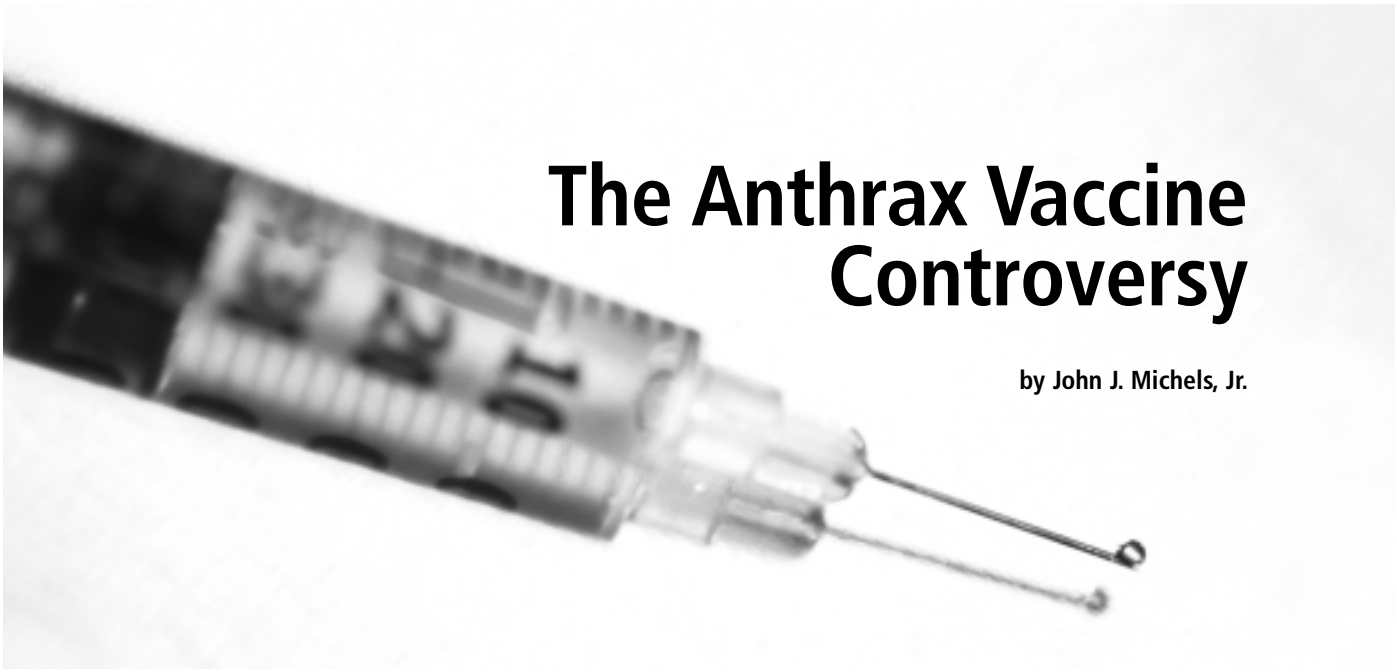

The Anthrax Vaccine Controversy

by John J. Michels, Jr.

The events of September 11, 2001, dramatically raised the profile of a little noticed program—the mandatory and involuntary vaccination of all members of the United States military with the anthrax vaccine adsorbed (AVA). The military's vaccination program for anthrax began in 1997 with an announcement by then-Secretary of Defense William Cohen. Cohen viewed anthrax as a significant threat to United States forces, and he announced his intentions to take appropriate preventative measures against that threat. Cohen directed the Department of Defense to establish a vaccination program for all active duty and reserve service members that would protect them from an attack using anthrax as a biological warfare agent.

From its very inception, the program was controversial. The debate intensified at the beginning of October 2001. The vaccination program has been plagued by the inability of the sole vaccine manufacturer, BioPort, a Michigan corporation, to produce any vaccine following a series of at least ten failed FDA inspections beginning in 1988. Service members, including both active duty and reserve members, have mounted a series of challenges to the vaccine and its manufacturer. They want to demonstrate that the vaccine is adulterated under the food and drug law of the United States, experimental under the FDA regulations, and improperly licensed under FDA procedures.

On May 4, 2001, Washington, D.C., attorney Mark Zaid and I filed suit in federal court in the District of Columbia, asking for a declaratory judgment that the vaccine was "an investigational new drug or a drug unapproved for its applied use" under the meaning of the FDA regulations and federal statutes. Other legal challenges have been mounted against the vaccine and its manufacturer.

