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JOHN DOE # 1 et al., Plaintiffs, v. DONALD H. RUMSFELD et al., Defendants.

Civil Action No.: 1:03CV00707(EGS)

UNITED STATES DISTRICT COURT FOR THE DISTRICT OF COLUMBIA

2003 U.S. Dist. Ct. Motions 707; 2004 U.S. Dist. Ct. Motions LEXIS 6277

April 7, 2004

Motion for Summary Judgment

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TITLE: [**1]

PLAINTIFFS' OPPOSITION TO DEFENDANTS' MOTION FOR SUMMARY JUDGMENT

TEXT: Plaintiffs John and Jane Doe one through six, by counsel, submit their Opposition to the Government's Motion for Summary Judgment, pursuant to *Fed. R. Civ. P. 56* and this Court's Order of January 16, 2004.

I. PRELIMINARY STATEMENT

Although the Defendants apparently treat this case as a routine challenge to administrative rulemaking, in reality, the straightforward issue before the Court affects the health of millions of service members and contractors who either received or will receive the Anthrax Vaccine Adsorbed ("AVA"). Because this litigation involves the first widespread use of a bioweapon vaccine in response to a public health threat, the questions raised with regard to the integrity of Defendants' approval process and decision to use the vaccine are critical to this nation's preparations for attacks with weapons of mass destruction.

The history of AVA dates back some 50 years. The primary FDA decision, albeit in a preliminary form, issued nearly 20 years ago. Defendant DoD's policies and decisions regarding AVA occurred during the last 15 years, and primarily in the last 7 years. Yet [**2] with all the information that exists concerning AVA, its development and its [*2] approval, comprising hundreds of thousands of pages of relevant documents, and with 9 lawyers analyzing the issues before the Court, the principal argument of Defendants DoD and FDA is that AVA is properly licensed "because we said so."

In fact, the Government's Motion for Summary Judgment and supporting Memorandum of Law systematically ignore FDA's complete failure to follow the requirements of the Administrative Procedures Act, *5 U.S.C. § 706* (2003). Instead, the Defendants ponderously retrace the licensing history of the vaccine, omitting key details along the way, in an attempt to obfuscate FDA's regulatory failure. In attempting to show that FDA's determination that the vaccine is

safe and effective (and therefore presumably properly licensed) against inhalation anthrax is proper, the government baldly distorts the record, misrepresents the findings upon which the vaccine's license is supposedly based, and provides key evidence demonstrating why AVA is still a drug unapproved for its intended use.

Plaintiffs respectfully ask the Court to keep in mind the nature of [**3] this case. The relevant statute, *10 U.S.C. § 1107*, says nothing about whether a drug or biologic is safe or effective or even licensed. The statute simply prohibits the use of investigational new drugs or drugs unapproved for their intended use on service members without the informed consent of those service members. In its decision suspending the anthrax vaccine immunization program ("AVIP") on December 22, 2003, this Court determined that the vaccine was investigational (or that the plaintiffs were likely to prove it was investigational) because FDA failed to complete its licensing review and because there was an outstanding investigational new drug application still in effect. See Memorandum Opinion at p. 29, December 22, 2003.

[*3] Eight days later, FDA hurriedly and (the government would have the Court believe) coincidentally completed processing on a final rule that had been pending for 18 years. See Biological Products; Bacterial Vaccines and Toxoids; Implementation of Efficacy Review, *69 Fed. Reg. 255* (Jan. 5, 2004) ("FDA Rule" or "Final Rule"). Base on the new Final Rule, this Court properly reassessed its ruling and lifted [**4] the injunction. The Court then asked the parties to move for summary judgment on the issue of whether the Final Rule issued by FDA was proper. But the real heart of this dispute remains whether the vaccine is an IND and/or a drug unapproved for its intended use. If the Court finds that FDA did not issue its Final Rule in accordance with statutory requirements, then the AVA is not properly licensed for its intended use as prophylactic against inhalation anthrax. Under the circumstances, the Court should reinstate its injunction until the FDA brings the vaccine's license into compliance.

The Defendants' Motion for Summary Judgment simply ignores the regulatory compliance issue. By submitting page after page of irrelevant factual information, the Defendants attempt to "paper" the Court into disposing of this case by telling the Court that FDA has found the vaccine to be safe, effective and not misbranded, and that this decision is effectively unreviewable.

