

March 25, 2005

Division of Dockets Management
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Attention: FDA Docket #1980N-0208; and Federal Register Docket #04-28322

Dear Dr. Lester Crawford, Acting Commissioner of Food and Drugs:

The following comments serve as our joint inputs for the FDA Dockets Management Branch case # 1980N-0208, as well as Federal Register Docket #04-28322. The inputs submitted in this letter are also attached electronically in PDF, and were signed and faxed to 301-827-6870.

In commenting on this docket we will cross-reference Citizen Petition Docket #2001P-0471, a document we co-authored and submitted to the FDA on October 15, 2001.¹ The FDA did not act on the Citizen Petition requested actions, instead having to be compelled to perform this congressionally chartered obligation following two federal court injunctions.²

The “*FDA's primary mission for 90 years has been to promote and protect the public health,*”³ Since the Agency was found by a federal court to have acted in an *arbitrary* manner regarding the actions requested in our Citizen Petition, we respectfully request the following actions prior to final rulemaking for anthrax vaccine adsorbed (also known as “AVA”):

1. The FDA must reconstitute the expert review panel, in accordance with Agency rules, prior to finalizing the license rulemaking for anthrax vaccine adsorbed.
2. The FDA must investigate DoD Inspector General Hotline Case #84142, referred to the Agency, as well as to the FBI’s Public Corruption Squad, for investigation by the Defense Criminal Investigative Service (DCIS) per memo dated November 20th, 2002. A copy of this complaint is included as a distinct submission to Docket #1980N-0208.
3. The FDA must review the investigation, if any, conducted by Mr. Stewart Simonson, DHHS Deputy General Counsel, resulting from an January 18, 2002 briefing by USAF Officers at DHHS HQ about the illegalities of anthrax vaccine adsorbed’s license and the AVIP.
4. The FDA should review a risk management analysis regarding anthrax vaccine adsorbed’s use by the DoD. The analysis, prepared in accordance with DOD directives, reviews the institutional and ethical risks faced by the DoD and FDA for knowingly implementing the

1 http://www.fda.gov/ohrms/dockets/dailys/01/Oct01/101501/101501.htm#_Toc527850400.

2 Doe v. Rumsfeld, 297 F. Supp. 2d 119 (D.C. Cir. 2003 & 2004): “[t]his Court is persuaded that AVA [anthrax vaccine] is an investigational drug and a drug being used for an unapproved purpose. As a result of this status, the DoD is in violation of 10 USC 1107, Executive Order 13139, and DoD Directive 6200.2.” See: <http://www.dcd.uscourts.gov/Opinions/2004/Sullivan/03-707c.pdf>.

3Michael A. Friedman, M.D., FDA Lead Deputy Commissioner, See: <http://www.fda.gov/ola/1997/423.html>.

AVIP in violation of U.S. law.⁴ This analysis has also been separately submitted to FDA's Docket #1980N-0208.

The remainder of the present docket entry concentrates on the 1st of the aforementioned requested actions, i.e., that **the FDA must reconstitute the expert review panel, in accordance with Agency rules, prior to finalizing the license rulemaking for anthrax vaccine adsorbed.** Requested actions #2 through #4 merely require the FDA to forthrightly investigate complaints referred to the Agency by the DCIS, as well as review the risks associated with ignoring the improprieties brought to the attention of the government.

The October 15, 2001 Citizen Petition, Docket #2001P-0471, cross referenced in this docket entry, requested action by FDA to finalize the anthrax vaccine license. Though acknowledging the need to do so, the FDA did not on its own accomplished this action to:⁵

“(1) Issue a Final Rule on the drug category placement of anthrax vaccine as Category II (unsafe, ineffective, or misbranded) amending the as yet to be finalized Proposed Rule as published in the Federal Register 13 December 1985.”

In addition to disregarding this primary requested action of Citizen Petition Docket #2001P-0471, until compelled to do so after being enjoined by federal court, the core issue of the anthrax vaccine's experimental use for inhalation anthrax also remains unresolved.

The FDA rebuffed the Citizen Petition's requests regarding this pivotal issue as well. As a result, the FDA's final rulemaking must clarify that any new licensing does not include this previously acknowledged experimental use. The 1973 expert review panel did not recommend inhalation anthrax protection as a use for anthrax vaccine adsorbed. This use is also known as aerosolized anthrax protection, and is also referred to as a weaponized biological defense indication for the vaccine.

