from sarin. 73 FR 42411 (2008).

The NAS issued its third report, titled "Gulf War and Health, Volume 3: Fuels, Combustion Products, and Propellants," on December 20, 2004. In that report, the NAS focused on the health effects of hydrazines, red fuming nitric acid, hydrogen sulfide, oil-fire byproducts, diesel-heater fumes, and fuels (for example, jet fuel and gasoline). VA published a **Federal Register** Notice announcing the Secretary's determination that the available evidence did not warrant a presumption of service connection for any disease discussed in that report. 73 FR 50856 (2008).

The NAS issued its fourth report, titled "Gulf War and Health Volume 4. Health Effects of Serving in the Gulf War," on September 12, 2006. In that report the NAS focused on the health status of veterans of the 1991 Gulf War. The report was intended to inform VA about illnesses and clinical issues including possible relevant treatments, which might have been overlooked among this population, regardless of the specific underlying cause. VA is drafting a **Federal Register** notice announcing the Secretary's determination that the available evidence does not warrant a presumption of service connection for any disease discussed in that report.

III. Gulf War and Health, Volume 5: Infectious Diseases

The NAS committee issued its fifth report, titled "Gulf War and Health Volume 5: Infectious Diseases" on October 16, 2006. The committee reviewed published, peer-reviewed scientific and medical literature on long-term health effects from infectious diseases associated with Southwest Asia. Based on the NAS's report, VA is currently drafting a proposed rule to establish presumptive service connection for nine infectious diseases discussed in the report and providing guidance regarding long-term health effects associated with these diseases.

However, the NAS additionally discussed several infectious diseases and agents that had been identified as possible causes of illnesses in veterans with service in Southwest Asia or that otherwise presented issues of special interest to such veterans. This notice provides the Secretary's determination that the scientific evidence in the report does not warrant a presumption of service connection for any illnesses caused by these diseases and agents. The diseases and agents are Al Eskan

disease, idiopathic acute eosinophilic pneumonia, wound and nosocomial infection, mycoplasmas, and biologic-warfare agents.

Al Eskan Disease

Al Eskan disease is named after a village in Saudi Arabia where U.S. military personnel lived during the 1991 Gulf War. These soldiers reported a vague systemic illness causing primarily respiratory symptoms that was termed Al Eskan disease or Desert Storm pneumonitis in three studies: Korenyi-Both *et al.* 1992; Korenyi-Both *et al.* 1997; Korenyi-Both *et al.* 2000. During Operation Desert Shield (ODSh) and Operation Desert Storm (ODSt), approximately 697,000 troops were deployed. Although researchers are unable to determine the exact number of troops affected by Al Eskan disease, data on respiratory illnesses in troops reveal that respiratory symptoms in general were more common in those with a history of lung disease, smoking, and longer deployment; more common in those with less outdoor exposure; and were most prominent in personnel who slept in air-conditioned facilities. Al Eskan disease or a similar illness has not been reported in troops deployed to Operation Iraqi Freedom (OIF) or Operation Enduring Freedom (OEF).

Al Eskan disease was first reported in 1992, and was characterized by sudden or insidious onset of chills, fever, sore throat, hoarseness, nausea and vomiting, and generalized malaise followed by respiratory tract complaints which included increasingly severe dry cough or expectoration of tan sputum (Korenyi-Both *et al.* 1992). The disease appears to be self-limited, and physical findings are minimal. Systemic description and precise definition of Al Eskan disease are unavailable.

Korenyi-Both and colleagues have ascribed Al Eskan disease to an immune response to sand-particle exposure, and argued that Al Eskan disease is most likely a form of acute silicosis aggravated by the pulmonary immune response and perhaps other genetic and environmental factors (Korenyi-Both *et al.* 1992; Korenyi-Both *et al.* 1997; Korenyi-Both *et al.* 2000). There are no clinical data to support this hypothesis and no reports of chronic lung disease consistent with silicosis in veterans. The hypotheses and conclusions of these researchers have not been uniformly accepted and have generated considerable debate (Clooman *et al.* 2000; Kilpatrick 2000).

The NAS found that no data link Al Eskan disease to any specific chronic

illness. Further, there is no evidence that the syndrome or disease observed in troops in Al Eskan village was caused by a communicable microbial pathogen. Korenyi-Both *et al.* have argued that the disease is caused by exposure to the unique sand dust of the central and eastern Arabian Peninsula and in particular to the silica in the sand. However, more than 13 years have passed since the initial description of Al Eskan disease appeared in the literature, and researchers have been unable to link chronic respiratory diseases in military personnel to exposure to Persian Gulf sand.