The numbing detail of the alleged FDA review does not save the Defendants' case because all of their recited facts are irrelevant to the real issues in this case. The numerous omissions in the Defendants' recitation of events n1 and [**5] the Defendants' continuing inability to explain the fact that both the original, and only, human study of an [*4] anthrax vaccine and the assessment of the FDA's own expert panel categorically conclude that there is insufficient evidence to license the vaccine against inhalation anthrax, effectively doom the Defendants' motion. Instead, the numerous intentional omissions of events and determinations in the record provide overwhelming evidence that the failure of the FDA to reopen the comment period for AVA is fatal to vaccine's license status. n2

n1 For example, Defendants simply fail to discuss, or even acknowledge, the IND applications and process begun in 1996; the application goes to the very issue under consideration now, i.e. did FDA properly issue its Final Rule?

n2 Defendants also mysteriously raise the issue of Plaintiffs' standing, although the Court dealt conclusively with this matter in its Opinion of December 22, 2003. See Memorandum Opinion at pp. 20-22.

The Defendants are not entitled [**6] to summary judgment on their motion because the undisputed facts in this case show that:

a. The FDA's Final Rule ignores the findings of both the studies and the expert report upon which the final rule is based;

b. There has never been a statistically valid trial of AVA against inhalation anthrax involving human subjects;

c. The FDA's Final Rule is improperly based on animal studies with the vaccine; and

d. The FDA engages in regulatory sleight of-hand to approve AVA when it is undisputed that the only controlled field study used to validate AVA effectiveness was performed with a different vaccine.

For these and other reasons, this Court should deny the Government's Motion for Summary Judgment, void the Final Rule issued on December 30, 2003, order the FDA to follow proper statutory requirements in its licensing process for AVA, and reinstate the injunction on further inoculations.

[*5] **II. ARGUMENT**

A. The FDA's Final Rule Relies on Invalid Studies

It is undisputed that the "most significant" piece of evidence relied on by FDA to establish the efficacy of the AVA is the so-called Brachman study; the only "controlled" field study of the vaccine involving [**7] human participants. See Defendants' Memorandum of Points and Authorities (filed March 3, 2004)("Defendants' Memo") at p. 36. FDA's reliance on the study to support its determination that the vaccine is effective against inhalation anthrax is flawed in at least two respects.

First, Brachman himself indicated at the time of the study, and on numerous occasions thereafter, that there was insufficient evidence (because of a paucity of cases) to determine if the vaccine was effective against inhalation anthrax. Although the government engages in pages of double talk in an effort to justify its complete reliance on the Brachman study for its finding, it cannot escape an essential fact, namely, that Brachman himself has never asserted that his study demonstrates AVA's effectiveness against inhalation anthrax. See Plaintiff's Memorandum in Support of Its Motion for Summary Judgment (filed March 3, 2004)(Plaintiff's Memo) at p. 8; Brachman, et al., "Field Evaluation of a Human Anthrax Vaccine," 52 Am. J. of Pub. Health 632 (1962).

Likewise, FDA's own expert panel determined in 1985 that there were too few instances of overlap between exposure to inhalation anthrax and vaccine [**8] use to validate AVA's effectiveness. It categorically stated that the vaccine's effectiveness against inhalation anthrax could not be determined, although it did recommend approving AVA as a Category I biologic. See Biological Products; Bacterial Vaccines and Toxoids; Implementation of Efficacy Review, *50 Fed. Reg. 51, 002* (December 13, 1985).

[*6] In an effort to get around this fatal limitation, the government engages in an analysis that can only be described as bizarre. Ignoring the clear language of the Brachman study, FDA simply notes that because Brachman included inhalation cases in his total count of cases for the determination of vaccine effectiveness, this must mean that the vaccine is effective regardless of route of exposure. See Defendants' Memo. at pp. 16-17; FDA Rule at 259-60.

In other words, even though the researcher himself repudiated any conclusion about the effectiveness of AVA against inhalation anthrax, the fact that he included inhalation cases (apparently by mistake) in determining the total effectiveness of the vaccine means that the FDA can disregard his specific determination with regard to efficacy and inhalation anthrax. This, [**9] of course, is pure nonsense.

Second, a recent statistical analysis of Brachman data, using analytical tools unavailable to Brachman in 1962, reveals that there is no statistical correlation between vaccination with AVA and inhalation anthrax protection. See Declaration of Dr. Walter Schumm, Colonel, USAR (Ret.) attached as Exhibit "1"; Schumm, et al., A Statistical Re-Analysis of the Relationship Between Anthrax Vaccination and Anthrax Infections in Goat Hair Mills in the 1950s, March 2004, attached as Exhibit "1-A". n3

n3 This Circuit has considered extra-administrative record documents when there are allegations that the agency either deliberately excluded from the record evidence adverse to its position, or was negligent in failing

> to include such documents. *Kent Cty, Del. Ct. v. US EPA, 963 F.2d 391, 395-6 (D.C. Cir. 1992),* citing *San Louis Obispo Mothers for Peace v. NRC, 751 F. 2d 1287, 1327 (D.C.Cir. 1984)* (subsequent history omitted). See also *Esch v. Yeutter, 876 F.2d 976, 991 (D.C. Cir. 1989)*(there are as many as eight different bases when extra-record evidence may be considered by the reviewing court, including *when agency action is not adequately explained*, when *the agency failed to consider relevant factors*, and in cases *where relief is at issue, particularly at the preliminary injunction stage*)(emphasis added).