Because the DoD knew the vaccine was experimental or investigational for use against inhalation anthrax, from 1996 to 2005 the Department attempted unsuccessfully to gain specific approval for this investigational use by submitting an Investigational New Drug (IND) Application to the FDA. The DoD's objective was to modify the product's labeling. The federal court documented its conclusions about these events in its 2003 injunction:⁶

“In the case of AVA, the 1985 panel found insufficient data to license the drug for use against inhalation anthrax. To date, no additional studies have been performed and AVA's label does not specify use of the vaccine for this purpose. Moreover, the Court is persuaded that the 1996 IND application remains pending today. The introduction to the application expressly states that one objective of the application is to obtain a specific indication for use of AVA

4 See: http://www.aviationmedicine.com/ORM_analysis_of_the_AVIP.doc.

5 http://www.fda.gov/ohrms/dockets/dailys/02/Sep02/091102/091102.htm#_Toc19593512.

6 See: <http://www.dcd.uscourts.gov/03-707.pdf>, see pgs 28-29.

*against inhalation anthrax. While the government states that the inhalation anthrax aspect of the IND is no longer active, the documents submitted to this Court under seal suggest otherwise. Finally, **statements made by DoD officials suggest that the agency itself has, at some point at least, considered AVA experimental with respect to inhalation anthrax.** Given all these factors, the Court would be remiss to conclude that the original license included inhalation anthrax. Having reached that conclusion, the DoD's administration of the inoculation without consent of those vaccinated amounts to arbitrary action."*

Despite the federal court's initial warning to the FDA through the injunction on December 22, 2003, the Agency attempted to disregard and circumvent the need for a renewed expert panel review in finalizing the anthrax vaccine license. The FDA had similarly disregarded cautions from the U.S. Congress in its 2000 House Report regarding the issue at question — the "experimental" use of anthrax vaccine adsorbed for inhalation anthrax.⁷

The federal court's second injunction, a permanent one based on summary judgment, on October 27, 2004 reaffirmed improper rulemaking and licensure. The court explained: *'Under the Administrative Procedure Act, a reviewing court may hold unlawful and set aside final agency action found to be "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with the law," or "without observance of procedure required by law."* 5 U.S.C. § 706(2).'

With these findings the federal court ruled against the FDA, remanding the license back to the Agency for proper rulemaking, and again found that the anthrax vaccine immunization program (AVIP) was *"illegal,"* and in violation of the Administrative Procedures Act — for the exact same reasons articulated in the 2000 Congressional Report and the 2001 Citizen Petition.

The court went on to caution defendants FDA and DoD in its decision by referencing in footnote #10 its judicial awareness of the *"numerous substantive challenges"* to the FDA's actions beyond its summary judgment on procedural grounds. The court wrote:

"Because the Court is granting plaintiffs' Motion for Summary Judgment, this Memorandum Opinion does not address plaintiffs' alternative argument for discovery or defendants' Motion for Summary Judgment. Moreover, since the Court's holding is based on procedural grounds, the Court does not reach plaintiffs' numerous substantive challenges to FDA's Final Rule and Order."

Following the federal court's injunction, under the rare admonition of summary judgment, the FDA pursued its latest steps to issue a new rule for anthrax vaccine adsorbed. The FDA previously validated, but did not act on, this requirement in its September 2002 response to Citizen Petition Docket #2001P-0471. The new rulemaking has now allowed the current series of public docket entries, allowing this attempt to implore the to FDA act responsibly and legally.

⁷ House Report 106-556 Findings excerpt: "Efficacy of the vaccine against biological warfare is uncertain. The vaccine was approved for protection against cutaneous (under the skin) infection in an occupational setting, not for use as mass protection against weaponized, aerosolized anthrax." See: http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=106_cong_reports&docid=f:hr556.106.

Based on the multiple previous attempts at requesting the FDA perform its “*primary mission*,” and due to the FDA’s reticence to do so in the past as requested by Congress, Citizens and the Court, it is now appropriate that we ask the FDA to exercise an abundance of caution as it proceeds in performing its mission — to “*protect the public [and servicemembers] health*.”

