UNITED STATES DISTRICT COURT
DISTRICT OF CONNECTICUT

HIFI DNA TECH, LLC, Plaintiff,	:	
v.	:	
U.S. DEPT. OF HEALTH AND HUMAN SERVICES, et al., Defendants.	:	Civil No. 3:08CV54(AVC)

MEMORANDUM OF DECISION

This is an action for review of an administrative determination made by the Food and Drug Administration ("FDA") regarding the classification of a medical device manufactured by the plaintiff, HiFi DNA Tech, LLC ("HiFi"). It is brought pursuant to 5 U.S.C. § 701 et. seq., which provides that the FDA's actions are subject to review under the Administrative Procedure Act ("APA").[1] HiFi seeks to reverse the denial of its petition to have its medical device reclassified from a Class III to a Class II device.[2]

The defendants United States Department of Health and Human Services, United States Food and Drug Administration, Michael O.

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[1] 5 U.S.C. § 706(2) states in pertinent part that a reviewing court may "hold unlawful and set aside agency action, findings, and conclusions found to be . . . arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law."

[2] Under the Medical Devices Amendments Act, before a medical device may be commercially distributed or marketed, notification must be given to the FDA so that the device can be classified according to the degree of regulatory control necessary to insure its safety and effectiveness. See 21 U.S.C. §§ 360(k), 360(c). Devices are classified as Class I, Class II, or Class III, with Class III devices subject to the most stringent controls, including "premarket approval." See 21 U.S.C. §§ 360(c), 360(e).

Leavitt, Secretary of Health and Human Services and Andrew Von Eschenbach, Commissioner of Food and Drugs, now move to dismiss the complaint pursuant to Federal Rule of Civil Procedure 12(b)(6), arguing that the complaint fails as a matter of law to state a claim upon which relief can be granted. The administrative record being appended to the file, the court shall construe the within motion as a motion for judgment, seeking affirmance of the FDA's determination.

_____The issue is whether the FDA's denial of HiFi's reclassification petition was arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law.

_____For the reasons that follow, the defendants' motion for judgment is GRANTED.

FACTS

Examination of the administrative record discloses the following:

The plaintiff HiFi is a corporation formed under the laws of the state of Connecticut, which manufactures certain reagents generally known as primer-defined DNA polymerase chain reaction ("PCR") amplification. PCR is the process of copying a targeted segment of a long DNA strand repeatedly and exponentially, called DNA amplification or replication.

HiFi intends to market a device for PCR amplification of

HPV[3] DNA ("the device"), to be used for preparation of sample materials suitable for accurate HPV genotyping by direct automated DNA sequencing. Genotyping can be used to determine which types of HPV are present in a particular specimen, which is useful identifying whether an HPV infection is caused by one of the high risk types of the HPV virus.

HiFi intends to use its device in order to screen patients with abnormal Pap test results in order to determine whether they should be referred for a colposcopy, and to screen patients over 30 years of age[4], in order to better guide patient management decisions.

The FDA has already approved two HPV DNA devices. Both of these devices have been classified as Class III devices. Class III devices are subject to the FDA's strictest regulations. Class III devices must obtain premarket approval ("PMA") from the FDA, a process in which the applicant must demonstrate that there is a reasonable assurance that the device is safe and effective. However, a new device can avoid a Class III classification and the PMA process if it can be shown that the new device is substantially equivalent to Class I or Class II device already on the market. In order to do so, an applicant

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[3] "HPV" refers to a group of approximately 80 strains of a virus. HPV is one of the most common sexually transmitted diseases, and certain "high risk" types of HPV can lead to the development of cervical cancer.

[4] Women over 30 years of age have a higher risk for developing cervical cancer.

must submit a so-called 510(k) submission to the FDA.

On December 7, 2006, HiFi sent its 510(k) submission to the FDA. By letter dated January 9, 2007, the FDA stated that "[w]e have determined that your type of device is classified as a class III device . . . [which] requires an approved PMA before it can be legally marketed, unless the device is reclassified."

On January 18, 2007, HiFi submitted a request for evaluation of automatic Class III designation ("de novo reclassification") to the FDA, seeking a determination of substantial equivalence, in order to reclassify the device from a Class III to Class II without undergoing the PMA process.

By letter dated February 27, 2007 to Heather Rosecrans of the FDA, HiFi voluntarily withdrew its request for evaluation of automatic Class III designation, and stated "per you[r] advice, the undersigned will re-submit the device application as a reclassification petition."

On March 7, 2007, HiFi sent a reclassification petition to the FDA. The FDA did not stamp the petition as received until May 22, 2007.

By letter dated December 14, 2007, the FDA denied HiFi's request for reclassification. In its 14-page letter, the FDA concluded that it "has determined that you have not demonstrated that there exists adequate valid scientific evidence establishing that special controls, when combined with the general controls .