Based on the NAS report, the Secretary has determined that there is insufficient evidence to conclude that there is a positive association between the condition described as Al Eskan disease and exposure to an agent, hazard, preventive medicine or vaccine associated with Gulf War service. To the extent the described condition involves respiratory symptoms of unknown etiology, current VA regulations provide a presumption of service connection for chronic disability due to undiagnosed illness manifest by respiratory signs and symptoms. See 38 CFR 3.317.

Idiopathic Acute Eosinophilic Pneumonia

Idiopathic Acute Eosinophilic Pneumonia (IAEP) is a syndrome characterized by a febrile illness, diffuse pulmonary infiltrates, and pulmonary eosinophilia (Allen *et al.* 1989; Badesch *et al.* 1989; Philit *et al.* 2002). Patients with IAEP have no history of asthma, allergy, or chronic lung disease and no discernible infection. Patients with IAEP present with fever, diffuse pulmonary infiltrates, cough, shortness of breath, and, not infrequently, respiratory failure. Most IAEP patients who survive the acute illness make a complete recovery. Eighteen soldiers deployed to Southwest Asia in OIF developed IAEP.

In many cases, IAEP has been associated with cigarette smoking and exposure to dust (Badesch *et al.* 1989; Pope-Harman *et al.* 1996; Rom *et al.* 2002). No causative pathogens were detected or implied by the immune repose of soldiers with IAEP (Allen *et al.* 1989; Shorr *et al.* 2004). Survey results failed to identify a common source of environmental, drug, or toxin exposure (Shorr *et al.* 2004). IAEP would not be expected to have long-term adverse health outcomes.

Based on the NAS report, the Secretary has determined that there is insufficient evidence to conclude that there is a positive association between IAEP and exposure to an agent, hazard,

preventive medicine, or vaccine associated with Gulf War service.

Wound and Nosocomial Infection

Soldiers can experience a wide variety of exposures to pathogens from explosives or combat (wound infections) or in health-care settings (nosocomial infections). One condition that is more prevalent in troops in Southwest Asia than in civilian settings is infection with *Acinetobacter calcoaceticus-baumannii* complex, a well-recognized cause of wound infection in general and among military troops in particular (CDC 2004; Davis *et al.* 2005). The complex is also a cause of nosocomially-acquired infection when wounded, infected soldiers are intermingled with other patients in the intensive care unit, emergency room, or hospital ward.

Research data has also revealed that *A. baumannii bacteremia* was common in OEF and OIF returnees who were hospitalized for injuries, although it was rare before the state of OEF and OIF (CDC 2004; Davis *et al.* 2005; Zapor and Moran 2005), and that nearly any war-theater injury, whether combat-derived or otherwise, may result in infection. The risk of infection is inherent in military service, training, readiness activities, transport, or combat (Zapor and Moran 2005).

Both wound infections and nosocomial infections are hazards for U.S. personnel deployed to Southwest Asia. Given modern medical and surgical treatment and the ability to evacuate injured military personnel rapidly, most infections will be seen within days or weeks of wounds.

The NAS found that both wound infections and nosocomial infections manifest within a short period after injury or exposure, such that making an epidemiological link between a particular infection and the precipitating wound or exposure is rarely difficult. The NAS further noted that, in rare cases, infections associated with chronic osteomyelitis could go undetected and become manifest after service, although it noted a "near absence" of case reports documenting that occurrence. In view of the possibility of infections from other military and civilian sources outside of Gulf War service, the NAS stated that determining whether any infections manifest after service were associated with such service or with other causes would require case-by-case evaluations of the epidemiologic, clinical, and microbiological characteristics of the infection.

Based on the NAS report, the Secretary has determined that there is insufficient evidence to conclude that

there is a positive association between wound or nosocomial infections manifest after service and any exposure to an agent, hazard, preventive medicine, or vaccine associated with Gulf War service. Any such infections manifest within service or within a short period following an in-service wound or exposure would be subject to service connection on a direct basis under current law.

Mycoplasmas

Mycoplasmas are ubiquitous microorganisms found as commensal colonizers and as pathogens in plants, insects, and animals. They are pleomorphic and filamentous and have a deformable membrane, which allows them to pass through filters that retain bacteria. They are fastidious and difficult to culture on cell-free media; at the same time, because of their common presence as nonpathogenic colonizers, they are common contaminants of cell cultures. The propensity for contamination of cell cultures can lead to false conclusions about the association of mycoplasmas with a variety of clinical syndromes (Baum 2005).

Culture of *Mycoplasma fermentans* on cell-free media (which decrease the risk of contamination) has been extremely difficult, and this has led to controversy over whether the organisms are true pathogens or merely contaminants.

