UNITED STATES DISTRICT COURT
DISTRICT OF CONNECTICUT

HIFI DNA TECH, LLC,	:	
	:	
Plaintiff,	:	
	:	
v.	:	Civil No. 3:08CV54 (AVC)
	:	
U.S. DEPT. OF HEALTH AND HUMAN SERVICES, U.S. FOOD AND DRUG ADMINISTRATION, MICHAEL O. LEAVITT, Secretary of Health and Human Services, and ANDREW VON ESCHENBACH, Commissioner of Food and Drugs,	:	March 24, 2008
	:	
Defendants.	:	

MOTION TO DISMISS AMENDED COMPLAINT

Pursuant to Federal Rule of Civil Procedure 12(b)(6), the defendants move to dismiss the complaint in this action. The basis for this motion is that the complaint fails, as a matter of law, to state a claim upon which relief can be granted, as explained further in the memorandum in support of this motion filed herewith.

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MEMORANDUM IN SUPPORT OF MOTION TO DISMISS AMENDED COMPLAINT

INTRODUCTION

In this action, plaintiff HiFi DNA Tech, LLC ("HiFi") challenges the denial of its petition to have its medical device reclassified from Class III to Class II. Class II devices are subject to less stringent standards than are Class III devices. Plaintiff's device is not currently on the market; HiFi has not attempted to have it approved as a Class III device. It is plaintiff's burden to demonstrate to the United States Food and Drug Administration ("FDA") that the device should be regulated as a Class II device; it is automatically a Class III device by law. Plaintiff submitted a petition seeking such reclassification and did not carry that burden. FDA has approved two other devices of the same type, and they were both approved as Class III devices.

Contrary to plaintiff's allegations, in denying the petition FDA properly applied the substantial scientific and technical expertise that Congress entrusted to it. Plaintiff's device is an

in vitro diagnostic assay that plaintiff intends to be used to detect the presence of Human Papillomavirus ("HPV"), an infection which may lead to cervical cancer. After a thorough review of plaintiff's petition, FDA concluded that the device may not be reclassified at this time because there is inadequate evidence to provide a reasonable assurance that, if the device were subject to the less rigorous regulatory oversight applicable to Class II devices, it would be safe and effective for its intended uses.

Plaintiff has filed a complaint under the Administrative Procedure Act ("APA") challenging the scientific judgment of FDA in denying its petition for reclassification. Review of FDA's decision under the APA is a matter of law, and, as a legal matter, plaintiff's claims must fail.[1] The administrative record demonstrates that FDA's scientific determination was reasonable and that its interpretation of both the statute it is charged with implementing and the accompanying regulations was fully in accord with the language and purpose of the Federal Food, Drug, and Cosmetic Act ("FDCA").[2] Thus, the FDA's determination should be upheld.

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[1] In MRCA Info. Servs. v. United States, 145 F. Supp. 2d 194 (D. Conn. 2000), this Court construed a summary judgment motion as a motion for judgment, noting the express disapproval of "the use of summary judgment procedure in cases where a court is reviewing an administrative action." Id. at 195 n.3 (quoting Olenhouse v. Commodity Credit Corp., 42 F.3d 1560, 1579-80 (10th Cir. 1994)). See also Marshall County Health Care Auth. v. Shalala, 988 F.2d 1221, 1226 (D.C. Cir. 1993) (Rule 12(b)(6) motion proper when court is reviewing agency action: "The entire case on review is a question of law, and only a question of law. And because a court can fully resolve any purely legal question on a motion to dismiss, there is no inherent barrier to reaching the merits at the 12(b)(6) stage.").

[2] The administrative record is being filed simultaneously with this motion, and is cited herein as "AR." FDA's Order denying plaintiff's petition is part of the administrative record, see AR 491-504; for the Court's convenience, a copy of the Order is also attached to this memorandum. In this memorandum, citations to the Order will be to the AR pages, 491-504.