A Brief History

In 1970, the Public Health Service licensed the AVA based on data from a trial study of an anthrax vaccine conducted in the 1950s. This trial, known as the "Brachman Study," used a vaccine prepared by Merck, Sharp & Dohme. Ironically, this vaccine differed substantially from the vaccine licensed in 1970 and in current use. According to the General Accounting Office, the vaccine licensed in 1970 used a different manufacturing process from the Brachman Study vaccine and a different strain of anthrax to grow the vaccine. The ingredients and/or formulation used to make the vaccine were changed from the Brachman Study vaccine. In other words, the original licensing of the AVA, then manufactured by the Michigan Department of Public Health (MDPH) was based on data derived from a different substance.[1]

The vaccine was originally licensed for individuals with occupations that involve the handling of animal carcasses or engaged in research on anthrax. The vaccination schedule requires 6 shots at intervals of 2 weeks, 4 weeks, 6 months, 12 months and 18 months.

In the 1980s, the Army began looking at various preventative measures regarding the use of biological weapons. Because anthrax was thought to be a likely biological weapons choice, the Army examined the AVA as a potential preventative, and found it lacking. In 1985, the Army published a "request for proposal," soliciting vaccine manufacturers to manufacture a new anthrax vaccine because "There is no vaccine in current use which will safely and effectively protect military personnel against exposure to [anthrax] . . . 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."[2]

Because there was a lack of controlled human field trials noted in the original licensing documents for the AVA, the FDA published a proposed rule for a specific product review of the vaccine in December 1985. However, a final rule fully affirming the vaccine

license was never published, apparently, because the manufacturer provided no human efficacy data on the vaccine to FDA.[3]

From 1985 until 1996, the Army continued its assessment of the AVA as inadequately licensed for use against inhalation anthrax threat. In 1995, the Army worked with an outside contractor to develop a plan to obtain FDA approval for a license amendment that would include aerosolized anthrax exposure. The plan submitted by the contractor and approved by the Army stated that: "this vaccine is not licensed for aerosol exposure expected in a biological warfare environment."[4]

As a result of its efforts in 1995, and close cooperation with the Michigan Department of Public Health, the Army and MDPH planned a submission to FDA to conduct experiments showing that the vaccine was effective against inhalation anthrax, and to reduce the number of shots required for effective vaccination from six to two or three. Over the course of a year, meetings between the Army, Joint Chiefs of Staff personnel and the Office of the Secretary of Defense concluded that it was necessary to obtain FDA approval of a license modification showing that the AVA was effective against inhalation anthrax before the Department of Defense could start mass anthrax vaccinations.

In September 1996, Michigan Biologic Products Institute, MDPH's successor, submitted an investigational new drug ("IND") application to the FDA. The IND application stated that it was being submitted for the purpose of securing a change to the license for the AVA to reflect an indication to include inhalation anthrax, a change in the number of shots required for vaccination, and a change in the route of vaccination.[5] The investigational new drug application, which outlined a plan of experiments to correlate inhalation anthrax survivability in animals with that of humans, as well as other experiments assessing the efficacy of the vaccine after two or three vaccinations, remains open. The manufacturer, whose filings indicate that the IND is for "inhalation anthrax", has supplemented it on an annual basis.

Despite this extended history of viewing the license as not including inhalation anthrax, on March 4, 1997 (approximately one month after William Cohen became Secretary of Defense), the Office of Secretary of Defense wrote a letter to the FDA saying that the Department of Defense had long maintained that the license for AVA included licensing against inhalation anthrax.[6] The FDA responded circumspectly, stating in a letter that the use of the AVA for inhalation anthrax "was not inconsistent" with an AVA license.[7] This curious phraseology has formed the basis for the Department of Defense's assertion that the vaccine is licensed for inhalation anthrax, despite the still pending IND application. Interestingly, Commissioner Friedman did not reference 21 CFR §10.85, which delineates the requirements for an official FDA advisory opinion. His failure to follow the requirements of this regulation renders his opinion a personal one, and not that of the FDA.[8]

In 1998 Congress passed 10 U.S.C. § 1107 regarding the use of investigational new drugs or drugs unapproved for their applied uses by members of the Armed Forces. The statute requires that service members consent before administration of an investigational new drug or a drug unapproved for its applied use in connection with the members' participation in a particular military operation.