The NAS noted that mycoplasmas are ubiquitous and did not suggest that they are more prevalent in the Gulf War theater than in other locations.

However, it addressed mycoplasmas as a matter of special interest to Gulf War veterans because certain researchers have suggested that many of the symptoms of Gulf War illness could be explained by aggressive mycoplasma infections present as contaminants in vaccines administered to service members before deployment to the Gulf.

Several studies by Nicolson and colleagues report a link between *Mycoplasma fermentans* and health problems in Gulf War veterans (Nicolson *et al.* 2002; Nicolson *et al.* 2003; Nicolson and Rosenberg-Nicolson 1995; Nicolson and Nicolson 1996). Nicolson and colleagues hypothesized that the source of such infections in Gulf War veterans may have been contamination of the multiple vaccines received by troops before and during deployment (Nicolson *et al.* 2003). It was suggested that many of the symptoms of Gulf War illness could be explained by "aggressive pathogenic mycoplasma infections, and they should be treatable with multiple courses of antibiotics, such as doxycycline or

macrolides" (Nicolson and Rosenberg-Nicolson 1995). However, independent attempts to confirm the results of studies conducted by Nicolson and his colleagues have been unsuccessful (Gray *et al.* 1999; Lo *et al.* 2000). One report noted that the methodology used by Nicolson and colleagues was "an inappropriate diagnostic method for detection of *M. fermentans*" and that neither the specificity nor the sensitivity of the test had been established (Dybvig 1998). Because of the conflicting data related to *M. fermentans* infections and their possible association with Gulf War illnesses and the suggestion of possible benefits of treatment with doxycycline, VA conducted a randomized placebo-controlled trial to determine whether doxycycline could improve functional status of persons with Gulf War illness (Donta *et al.* 2004). Overall, the results of this study revealed no statistically significant difference between the doxycycline-treated and placebo groups.

Although several studies by Nicolson and colleagues report a link between *Mycoplasma fermentans* and health problems in Gulf War veterans (Nicolson *et al.* 2002; Nicolson *et al.* 2003; Nicolson and Rosenberg-Nicolson 1995; Nicolson and Nicolson 1996), other investigators were not able to duplicate their work and there are concerns about the nuclear gene tracking technique used by Nicolson *et al.* (Dybvig 1998; Gray *et al.* 1999; Lo *et al.* 2000). After reviewing the evidence, mycoplasma infection is not believed to be related to the symptoms reported by Gulf War veterans.

Based on the NAS report, the Secretary has determined that there is insufficient evidence to conclude that there is a positive association between mycoplasma infections and any exposure to an agent, hazard, preventive medicine, or vaccine associated with Gulf War service. The evidence does not show that mycoplasma infections are associated with Gulf War illness or any other chronic health outcome.

Biologic-Warfare Agents

Biologic warfare is defined as the use of microorganisms or toxic products derived from microorganisms to inflict mass casualties in military and civilian populations (Horn 2003). At the time of the 1991 Gulf War, Iraq had an active biologic warfare program. Iraq developed bombs, missile warheads, aerosol generators, and helicopter and jet spray systems for dispersal of biological warfare agents (Leitenberg 2001). Iraqi sources reported that aflatoxin, botulinum toxin, and *Bacillus anthracis* were loaded in missiles and air-delivery bombs in preparation for

the Gulf War (Roffey *et al.* 2002). Of the four biological warfare agents that Iraqi sources reported weaponized: aflatoxin, botulinum toxin, *Bacillus anthracis*, and ricin, only anthrax is a living microorganism and capable of multiplying in infected people. However, no evidence has been found that Iraq deployed any weapons containing biological warfare agents (Roffey *et al.* 2002; Zilinskas 1997).

Based on the NAS report, the Secretary has concluded that a presumption is not warranted for any disease associated with exposure to biological warfare agents because such weapons were not shown to have been deployed in the Gulf War.

IV. Conclusion

After careful review of the findings of the 2006 NAS report, "Gulf War & Health Volume 5: Infectious Diseases," the Secretary has determined that the scientific evidence presented in the report and other information available to the Secretary indicate that no new presumption of service connection is warranted for Al Eskan disease, idiopathic acute eosinophilic pneumonia, wound and nosocomial infection, mycoplasmas, or for any illness based on exposure to biological warfare agents.

Approved: March 26, 2009.

John R. Gingrich,

Chief of Staff, Department of Veterans Affairs.