. . are sufficient to provide reasonable assurance of safety and effectiveness [of the device]."

_____"Specifically, FDA has determined that: (1) the supporting data you submitted are inadequate; (2) the special controls you propose do not provide reasonable assurance of the safety and effectiveness of the device; and (3) there is insufficient information to establish adequate special controls at this time."

_____The FDA determined that, based upon HiFi's own intended use statement, "that the device is purported or represented to be for a use which is of substantial importance in preventing impairment of human health." The FDA concluded that because the device is "intended to help physicians make a potentially significant decision: whether to immediately refer patients to colposcopy, which can in turn lead to biopsy and intervention, or to advise patients to wait and be screened again later."

The FDA also determined that HiFi's "device presents a potential unreasonable risk of illness or injury because its rate of false negative results is not known." The FDA found that "[a] false negative result from your device may lead to delays in timely diagnosis and treatment, allowing an undetected condition to worsen and potentially increasing morbidity and mortality from cervical cancer . . . [d]espite the potential harms from false negative results, you have neither established the risk of false negative results for your device nor shown that the risk is

reasonable."

The FDA noted that it had "carefully analyzed" the studies and supporting data submitted by HiFi. The FDA highlighted various deficiencies in HiFi's data, including: 1) failure to perform any cross reactivity or interfering substances studies; 2) failure to adequately establish the limit of detection, because proper specific types were not used; 3) failure to collect information on the age distribution and cervical pathological conditions of the study subjects; 4) inadequacy of specificity study because the FDA cannot determine the precise degree to which the device detects non-carcinogenic or low-risk HPV; 5) HiFi's intended uses indicate that the device will be used in conjunction with HPV genotyping, but the FDA has not approved any HPV genotyping test yet to date; 6) HiFi's study regarding reproducibility failed to account adequately for multiple operators, laboratories, days and reagent lots as applicable, and therefore HiFi did not establish that the device would perform consistently; 7) stability was not established in a clinically valid manner, and such failure may lead to inappropriate storage and handling recommendations.

The FDA also found the proposed special controls to be inadequate.

In addition, the FDA's "memo to the record" which reflects the FDA's review of HiFi's petition, contains a 30-page narrative

specifically addressing each of HiFi's intended uses for the device, each of HiFi's studies, and each of HiFi's proposed special controls. The memo also notes that the "majority of literature cited by the petitioner is general literature on HPV and cervical cancer," and "[o]nly a single article was provided that contains data generated by the petitioner's device." The memo also references over 15 scholarly articles and studies.[5]

On January 11, 2008, HiFi filed the complaint in the instant action. Count one of the complaint alleges that the FDA improperly denied the reclassification petition. Count two alleges that the FDA should have permitted HiFi to obtain "de novo" reclassification under the less burdensome provisions of 21 U.S.C. 360c(f)(2).[6]

STANDARD

Section 706 of the APA provides that a court may set aside an agency action only where it finds the action "arbitrary, capricious, an abuse of discretion, or otherwise not in

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[5] These articles included "HPV DNA testing in cervical cancer screening; results from women in high-risk province of Costa Rica"; "The expanded use of HPV testing in Gynecologic practice per ASCCP-guided management requires the use of well validated assays"; "2006 consensus guidelines for the management of women with abnormal cervical cancer screening tests"; "The 2001 Bethesda System: terminology for reporting results of cervical cytolology."

[6] HiFi has waived the argument regarding whether the FDA should have permitted the device to be evaluated under the less burdensome provisions of 21 U.S.C. § 360c(f)(2), known as de novo review. The administrative record indicates that HiFi voluntarily withdrew its petition for de novo review by letter dated February 27, 2007, in order to submit its reclassification petition. Accordingly, the FDA never issued a determination regarding the de novo petition.

accordance with law." 5 U.S.C. § 706(2)(A). Under this standard, there is a presumption in favor of the validity of administrative action and a court cannot substitute its judgment for that of the agency. See Citizens to Preserve Overton Park v. Volpe, 401 U.S. 402, 416 (1971). The arbitrary and capricious standard of review is narrow and particularly deferential. See Erie Niagara Rail Steering Comm. v. Surface Transp. Bd., 247 F.3d 437, 441 (2d Cir. 2001).

A decision is arbitrary and capricious if the agency "has relied on factors which Congress has not intended it to consider, entirely failed to consider an important aspect of the problem, offered an explanation for its decision that runs counter to the evidence before the agency, or is so implausible that it could not be ascribed to a difference in view or product of agency expertise." Motor Vehicle Mfrs. Ass'n. v. State Farm Mut. Auto. Ins. Co., 463 U.S. 29, 43 (1983). "[The court's] task under this standard is to decide if the agency has considered the evidence, examined the relevant factors, and spelled out a satisfactory rationale for its action including the demonstration of a reasoned connection between the facts it found and the choice it made." Environmental Defense v. U.S. E.P.A., 369 F.3d 193, 201 (2d Cir. 2004).

