

Food and Drug Administration
Rockville MD 208574858 '02 JAN 18 P2:30
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Mr. Mark S. Zaid
The James Madison Project
1275 K Street, N.W.
Suite 770
Washington, D.C. 20005

Re: Docket No. 00P-0653/CP1

Dear Mr. Zaid:

In your citizen's petition dated February 11, 2000, and filed with the Dockets Management Branch on February 16, 2000, you request that the Food and Drug Administration amend the product insert and/or label for Anthrax Vaccine Adsorbed, U.S. license number 1260 to reflect additional information concerning systemic adverse reactions. You have submitted a summary of studies, surveys, Department of Defense brochures, slide presentations, web site information and GAO documents to support the petition. Your specific recommendation for the Adverse Reactions section of the label is as follows:

Systemic Reactions: Systemic reactions occur in 5-35 per cent of recipients, and have included reports of malaise, lassitude, chills, rashes, headaches and low-grade fever. In such cases, immunization should be discontinued. Women report these symptoms more often than men.

We acknowledge that these proportions of systemic reactions have been reported in the information you cite. Also, the cited information indicates that a higher percentage of women participants reported adverse events compared to men.

However, the information you cite, which includes recent studies and retrospective surveys, has significant methodologic limitations. Specifically, these studies, such as the "Fort Bragg Booster Study" and the "USAMRIID SIP AVA Primary Series Reactions," are not randomized and well-controlled. These studies also do not adjust for factors such as occupation, physical activity level, and age. For example, it is unknown whether subjects would have experienced a headache (or other systemic reactions) during the same period of observation in the absence of anthrax vaccination.

Furthermore, in some retrospective surveys cited in your petition, such as the U.S. Forces, Korea survey, and the Tripler Army Medical Center survey, there is insufficient information to determine the definitive surveillance time (e.g., one week, one month, two months) post-vaccination. Also, the Korea survey, a mandatory, self-administered prevaccination questionnaire, was initially designed to record adverse reactions from service members' previous

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doses of AVA to promote risk communication between health-care providers and service members. Any service members who were medically deferred or transferred after a previous AVA dose would have been missed by the survey; therefore, information from this study about the adverse events may not accurately reflect the immunized group.

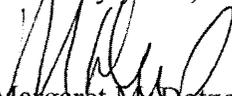
The Tripler Army Medical Center data on local reactions in a cohort of U.S. military health-care workers were collected retrospectively after the first three doses and prospectively for the remaining doses, potentially resulting in observational bias. There is also a large group that was lost to follow-up. In addition, in the Tripler survey, there is the absence of an unvaccinated control group.

Any label change based on these data should include a description of the limitations. FDA is, in fact, revising the Adverse Reactions section of the label for *Anthrax Vaccine Adsorbed*. We intend to modify the systemic adverse event rates in the label and note the gender differences, as well as identify the limitations of the studies. *However, we generally do not recommend discontinuation of vaccination for adverse events that are not serious. We have concluded, therefore, that discontinuation of the series is not to be automatically recommended for all systemic adverse events.*

We have enclosed a copy of a letter dated November 26, 1999, from Melinda K. Plaisier, Associate Commissioner for Legislation, issued to The Honorable Dan Burton. This letter provides further information concerning the anthrax vaccine and the references you have cited.

We appreciate the time and research that went into the formation of your petition. After FDA revises the labeling, we will forward a copy to you.

Sincerely yours,



Margaret M. Detzel

Associate Commissioner for Policy

Enclosure