[FR Doc. E9-7342 Filed 4-1-09; 8:45 am]

BILLING CODE

DEPARTMENT OF VETERANS AFFAIRS

Advisory Committee on Cemeteries and Memorials; Notice of Meeting

The Department of Veterans Affairs (VA) gives notice under Public Law 92-463 (Federal Advisory Committee Act) that a meeting of the Advisory Committee on Cemeteries and Memorials will be held on May 5-6, 2009, at the El Paso Marriott, 1600 Airway Boulevard, El Paso, Texas. On May 5, the meeting will begin at 8 a.m. and end at 3:45 p.m. and on May 6, the meeting will begin at 8:30 a.m. and end at 4 p.m. The meeting is open to the public.

The purpose of the Committee is to advise the Secretary of Veterans Affairs on the administration of national cemeteries, soldiers' lots and plots, the selection of new national cemetery sites, the erection of appropriate memorials, and the adequacy of Federal burial benefits.

On May 5, the Committee will receive updates on National Cemetery Administration issues. On May 6, the Committee will tour Fort Bliss National Cemetery, located at 5200 Fred Wilson Boulevard, El Paso, Texas, and then reconvene at the hotel for a business session in the afternoon. The May 6 session will include discussions of Committee recommendations, future meeting sites, and potential agenda topics at future meetings.

Time will not be allocated for receiving oral presentations from the public.

Any member of the public wishing to attend the meeting should contact Mr. Michael Nacincik, Designated Federal Officer, at (202) 461-6240. The Committee will accept written comments. Comments may be transmitted electronically to the Committee at *Michael.n@va.gov*, or mailed to the National Cemetery Administration (41C2), 810 Vermont Avenue, NW., Washington, DC 20420. In the public's communications with the Committee, the writers must identify themselves and state the organizations, associations, or persons they represent.

Dated: March 27, 2009.

By Direction of the Secretary.

E. Philip Riggan,

Committee Management Officer.

[FR Doc. E9-7455 Filed 4-1-09; 8:45 am]

BILLING CODE 8320-01-P

DEPARTMENT OF VETERANS AFFAIRS

Advisory Committee on OIF/OEF Veterans and Families; Notice of Meeting

The Department of Veterans Affairs (VA) gives notice under Public Law 92-463 (Federal Advisory Committee Act) that the Advisory Committee on OIF/OEF Veterans and Families will meet on April 15-16, 2009, at the St. Regis Hotel, 923 16th Street, NW., Washington, DC, from 8:30 a.m. to 4:30 p.m. each day. The meeting is open to the public.

The purpose of the Committee is to advise the Secretary of Veterans Affairs on the full spectrum of health care, benefits delivery and related family support issues that confront servicemembers during their transition from active duty to veteran status and during their post-service years. The Committee focuses on the concerns of all men and women with active military service in Operation Iraqi Freedom and/or Operation Enduring Freedom, but pays particular attention to severely disabled veterans and their families.

The agenda for April 15 and 16 will feature a review of information gathered by the Committee during the past two years. The Committee will also discuss the possibility of transferring records and sharing the results of its various fact-finding initiatives with other VA advisory committees which have complementary jurisdictions and similar areas of interest.

The public may submit written statements for the Committee's review to the Advisory Committee on OIF/OEF Veterans and Families (008), Department of Veterans Affairs, 810 Vermont Avenue, NW., Washington, DC 20420. Any member of the public seeking additional information should contact Laura O'Shea, Designated Federal Officer, at (202) 461-5765.

Dated: March 31, 2009.

By Direction of the Secretary.

E. Philip Riggan,

Committee Management Officer.

[FR Doc. E9-7456 Filed 4-1-09; 8:45 am]

BILLING CODE 8320-01-P

DEPARTMENT OF VETERANS AFFAIRS

Genomic Medicine Program Advisory Committee; Notice of Meeting

The Department of Veterans Affairs (VA) gives notice under Public Law 92-463 (Federal Advisory Committee Act) that the Genomic Medicine Program Advisory Committee will meet on April 27, 2009, at the Madison Hotel, 1177 15th St NW., Washington, DC. The meeting will start at 8 a.m. and end at 5 p.m.

The purpose of the Committee is to provide advice and make recommendations to the Secretary of Veterans Affairs on using genetic information to optimize medical care of Veterans and to enhance development of tests and treatments for diseases particularly relevant to Veterans.

The Committee will meet in an open session from 8 a.m. until 3:30 p.m. to receive updates from the VA program staff; discuss optimal ways for VA to incorporate genomic information into its health care program while applying appropriate ethical oversight and protecting the privacy of Veterans; and receive an overview of the recent Institute of Medicine report on privacy protections in health research and discussions of potential areas of research in diseases/conditions prevalent in Veterans such as diabetes, women's health, specifically breast cancer, and the application of pharmacogenomics in clinical care.