DISCUSSION

The FDA argues that the "administrative record demonstrates

that FDA carefully reviewed HiFi's reclassification petition and reasonably concluded, in an exercise of its considerable scientific and technical expertise, that the HPV device could not be reclassified into Class II because HiFi failed to adduce sufficient evidence to establish . . . a reasonable assurance of the safety and effectiveness of the HPV device for its intended uses."

Specifically, the FDA contends that HiFi's "supporting data are inadequate to support reclassification," and "[c]omplex scientific judgments such as these, regarding the magnitude and quality of scientific evidence provided by HiFi and the sufficiency of that evidence in demonstrating the safety and effectiveness of its HPV device, lie at the very heart of FDA's specialized expertise."

HiFi responds by arguing that the "FDA's denial of HiFi's petition is arbitrary, capricious and an abuse of discretion delegated to it by Congress." Specifically, HiFi contends that the FDA's denial "ignores the current state of the science of DNA testing," "ignores court recognition of this science as legally acceptable," "violates FDA's own statements regarding the type of test being done," "ignores the evidence presented as to safety and efficacy," and "misapplies the standards regarding classification." HiFi concedes that under the arbitrary and capricious standard, it has a "high burden in asking a Court to

overrule an agency decision, especially one so scientifically based."

The court concludes that the FDA's denial of HiFi's reclassification petition is not "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2)(A).

The FDA's authority to regulate medical devices is founded upon the Medical Devices Amendments Act of 1976. See 21 U.S.C. §§ 360(k), 360c, 360e, 360j. Under this Act, medical devices are classified as Class I, Class II, or Class III. See 21 U.S.C. § 360(c).

Class III devices are either: (1) "purported or represented to be for use in supporting or sustaining human life, or for a use which is of substantial importance in preventing impairment of human health," or (2) "[devices that] present a potential unreasonable risk of illness or injury [and] insufficient information exists . . . to provide a reasonable assurance of safety." 21 U.S.C. § 360c(a)(1)(c); 21 C.F.R. § 860.3(c)(3).

All medical devices are classified automatically as Class III devices, and therefore subject to the most stringent approval process. See 21 U.S.C. § 360c(f)(1). In order for a device to be reclassified as a Class II device, a petitioner must identify "special controls" that will "provide adequate assurance of safety and effectiveness and describe how such controls provide

such assurance." 21 U.S.C. § 360c(a)(1)(B).

_____When submitting a petition for reclassification to the FDA, a manufacturer should submit valid scientific evidence, which includes "evidence from well-controlled investigations, partially controlled studies, studies and objective trials without matched controls, well-documented case histories conducted by qualified experts, and reports of significant human experience with a marketed device, from which it can fairly and responsibly be concluded by qualified experts that there is reasonable assurance of the safety and effectiveness of a device under its conditions of use." 21 C.F.R. § 860.7.

_____Here, the FDA's determination involved the interpretation of its own statutes and regulations. When the agency action at issue involves an interpretation by the agency of its own statute and regulations, the court must be especially deferential. See United States v. Rutherford, 442 U.S. 544, 553 (1979). Indeed, the decision need not even be one that this court would independently reach, given the findings and the law; it need only be reasonable. See Aluminum Co. of America v. Central Lincoln Peoples' Utility District, 467 U.S. 380, 389 (1984); Henley v. FDA, 77 F.3d 616, 621 (2d Cir. 1996) (noting that "we might not have chosen the FDA's course had it been ours to chart. But that is hardly the point . . . the APA precludes us from substituting our judgment for that of the agency.").

The FDA's 14-page denial of HiFi's petition clearly sets forth the basis for the FDA's determination. In addition, the FDA's "memo to the record" which reflects the FDA's review of HiFi's petition, contains a 30-page narrative specifically addressing each of HiFi's intended uses for the device, each of HiFi's studies, and each of HiFi's proposed special controls. The memo also notes that the "majority of literature cited by the petitioner is general literature on HPV and cervical cancer," and "[o]nly a single article was provided that contains data generated by the petitioner's device." In sum, after a thorough review, the FDA determined that the scientific evidence submitted by HiFi to be insufficient to provide a reasonable assurance of the safety and effectiveness of the device for its intended uses. As such, this determination is not arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law.

CONCLUSION

For the reasons stated above, the defendants' motion for judgment (**document no. 13**) is GRANTED.

It is SO ORDERED this 24th day of March, 2009, at Hartford, Connecticut.

/s/
Alfred V. Covello
United States District Judge