BACKGROUND

I. STATUTORY AND REGULATORY SCHEME

The regulation of medical devices in the United States is governed by the FDCA and the amendments thereto, most notably, the Medical Device Amendments of 1976 ("MDA"), Pub. L. No. 94-295, 90 Stat. 539. "Congress enacted the [MDA], in the words of the statute's preamble, 'to provide for the safety and effectiveness of medical devices intended for human use.'" Medtronic, Inc. v. Lohr, 518 U.S. 470, 474 (1996) (quoting the MDA).

The FDCA, as amended by the MDA, establishes three regulatory classes for medical devices: Class I, Class II, and Class III. See 21 U.S.C. § 360c(a). Depending on its classification, a device will be subject to different regulatory controls. See Yale-New Haven Hosp. v. Leavitt, 470 F.3d 71, 74 (2d Cir. 2006) ("Under the MDA, each medical device is classified according to the stringency of regulatory control necessary to ensure safety and effectiveness."). "Devices that present no unreasonable risk of illness or injury are designated Class I and are subject only to minimal regulation by 'general controls.'" Medtronic, 518 U.S. at 476-77 (citing 21 U.S.C. § 360c(a)(1)(A)). These general controls include prohibitions against adulteration and misbranding and compliance with establishment registration and listing, good manufacturing practice, and recordkeeping and reporting requirements. See 21 U.S.C. § 360c(a)(1)(A); 21 C.F.R. § 860.3(c)(1).

"Devices that are potentially more harmful [than Class I] are designated Class II." Medtronic, 518 U.S. at 477. Class II devices are subject to both general controls and additional "special controls" deemed by FDA to be sufficient to provide a reasonable assurance of the safety

and effectiveness of particular device types. See 21 U.S.C. § 360c(a)(1)(B); 21 C.F.R. § 860.3(c)(2). Special controls for Class II devices may include performance standards, postmarket surveillance, patient registries, guidelines, recommendations, and other particularized requirements. Id.

Class III devices "incur the FDA's strictest regulation." Buckman Co. v. Plaintiffs' Legal Comm., 531 U.S. 341, 344 (2001). They are devices that are either "purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health," or that "present[] a potential unreasonable risk of illness or injury," and for which "insufficient information exists to determine that the application of general [or special] controls are sufficient to provide reasonable assurance of [their] safety and effectiveness." 21 U.S.C. § 360c(a)(1)(C); 21 C.F.R. § 860.3(c)(3). Class III devices must comply with general controls and obtain premarket approval ("PMA") from FDA. See id.; 21 U.S.C. § 360e. "Despite its relatively innocuous phrasing, the process of establishing this 'reasonable assurance,' which is known as the 'premarket approval,' or 'PMA' process, is a rigorous one." Medtronic, 518 U.S. at 477. FDA can approve a PMA application only if the information in the application demonstrates, based on valid scientific evidence, that there is a reasonable assurance that the device to be marketed is safe and effective for its intended use. See 21 U.S.C. § 360e(d); 21 C.F.R. §§ 814.45(c), 860.7(c).

All devices that were introduced for commercial distribution after May 28, 1976 (the effective date of the MDA), commonly referred to as "post-amendments devices," are classified automatically by statute into Class III and are subject to the FDCA's premarket approval requirements. See 21 U.S.C. § 360c(f)(1). A post-amendments device remains in Class III

unless, pursuant to Section 510(k) of the Act, 21 U.S.C. § 360(k), the device is shown to be substantially equivalent to a Class I or II device that is already legally on the market or FDA reclassifies the device into Class I or II. 21 U.S.C. § 360c(f). A manufacturer seeking to remove its device from Class III "carries the burden of proving that the device meets the requirements for reclassification set up by the [Medical Device] Amendments" to the FDCA. Gen. Med. Co. v. FDA, 770 F.2d 214, 219 (D.C. Cir. 1985).

