

My name is Sarah Berdugo. I am a certified professional engineer, a Captain in the Air Force Reserves, and a veteran. I thank you for the opportunity to comment on Docket No. 1980N-0208, Biological Products; Bacterial Vaccines and Toxoids; Implementation of Efficacy Review.

I have several concerns about the content of this Docket and its effects on vaccine recipients based on my review and personal experience. My concerns and questions follow:

- Section IV.A: This Section states that, “During the comment period for the December 1985 proposal, FDA received no comments opposing the placement of AVA into Category I.” Was this lack of comments considered in the decision to approve placement of AVA into Category I? While this information is good to note, it does not verify or even imply tacit approval; there can be many reasons why comments were not received.

- Section IV.A: This Section says that the Panel based its evaluation of the safety and efficacy of AVA in part on “the Brachman study”. This was conducted in the 1950’s. How commonly does the FDA base evaluations on such outdated studies? Many advances in the field of medicine have taken place since this time so that even solid data from the past could be reinterpreted in different ways. For such a controversial vaccine, a new study should be conducted.

- Section IV.A: This Section explains that the Panel based its evaluation of the safety and efficacy of AVA on “the Brachman study”, an open-label safety study conducted by the National Center for Disease Control, and by considering surveillance data on the occurrence of anthrax disease in the United States in at-risk industrial settings. I am concerned about the likelihood that the persons involved in these three sources are not a representative sample of either the military personnel who have been given AVA or the civilian population who may be given AVA in the future. What was the personnel make-up of these three data sources? It seems likely that the participants were primarily men. Did they include a statistically significant number of both genders, different races, and persons of different weight and of different ages? This is very important because a vaccine must be made strong enough to be effective in your largest and least sensitive individual while ensuring the safety of the smallest and most sensitive (for example, expecting mothers).

- Section IV.A: This Section says that, “In its proposed determination that the data support the safety and efficacy of AVA, FDA has identified points of disagreement with statements in the Panel report.” What are the FDA-identified points of disagreement and how did the FDA answer them or find them acceptable such that they continued to support the safety and efficacy of AVA?

- Section IV.B: This Section says that “the Brachman study” used an earlier version of the protective antigen-based anthrax vaccine. How commonly does the FDA base the safety and efficacy of a vaccine on the results of studies from a different version of that vaccine? How can the FDA be sure that the change from the earlier version of the vaccine to the current one did not alter or negate its efficacy? In addition, there have been many reports of adverse reactions to the AVA by military personnel. How can the FDA be sure that the change from the earlier version of the vaccine to the current one did not alter or negate its safety?

- Section IV.B. Note 5: The Panel said that it would be very difficult, if not impossible, to clinically study (and therefore determine) the efficacy of any anthrax vaccine. Based on this information, how can the Panel and the FDA place the vaccine in Category I, "Licensed biological products determined to be safe and effective and not misbranded."
- Section IV.B. Note 5: If the Panel thought it would be difficult or impossible to clinically study (and therefore determine) the efficacy of the anthrax vaccine, how did it determine that it was possible and acceptable to determine the safety?
- Section IV.B. Note 5: The Panel noted that efficacy studies raise ethical considerations. Why is this a concern for studies, but not for administration, without information or consent, to military personnel?
- Section IV.B. Note 5: The Panel noted that, "...the low incidence and sporadic occurrence of anthrax disease also makes further adequate and well-controlled clinical studies of effectiveness not possible." If the incidence is low and occurrence of anthrax sporadic, why did the FDA push for quick acceptance of the vaccine; why did the DoD implement mandatory vaccination of all troops; and why is this vaccine being considered for administration to the general public—especially in light of the availability of antibiotics as a remedy?
- Section IV.B: Data was collected on the occurrence of anthrax disease in at-risk industrial settings by the CDC and summarized for the years 1962-1974. Some individuals, from whom data was collected, received an earlier version of the anthrax vaccine. This data was included as supportive of the effectiveness of AVA. How can the FDA be sure that the change from the earlier version of the vaccine to the current one did not alter or negate its efficacy? In addition, why was this collected data not also included as supportive of the safety of AVA?
- Section IV.C: The CDC's open-label study included textile employees, laboratory workers, and other at-risk individuals. Again, I am concerned about the likelihood that the persons involved in this study are not a representative sample of either the military personnel who have been given AVA or the civilian population who may be given AVA in the future. What was the personnel make-up of this study? Did it include a statistically significant number of both genders, different races, and persons of different weight and of different ages?
- Section IV.C: In its report, the Panel found that the CDC data "suggests that this product is fairly well tolerated with the majority of reactions consisting of local erythema and edema. Severe local reactions and systemic reactions are relatively rare." The underlined language used by the CDC provides a weak recommendation. Is there a standard method or standard language by which such recommendations are accepted or is it a subjective process? If it's the former, please explain the method.
- Section IV.C: The DoD conducted a small, randomized clinical study of the safety and immunogenicity of AVA. Were the results of this study the driving factor in updating the product label to reflect a much greater percentage of adverse reactions than originally printed? Why was a small study conducted when a larger data set was available? What were the results of this study? Did the results support the efficacy, as well as the safety of AVA?

- Section IV.C: This Section says that post licensure adverse event surveillance data available from the Vaccine Adverse Event Reporting (VAER) further support the safety of AVA. While the VAER system was an important step in post-vaccine accountability, it cannot support the safety of AVA. From experience, I know that many, if not most, military personnel who have had adverse reactions to AVA did not complete a VAERS. This is for many reasons: uninformed/misinformed about VAERS; fear of reprisal; military culture which discourages speaking out, “making waves”, and acknowledging personal health problems; previous inability to submit the form anonymously. This data should either be removed as a supporting source or should be supplemented by a survey from all military members who received the vaccine.

- Section IV.F: It is stated that, “the labeling seems generally adequate.” This is a very weak acknowledgement. Either the labeling is or is not adequate. At some point during administration of AVA, the product label was updated to reflect a much greater percentage of adverse reactions than originally printed. This is not consistent with the statement that “labeling seems generally adequate.” How was the labeling determined to be adequate?

- General: The largest data pool to-date on the safety of AVA is available in the form of military members who have been vaccinated since 1998. To ensure the safety of future military and civilian personnel, the FDA should perform a comprehensive survey using this data. The survey would need to be very carefully crafted to ensure that leading questions were not asked while at the same time identifying problems that may have been attributed to other causes, to ensure that a representative sample of different individuals was included, and to ensure that there was an anonymous environment that encouraged open and honest participation.

- General: New data during the course of administering AVA to military personnel resulted in updating the AVA product label to reflect a much greater percentage of adverse reactions than originally printed. Why didn't this new data also cause concern that other aspects of AVA's safety and efficacy could be understated or incorrect?

- General: The circumstances under which these comments are being collected verify that the anthrax vaccine is very controversial. Many military personnel have quit their careers, faced punishment, or lost their health or perhaps even lives. According even to this Docket, incidence of anthrax is low and unlikely. I strongly urge that the FDA work with the DoD to re-evaluate the ratio of risk-to-need in order to determine if this vaccine is necessary for the military. If it is determined to be, I strongly urge that the FDA/DoD perform further studies (see General comment above) to validate safety and efficacy. In addition, I recommend that the FDA work with the Department of Veterans Affairs to ensure that the vaccine is not approved for use until studies on the cause and treatment of adverse reactions are performed and a clear avenue for receiving support (treatment, disability, etc.) is established for these individuals.

Thank you for the opportunity to comment.

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