Following the current open 90 public docket period, closing on March 29, 2005, the FDA would be remiss once again if it fails to reconstitute an expert review panel as delineated in its own rule making guidelines. The Court specifically referenced the requirement that the FDA “*must*” follow its rules.⁸ Such prudence will ensure that the FDA’s future actions will not for a third time be found to be “*arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with the law,*” or “*without observance of procedure required by law.*”

According to the court, when the FDA’s experts “*review the labeling*” of a vaccine the Agency follows a “*two-stage*” process whereby the expert review panel evaluates the scientific data and submits a report to the FDA Commissioner prior to a proposed rule. Currently the FDA is circumventing this normal requirement, moving directly to a proposed ruling for full vaccine licensure. But in doing so, the Agency is altering the recommendations of the original review panel. FDA’s new interpretations contradict the explicit wording of the 1973 expert review panel’s 1985 proposed rule.⁹ Thus, FDA’s new interpretations require renewed expert review.

The federal court’s ruling on the illegality of the anthrax vaccine mandate also captured the DoD's attorney's admitting that the original, never finalized, proposed rulemaking for anthrax vaccine adsorbed in 1985 didn't contemplate the vaccine's mass use for inhaled anthrax. The attorney for the DoD and FDA candidly admitted: “*But it’s absolutely right, Your Honor, that the possibility of weaponized anthrax was not in the minds of the advisory panel and probably not in the minds of the FDA.*”¹⁰

In addition to this admission, the federal court ruling also reiterated the language in the original 1985 review of the vaccine as published in the Federal Register: “*Anthrax vaccine poses no serious special problems other than the fact that its efficacy against inhalation anthrax is not well documented.*” Considering these admissions and facts, the FDA “*must*” reform an expert panel to review all new data and uses. The original 1985 experts never contemplated such uses. Therefore, unbiased expert review is finally required for any data generated on a post-facto basis.

Even the original Chairman of the 1973 expert review panel commented on the previous scientific, versus the current legal, foundations of the 1985 Proposed Rule’s recommendations in an article for *Nature Medicine* in February 2004. Gene Stollerman affirmed, “*I will defend our [1973] interpretation ... Any other interpretation has to do with legal issues.*”

Given these inconsistencies, the American public will now view with increased scrutiny any new interpretations by the FDA for legal reasons, particularly because they are contrary to previously documented scientific conclusions about anthrax vaccine adsorbed. Multiple examples include:

8 See: <http://www.dcd.uscourts.gov/Opinions/2004/Sullivan/03-707c.pdf>.

9 <http://www.fda.gov/ohrms/dockets/dockets/80n0208/1980N-0208.htm>.

10 See: <http://www.dcd.uscourts.gov/Opinions/2004/Sullivan/03-707c.pdf>. See page 30, footnote 9.

January 22, 1969, letter from CDC to NIH: *“There have been no controlled evaluation studies with the Michigan anthrax product as was done by Dr. Phillip Brachman using the Merck, Sharp and Dohme product.”*

1985 U.S. Army Request For Proposal (RFP) for a replacement anthrax vaccine: *“There is no vaccine in current use which will safely and effectively protect military personnel against exposure to this hazardous bacterial agent. A licensed vaccine against anthrax, which appears to afford some protection from the disease, is currently available for human use...The vaccine is, however, highly reactogenic, requires multiple boosters to maintain immunity and may not be protective against all strains of the anthrax bacillus.”*

1985 FDA expert panel product review panel for anthrax vaccine adsorbed: *“The vaccine manufactured by the Michigan Department of Public Health has not been employed in a controlled field trial... efficacy against inhalation anthrax is not well documented...No meaningful assessment of its value against inhalation anthrax is possible due to its extremely low incidence...”*

1989 letter by Assistant Secretary of Defense Robert B. Barker to Senator John Glenn, Chairman of the Senate Governmental Affairs Committee: *“Current vaccines, particularly the anthrax vaccine, do not readily lend themselves to use in mass troop immunization for a variety of reasons: the requirement in many cases for multiple immunizations to accomplish protective immunity, a higher than desirable rate of reactogenicity, and, in some cases, lack of strong enough efficacy against infection by the aerosol route of exposure.”*

March 1990 article in Infectious Disease Clinics of North America by Col. (Dr.) Takafuji and Col. (Dr.) Philip K. Russell: *“Limited use vaccines and products are defined as those unlicensed experimental vaccines...used in specific contingency situations...Limited use vaccines include...anthrax.”*