[**10]

[*7] Of particular note in Dr. Schumm's analysis is his validation of Dr. Brachman's initial assessment that it was impossible to determine any correlation of effectiveness for AVA against inhalation anthrax. Dr. Schumm's studies also validate the Institute of Medicine's similar determination that the small number of inhalation cases makes it impossible to validate the effectiveness of the vaccine. Id. at para. 5; See also Strom, et.al., Institute of Medicine, "The Anthrax Vaccine: Is it Safe? Does it Work?" (2002) ("IOM Report") found at (http: //www.nap.edu/catalog/10310.html) at pp. 58-59.

In addition to statistically validating the findings of Brachman and the Expert Panel that there was no valid evidence of efficacy for inhalation anthrax, Dr. Schumm's analysis notes that the CDC surveillance data, used by FDA to support the effectiveness of the vaccine, is statistically invalid and entitled to no weight whatsoever. Schumm, et al., at para. 5. Schumm further notes that, using modern statistical analyses, the vaccine used in the Brachman field trial (which FDA uses as a surrogate for AVA) does not protect against infection by any route in the majority of [**11] cases.

> Even taking both cutaneous and inhalation anthrax into account, we found that the vaccine's protective effects were not significant in 75% of the mills tested. In addition, partial vaccination status was never a significant predictor of infection risk, suggesting that incomplete vaccinations were relatively ineffective, even in preventing cutaneous anthrax infection.

Id., at para. 4.

Of course, had the FDA properly reopened the rule-making comment period for the vaccine when it began considering new information after 1985, as required by law, this information could have been before the FDA and a meaningful assessment of the vaccine' s efficacy could have been made. Instead, the FDA elected to proceed with certifying the Final Rule as quickly as possible, given that this Court was aware of the [*8] numerous deficiencies in the DoD's anthrax vaccination program. n4 The end result is a Final Rule that not only contradicts the specific determinations found in the reports upon which the Final Rule ostensibly relies, but also uses a tortured analysis in an effort to escape those inherent contradictions.

> n4 In its press statement of December 30, 2003, announcing the Final Rule, the FDA calmly announced that it issued its determination in an effort to influence this litigation:
>
> > A recent ruling by United States District Court for the District of Columbia gave the opinion that the anthrax vaccine should be classified as "investigational" with regard to protecting against inhalation anthrax. Today's Final Rule and Order make it clear that FDA does not regard the approved anthrax vaccine as "investigational" for protection against inhalation anthrax. FDA's final determination of the safety and effectiveness of the anthrax vaccine, independent of route of exposure, as well as its conclusion regarding the Expert Panel's Report, being announced today in the Final Order, are relevant and should be considered in any further litigation in this matter."
>
> A copy of this press statement can be found at *http: //www.fda.gov/bbs/topics/News/2003/ New01001.html*. It is

a rare event indeed for a federal agency to issue an administrative ruling followed by a press release, noting the agency's specific intent to influence ongoing litigation.

[**12]

Accordingly, there are numerous issues of material fact at the heart of the FDA's action in issuing the final rule approving the status of the vaccine as safe and effective. Their own documents show that Defendants cannot demonstrate that the approval of AVA was done in a proper manner. On this basis the court should deny the Government's motion.

B. The FDA's Decision Also Relies on the Inappropriate and Improper Use of Animal Data to Validate the Vaccine's Effectiveness

The FDA does not limit the basis for its Final Rule to unjustified reliance on the flawed Brachman study. Other assessments of AVA relied on by the FDA are heavily [*9] influenced by the use of various animal studies conducted by the DoD in effort to determine AVA's efficacy against inhalation anthrax. See Defendants' Memo at p. 41.

Defendants in their brief admit that use of animal studies to substantiate AVA's effectiveness is improper under the requirements of *21 CFR § 601.25 (d)(2)*. Id. at p. 41, n. 35. Defendants try to dance away from this particular problem by noting that FDA relied solely on the Brachman study as "proof of effectiveness" for purposes of § 601.25 (d) (2), and [**13] the animal studies, CDC surveillance data and other support data and studies were considered merely as "corroborating" evidence. See Defendants' Memo. at p. 41, n. 35.

But, as has been discussed previously, the Brachman study specifically states that it could not determine the effectiveness of AVA with regard to inhalation anthrax. The FDA's own expert panel also found that it could not rely on the Brachman study to determine inhalation anthrax efficacy. Under the circumstances, the government's reliance on animal data for any corroboration is improper, especially since it is undisputed that no correlate of immunity has been found between any of the animals tested and human beings, a requirement for use of animal studies. See Plaintiff's Memo. at pp. 12-15 and authorities cited therein.

