DEPARTMENT OF DEFENSE
ARMED FORCES EPIDEMIOLOGICAL BOARD
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AFEB

MEMORANDUM FOR JUN 18 2004

The Assistant Secretary of Defense (Health Affairs)
The Surgeon General, Department of The Army
The Surgeon General, Department of The Navy
The Surgeon General, Department of The Air Force

SUBJECT: DoD Immunization Program for Biological Warfare Defense AFEB 2004-08

1. References:

a. Department of Defense Directive 6205.3, "DoD Immunization Program for Biological Warfare Defense," dated November 26, 1993.

b. Department of Defense Directive 6200.2, "Use Of Investigational New Drugs For Force Health Protection," dated August 1, 2000.

c. Memorandum, OASD(HA)/FHP&R, March 13, 2002, Therapeutics Against Biowarfare Agents.

d. Memorandum, AFEB 2002 - 09, August 12, 2002, Therapeutics Against Biowarfare Agents.

2. The Armed Forces Epidemiological Board (AFEB) meets annually as required under DoD Directive 6205.3 to provide recommendations to the Assistant Secretary of Defense for Health Affairs and the DoD Executive Agent on protocols necessary to enhance protection against validated biological warfare threat agents. Specifically, DoD Directive 6205.3 requires that "on an annual basis the President of the Armed Forces Epidemiological Board (AFEB) shall identify to the Assistant Secretary of Defense for Health Affairs vaccines available to protect against validated biological warfare threat agents, and recommend appropriate immunization protocols."

3. On 11-12 May 2004, the Board met to consider the biological threat agents designated by the Chairman of the Joint Chiefs of Staff and to discuss appropriate medical countermeasures. The current Chairman of the Joint Chiefs of Staff validated threat list was last validated in September 2002. The Board received briefings on the Chairman's threat list, the use of investigational new drugs in the combatant theater for force health protection, and updates on the medical biological defense research program and the advanced development of chemical and biological medical countermeasures. In addition, the Board received updates on the status of the military vaccine

program (MILVAX) and on rare adverse event reporting through the Vaccine Healthcare Centers (VCH) network. Presentations were given on follow-up studies of reported smallpox vaccine-associated cases of myopericarditis and dilated cardiomyopathy, plans for a case-control study of smallpox vaccine-associated cardiac events, and follow-up studies of reproductive health outcomes associated with receipt of smallpox vaccine during pregnancy. In the Joint Staff preventive medicine report, the Board heard about proposals for extending current policies to total force protection for smallpox and anthrax.

4. The Board was very impressed with the extensive and carefully conducted follow-up studies on personnel with cardiac adverse events linked to smallpox vaccination. The Department is to be commended for this work, which has led to several peer-reviewed publications in the scientific literature. As stated in an accompanying editorial in the *Journal of the American Medical Association*, "This is a model for how military and civilian cooperation can effectively serve the public health of the entire nation." (Wright ME, Fauci AS, JAMA 2003, 289:3306-8) The myopericarditis studies demonstrate a consistent syndrome marked by transient inflammation that occurs in approximately one in eight thousand primary vaccine recipients in the one-to-two weeks following vaccination. Extended follow-up, as requested by the Board, has not shown any sustained cardiac injury by objective measures, and most affected personnel are now asymptomatic. A small proportion of these individuals continue to have subjective complaints of chest discomfort. There are no persuasive data demonstrating a link between dilated cardiomyopathy and smallpox vaccination among military personnel.

5. The Board was also impressed by the careful follow-up of reproductive health outcomes performed by the Naval Health Research Center. These studies show that the number of inadvertent vaccinations during pregnancy appears to have been substantially reduced through screening programs, that the majority of episodes where this occurred could not have been detected with current screening measures, and found no evidence of fetal vaccinia or unexpected rates of pregnancy-related complications. Nonetheless, a small proportion of inadvertent pregnancy-related smallpox vaccinations were clearly preventable, demonstrating a continued need for vigilance and close monitoring of the quality of pregnancy screening programs.

6. The Board supports the work and role of the VHC network. This activity not only provides important signals concerning potential adverse events related to DoD-administered vaccines but also is a highly valued source of information for health care providers and service members with concerns about vaccines and health. We believe the VHCs have been an important factor in mitigating communications problems that have arisen with past vaccination campaigns.

7. The Board remains impressed with the quality and range of biological countermeasures research conducted in the Department. Structural changes that have occurred in the last year in the DoD medical chem-bio defense acquisition arena appear to have resulted in improved management of this activity. However, the Board remains concerned about the continued slow translation of research activities into useable licensed products for medical countermeasures.

8. In the 2003 review, the Board recommended that DoD Directive 6205.3 be rewritten to expand the annual review from the current focus on vaccine countermeasures to all available medical countermeasures. The Board understands that the revision process is underway and would appreciate the opportunity to review the new directive when it is available. The Board is concerned that the validated Chairman's threat list has not been updated since September of 2002. International events of the past year make it highly likely that there will be significant modifications to the current threat matrix, and in order to best serve the Department our deliberations are best guided by the latest threat assessments.

9. The Board is very concerned about proposals to expand current vaccination policies for smallpox and anthrax beyond the current capabilities and risk-based approach to one that supports full-force protection. The Board has repeatedly made recommendations endorsing the use of a threat-based approach by DoD. We believe this approach appropriately balances threat with the adverse health profiles of these products and the unique circumstances of military deployments and personnel. We have no basis upon which to endorse an expansion of the current approach, and the adverse events documented to date argue against deviation from current policy from the medical perspective. However, we do believe it is appropriate for DoD to maintain adequate stockpiles of vaccine and other countermeasures to assure full-force protection should the threat circumstances deteriorate at a future time.

10. Based on the above information, the Board makes the following recommendations:

a. The current approach for anthrax and smallpox vaccination, focused on deployments to high-threat theaters of operations, should remain the basis for decisions about the need for pre-exposure vaccination against biowarfare threats (such as anthrax and smallpox). It also is reasonable to follow a threat-based approach as future countermeasures become available, including next generation products for anthrax and smallpox, and products to protect against other biowarfare threats.

b. The Department should maintain an adequate stockpile of countermeasures to accomplish full-force protection should this become necessary.

c. While the Board is impressed with the largely negative findings of the follow-up of persons with cardiac complications of smallpox vaccination to date, continued study of a sample of this cohort would provide additional data points on which to base countermeasure recommendations and provide invaluable information on the consequences of this complication. DoD should support continued epidemiological evaluation of the cohort.

d. Opportunities to further reduce the potential for vaccinating pregnant women and for educating females about the importance of avoiding conception in the peri-vaccination period should be explored. We continue to support the smallpox vaccine pregnancy registry and the continued follow-up of infants born to this cohort.

e. Methodologic concerns were raised about the case-control study of myopericarditis complications, which is about to be initiated. Since the Board recommended this study we would appreciate the opportunity to review the current protocol and questionnaire before the study begins, to assure that optimal and scientifically valid information is derived from this important study.

f. The current scientific understanding of vaccinia adverse events is based upon the careful collection and thorough investigation of post-vaccination adverse event information primarily through the Vaccine Adverse Event Reporting System and other data sources within the Department of Defense. The Board recommends continued support for robust adverse event surveillance among military vaccinees.

g. The Board recommends that the countermeasures/threat matrix previously developed by DoD be updated when the revised Chairman's threat list becomes available.

11. The above recommendations were unanimously approved.

FOR THE ARMED FORCES EPIDEMIOLOGICAL BOARD:

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