1991 letter by the Secretary of the Army indemnifying the anthrax vaccine manufacturer (a similar letter was also signed by Louis Caldera, Secretary of the Army, September 3, 1998): *“... unusually hazardous risks associated with potentially severe adverse reactions and the potential lack of efficacy of the AVA. These concerns stem from: a) the limited use of the vaccine to date, i.e., tests prior to approval of the vaccine by the Food and Drug Administration are on too small a scale to permit accurate assessment of types and severity of adverse reactions (only widespread use can provide this assessment); and b) insufficient experience in mass immunization programs to truly evaluate the efficacy of the vaccine. Moreover, there is no way to predict whether the pathogen against which the vaccine may be used will be sufficiently similar to the pathogen used in tests to ensure vaccine efficacy.”*

December 8, 1994 Senate Veterans Affairs Committee Staff Report 103-97: *“Therefore, the efficacy of the vaccine against biological warfare is unknown. ... The vaccine should therefore be considered investigational when used as a protection against biological warfare.”*

September 29, 1995 SAIC Corporation study for the DoD regarding anthrax vaccine adsorbed's IND application for inhalation anthrax (submitted by the manufacturer on 20 Sep 1996): "This vaccine is not licensed for aerosol exposure expected in a biological warfare environment."

1999 article in *Vaccines* by Col (Dr.) Arthur Friedlander and Dr. Philip S. Brachman, p. 635: "There have been no controlled clinical trials in humans of the efficacy of the currently licensed U.S. vaccine."

The above examples abundantly demonstrate that the DoD and FDA have altered the previous commonly accepted scientific conclusions about the anthrax vaccine to support policy over science. This may be due to the complex "*legal issues*," versus the original intellectually honest "*interpretation*" of the 1973 expert review panel as suspected by its Chairman, Gene Stollerman. Yet still more examples exist through internal efforts within the DoD to halt the shift of opinion.

The DoD's Assistant Secretary of Defense for Health Affairs (ASDHA) was placed on notice with a briefing by USAF Officers about the legal improprieties and misinformation of the AVIP on January 14, 2002 in Pentagon Room 3E1082. This rejection of the recommendations of the official meeting marks an additional example of the DoD's reluctance to reverse the wrongdoing associated with the AVIP. More importantly, the DoD's dismissive official response concerning their notification about the impropriety of the non-finalized status of the vaccine's license was significant. The DoD response commented on the irrelevance of the lack of a final rule saying:¹¹

*"The panel reviewing anthrax vaccine recommended its continued licensure and FDA accepted this recommendation. FDA apparently never adopted a Final Rule to conclude this review process. Several vaccines are subject to this **bureaucratic loose end** ... which apparently has no regulatory meaning."*

Despite the DoD's dismissal of these internal warnings, the federal court found the DoD's shortsighted interpretation of this "**bureaucratic loose end**" to be incorrect. Instead, the "**bureaucratic loose end**" became a partial basis of the AVIP's illegality, and resulted in this rulemaking. Though the DoD and the FDA bureaucracies are seemingly intertwined in this dilemma, the FDA has the statutory responsibility under the strict guidance of the Federal Food, Drug, and Cosmetic Act to bring these events to a scientifically and legally supportable closure.

Ultimately, the FDA must proceed with caution in its considerations to alter the basis of scientific conclusions. This is especially vital in light of the FDA's acknowledgment of the "*DoD's continuous involvement*"¹² with manufacturing of, and the manufacturing changes made to, anthrax vaccine adsorbed. Because FDA has described that the "*DoD is thus similar to a manufacturer*" they must hold DoD, and other responsible entities, accountable for the previous illegal actions documented in the public record, and affirmed by the federal court. These include

¹¹ Position Paper by the Office of the Assistant Secretary of Defense, Col. John Grabenstein, Deputy Director, AVIP Agency.

¹² Ibid, http://www.fda.gov/ohrms/dockets/dailys/02/Sep02/091102/091102.htm#_Toc19593512.

the use of a vaccine for the unapproved purpose for inhaled anthrax, as well as the previous illegal adulteration of anthrax vaccine adsorbed due to unapproved manufacturing alterations in violation of the specific guidance of the Federal Food, Drug, and Cosmetic Act.¹³

The legal chaos created by altering original interpretations of the 1973 expert review panel cannot be erased. The original assessment was that the proof of efficacy for inhalation anthrax was not supportable. Significantly, Dr. Phillip S. Brachman was the original researcher responsible for the study of the inhalation anthrax epidemic at the Arms Mill in Manchester, NH in 1957. Dr. Brachman's study is now being used as the primary basis of the FDA attempt to justify license changes to support inhalation anthrax. It is imperative to highlight Dr. Brachman's 2002 view on vaccine efficacy in the American Journal of Epidemiology:¹⁴

“The results showed a 92.5 percent efficacy in preventing cutaneous anthrax. Although five cases of inhalational anthrax occurred in one of the field trial mills (two in placebo recipients and three among nonparticipants), the results were not statistically significant in view of the small number of events to address the efficacy of the vaccine in preventing inhalation anthrax.”