A presidential executive order, signed in September 1999, goes even further. It states that before administering an investigational drug to members of the Armed Forces, the Department of Defense must obtain informed consent from each individual unless the secretary can justify to the president a need for a waiver of informed consent in accordance with 10 U.S.C 1107.[9]

In other words, there is an informed consent requirement before an investigational new drug can be given to a service member. Only the president can waive the requirement. The Department of Defense has steadfastly refused to acknowledge this requirement in the case of the AVA, although it has promulgated its own internal regulation that specifically adopts the requirements of 10 U.S.C. 1107 and Executive Order 13139.[10]

Interplay Between the Law and the Facts

The upshot of the history of the vaccine, coupled with the relatively recent statutory and executive order changes in use of investigational drugs, means that if the AVA is an investigational new drug, the Department of Defense's program of mandatory inoculation is illegal.

A drug can be placed into investigational new drug status in several ways.

The drug can be administered in a manner inconsistent with its labeling. Or a manufacturer might file an investigational new drug application and conduct experiments pursuant to that application.[11] The Department of Defense and the manufacturer have made the drug an IND using both methods.

In the summer of 2000, DoD began a drastic reduction in the vaccination program as a result of the manufacturer's inability to pass FDA inspections relating to the vaccine. Hundreds of individuals stopped their vaccinations in mid-sequence. For those individuals who had at least two shots, DoD unilaterally announced that they would not be required to restart the vaccination sequence as long as they received the next injection within two years of their last shot.

This unprecedented modification of a licensed vaccination sequence almost certainly renders the vaccine investigational, as used by DoD. Several FDA managers told Congress, that while

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the vaccine was properly used in 1998 and 1999, any deviation from the licensed shot sequence would revert the drug to investigational status.[12]

Although DoD maintained in court filings as late as the summer of 2000 that it followed the FDA approved immunization schedule for the vaccine, it has been policy for the last 15 months that DoD use the vaccine "off label" in an unlicensed manner—causing the vaccine to be investigational.

Now, the military involuntarily vaccinates its soldiers against inhalation anthrax with a vaccine for which an investigational new drug application for inhalation anthrax currently exists, and has existed for over five years. In addition, DoD unilaterally modified the FDA approved and licensed shot schedule, telling service members that they will not need additional shots even if there is as much as a two-year break in the shot sequence.

These two factors—the investigational new drug application and the deviation from the FDA licensed shot schedule—form the basis of the declaratory judgment case filed in May, 2001. In addition to the declaratory judgment action, the manufacturer faces other legal challenges in the form of a Citizens' Petition filed with the FDA seeking revocation of the manufacturer's license to make the vaccine. The petition also asks for the revocation of federal contracts to manufacture the vaccine. A *qui tam* action filed by former service members' claims that the manufacturer knowingly produced a vaccine that was not effective and in accordance with the government specifications.

As people clamor for access to the vaccine, these legal actions may well determine whether the public will have access to something that effectively is untested for the purpose for which it is being offered and whether the government tries, again, to develop a truly effective prophylaxis against anthrax. ⚖

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Endnotes

1 *See* GAO report of 29 April, 1999, found at http://www.gao.gov/AindexFY99/abstracts/ns99148t.htm.

2 RFP No. DAMD 17-85-R-0078, US Army Medical Research Acquisition Activity, Fort Dietrich, Frederick, Maryland, May 16, 1985. The Army proposal was prophetic, the vaccine would not have protected the Florida man who died of inhalation anthrax in October 2001.

3 December 13, 1985, FDA Product Review & Proposed Rule, found at http://www.house.gov/reform/hearings/healthcare/00.10.03/timeline.doc

4 September 29, 1995 enclosure to memorandum from Dr. Anna Johnson-Winegar, US Army Medical Research and Material Command, Ft. Dietrich, Frederick, Maryland, October 5, 1995.

5 IND application dated 20 September, 1996

6 March 4, 1997 letter of Steven Joseph to FDA Commissioner Michael Friedman

7 March 13, 1997 letter from Michael Friedman to Steven Joseph

8 *See* 21 CFR 10.85 which states in full: "a statement made or advice provided by a FDA employee constitutes an advisory opinion only if it is issued in writing under this section. A statement or advice given by a FDA employee orally, or given in writing but not under this section or Section 10.90, is an informal communication that represents the best judgment of that employee at that time but does not constitute an advisory opinion, does not necessarily represent the formal position of FDA, and does not bind or otherwise obligate or commit the agency to the views expressed."

9 Executive Order 13139, September 30, 1999.

10 *See* DoD Directive 6200.2.

11 *See generally* 21 CFR§312.

12 *See* February 18 1997 memorandum from Dr. Karen Goldenthal to Admiral Martin regarding Anthrax vaccine, for example.