A cursory review of information contained in the Defendants' Memo. clearly shows that the FDA's use of animal data is key to its finding that AVA is safe and effective, if for no other reason than AVA's only controlled study of AVA does not support such a conclusion. See Defendant's Memo at pp.40-41, n.35. Following the determination of FDA's Expert Panel that there was insufficient evidence [**14] to establish the effectiveness of the vaccine against inhalation anthrax, FDA realized it needed some [*10] other source of information to support its rejection of the Panel's conclusions. The only testing data in the record on efficacy that came into existence after the Expert Panel made its findings is animal testing data. See Administrative Record Document ("AR") AR 3385-88. The use of such impermissible data is clear evidence of the arbitrary and capricious nature of the FDA decision-making process with regard to AVA. This improper reliance on questionable data provides yet another basis for the Court to deny the Government's motion.

C. There Has Never Been a Properly Controlled Field Test of AVA Because it is a Different Vaccine From the Vaccine Used in the 1962 Brachman Study

As noted in both the Final Rule and the Defendants' Memo., the vaccine used in the Brachman study was not the same vaccine that is the subject of this litigation. In fact, the original vaccine was manufactured by the DoD at Fort Detrick, Maryland, and went through at least two other manufacturing variations to arrive at its current formulation AVA. See Defendant's Memo at pp.11-12. [**15]

As noted in the Plaintiff's Memorandum at p. 15-16, a manufacturer may not validate the safety and efficacy of its product by relying on testing data from a product manufactured by another entity, absent special circumstances. In

contrast, FDA's so-called "comparability policy" allows a single manufacturer to make manufacturing changes to a product without performing additional clinical studies to demonstrate the safety and efficacy of the successor product. See Guidance Concerning Demonstration of Comparability of Human Biological Products Including Therapeutic Biotechnology-Derived Products Center for Biologics Evaluation and Research (CBER), April 19, 1996, found at http: //www.FDA.gov/cber/gdlns/comptest.txt ("FDA Guidance").

[*11] But of course in this case there is no manufacturer creating a successor product. Instead, there are four different variations of the vaccine -- the original vaccine used by Brachman, and manufactured by DoD; a later variation of the Brachman vaccine, also manufactured by DoD; a third version of the vaccine manufactured by Merck, Sharp & Donne; and a fourth variation of the vaccine manufactured by the Michigan Department of Public Health, [**16] which was ultimately licensed in 1970. See FDA Response to Citizen's Petition, p. 8, Plaintiff's First Amended Complaint, Atch D., (filed January 6, 2004).

In order to overcome this glaring discrepancy, FDA fabricates a new status for DoD, specifically for the purpose of thwarting this challenge to the vaccine. FDA converts the DoD into a de facto vaccine manufacturer.

There is no FDA precedent for this arbitrary and capricious action. Defendant's citation to *Berlex Laboratories, Inc. v. FDA, 942 F. Supp. 19 (D.D.C. 1996)* is readily distinguishable. Berlex deals with a situation involving a single manufacturer doing precisely what the FDA Guidance contemplates, namely, developing a biologic on which it conducted a complete round of human clinical testing, and then seeking FDA approval of a derivative product in the United States. Under these circumstances, FDA had little difficulty in approving the successor product with no additional testing because of its similarity to the previous product, and because a single manufacturer created and developed the biologic product in question. *Berlex, 942 F. Supp. at 22-23.*

The situation could hardly [**17] be more different with AVA. Four different variations of the vaccine, manufactured by three different manufacturers, are at issue. Indeed, AVA's human clinical tests were performed with the earliest version of the vaccine only and are now more than 40 years old. The time between the initial clinical tests of the [*12] product in question in Berlex and its approval by FDA was two years, 1994 to 1996. There were only two variations of the Berlex drug to connect together, while here there are at least four. n5

n5 For the record, Plaintiff's note a fifth AVA variant which was created following the dramatic change in AVA's manufacturing status in the early 1990s in response to DoD's demand for vaccine during the first Gulf War. See testimony of Nancy Kingsbury, United States General Accounting Office, before the Sub-Committee on National Security, Veteran's Affairs, and International Relations, Committee on Government Reform, House of Representatives, October 23, 2001, pp. 5-6, Plaintiff's First Amended Complaint, attachment F (filed Jan. 6, 2004).

[**18]

III. CONCLUSION

Because the AVA currently used is substantially different from the vaccine originally tested vaccine, and because the FDA has provided no reasonable basis for certifying the current vaccine, its action in drafting the Final Rule is factually unsupportable, arbitrary and capricious. The Court should so find, and order Defendant's to properly complete the licensing process.

Date: April 7, 2004

Respectfully submitted,

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