The FDA should not alter the previous anthrax vaccine adsorbed expert review panel's conclusions about the anthrax vaccine, or accept any evolving opinions of the DoD or Dr. Brachman, despite the fact that he has submitted opinions now favorable to the FDA. Dr. Brachman, the federal court, the U.S. Congress, and the original FDA expert review panel chair currently all have disagreed with the FDA's new interpretations of use for inhalation anthrax.

It is important for the FDA to weigh the public's realization of these shifting of opinions as it proceeds with its rule-making mission. To yield as a bureaucratic skill to the institutional goals and interpretations of the DoD in this matter is not in the best interest of the public health or the reputation of the FDA as an executive branch agency. It is paramount that the FDA prudently assess the ethical and legal risks it accepts if it acquiesces to DoD objectives, particularly in light of that fact that the *“DoD is thus similar to a manufacturer.”* Our soldiers, and the protection of their rights, rely on the FDA's good judgment, regulatory discretion, and proper use of power.

Based on the FDA's *“primary mission”* — *“to promote and protect the public health,”* the Agency must remain strong in its role as the enforcement arm for the public and the government. Nowhere in the preamble of the FDA's mission does it say that its primary mission is to promote and protect DoD policies. To the contrary, the FDA must protect the America's public and the members of her armed forces from illegal policies and vaccines that lack proper approval.

As the Deputy Defense Secretary Rudy de Leon previously maintained, the DoD is *“willing to accept the independent judgment of FDA on this question.”*¹⁵ The DoD will comply with the FDA's judgments, but compelling the DoD will require decisiveness and fortitude by the FDA, as well as the initiation of firm actions, to avoid further abuses of discretion. The FDA *must*:

13 GAO-02-181T Anthrax Vaccine: Changes to the Manufacturing Process, See: <http://www.gao.gov/new.items/d02181t.pdf>.

14 Bioterrorism: An Update with a Focus on Anthrax Brachman Am. J. Epidemiol..2002; Vol. 155, No. 11, 2002, page 984, Column 2

15 Inside the Pentagon, May 11, 2000, page 2.

1. Reconstitute the expert review panel in accordance with Agency rules prior to finalizing the license rulemaking for anthrax vaccine adsorbed.
2. Investigate previous unresolved complaints referred to the Agency, and the FBI's Public Corruption Squad, by the Defense Criminal Investigative Service.
3. Investigate the internal inquiries made by DHHS officials, such as Mr. Stewart Simonson, Deputy General Counsel, with particular focus on involvement in WI ANG pilot expulsions.
4. The FDA should conduct a thorough risk analysis regarding anthrax vaccine adsorbed's unprecedented and alarming safety profile (4094 reports of adverse reactions since the 1999 — a hundred-fold increase).¹⁶ FDA's analysis should focus on the ethical risks FDA faces if it continues to support the DoD's AVIP, versus holding the Department accountable as a "*manufacturer*" for both illegally experimenting with anthrax vaccine adsorbed, as well as allowing the manufacturing process to be changed and adulterated without approval.¹⁷

FDA's proper execution of its mission, and the rulemaking process specific to this docket, will guarantee the public's confidence and trust, as well as that of the members of the armed forces.

Respectfully submitted,

//Signed//

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¹⁶ As of March 24, 1999 Congressional testimony the FDA reported that only 42 Vaccine Adverse Event Reporting System (VAERS) reports were submitted to the FDA and CDC since 1990 for anthrax immunizations given to over 223,000 servicemembers. By 2004 the FDA admitted to at least 4,136 adverse reactions for immunizations given to 1.3 million servicemembers. This equates into a 100-fold increase in adverse reactions for only slightly over five times more shots given to soldiers. Clearly something doesn't add up. See latest FDA VAERS data listed in this docket: <http://www.fda.gov/ohrms/dockets/dockets/80n0208/80n-0208-cr00001-02-vol128.pdf>.

¹⁷ GAO-02-181T Anthrax Vaccine: Changes to the Manufacturing Process, See: <http://www.gao.gov/new.items/d02181t.pdf>.