A. Classification Through Substantial Equivalence Under Section 510(k)

A post-amendments device can avoid a Class III designation and the attendant premarket approval process if it can be shown, pursuant to a premarket notification submission under Section 510(k) of the Act, 21 U.S.C. § 360(k) (commonly called a "510(k) submission"), to be of the same type as and "substantially equivalent" to a Class I or II device that is already legally on the market (commonly called a "predicate device"). 21 U.S.C. § 360c(f)(1)(A). A device may be found substantially equivalent to a predicate device if it has the same intended use and either has the same technological characteristics or has different technological characteristics but the information submitted demonstrates that the device is as safe and effective as the legally marketed predicate device and does not raise different questions of safety and effectiveness. See 21 U.S.C. § 360c(i)(1)(A).

When it enacted the MDA, "Congress realized that existing medical devices could not be withdrawn from the market while the FDA completed its PMA analysis for those devices. The statute therefore includes a 'grandfathering' provision which allows pre-1976 [Class III] devices to remain on the market without FDA approval until such time as the FDA initiates and completes the requisite PMA." Medtronic, 518 U.S. at 477-78. Thus, a manufacturer of a post-

amendments Class III device may also use the 510(k) process to initially enter the market as a Class III device without first obtaining an approved PMA if it can show that its device is the same type of device and substantially equivalent to either a grandfathered "pre-amendments" Class III predicate device that does not yet require premarket approval or to another post-amendments Class III device found to be substantially equivalent to a grandfathered Class III device that does not yet require premarket approval. See 21 U.S.C. § 360e(b). This provision is inapplicable in the present case, however, because HiFi seeks reclassification into Class II, and demonstration of substantial equivalence to a grandfathered Class III device does not remove a device from Class III. Moreover, HiFi has not identified, nor is FDA aware of, any Class III device not subject to the requirement of premarket approval that could serve as a predicate for HiFi's device. The Class III device cited as a predicate in HiFi's 510(k) filing was itself a post-amendments Class III device that required premarket approval.

B. Reclassification Under 21 U.S.C. § 360c(f)(3)

The manufacturer of a post-amendments device may also petition FDA, pursuant to 21 U.S.C. § 360c(f)(3), for reclassification of its device from Class III into Class I or II on the grounds that the device meets the statutory requirements for the less rigorous regulatory oversight afforded devices in those classifications. See also 21 C.F.R. §§ 860.123, 860.134. In order for FDA to reclassify a device into Class II, the manufacturer's petition must provide sufficient information, in the form of valid scientific evidence, to establish special controls that, in conjunction with general controls, will provide reasonable assurance of the safety and effectiveness of the device for its intended use. 21 U.S.C. § 360c(a)(1)(B). Valid scientific evidence includes "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(c)(2).

In reaching a decision regarding the reclassification of a device, the Commissioner "may for good cause shown refer the petition to an appropriate panel . . . [to] make a recommendation to the [Commissioner] respecting approval or denial of the petition." 21 U.S.C. § 360c(f)(3)(B).[3] Within 90 days from the date that a panel's recommendation is received if the Commissioner refers a petition to a panel, and in no event later than 210 days from the filing date of a petition, the Commissioner shall issue an order, in the form of a letter to the petitioner, approving or denying the petition for reclassification. See id.; 21 C.F.R. § 860.134(b)(6).

C. De Novo Reclassification Under 21 U.S.C. § 360c(f)(2)

Certain post-amendments devices may also be eligible for a streamlined reclassification from Class III into Class I or II, pursuant to 21 U.S.C. § 360c(f)(2). A manufacturer of "a type of device that has not been previously classified under this Act" may petition FDA for an Evaluation of Automatic Class III Designation, or so-called "de novo" reclassification, on the grounds that the device fits the criteria of a Class I or II device. 21 U.S.C. § 360c(f)(2); see also 21 U.S.C. § 360c(f)(1)(A)(ii). Devices are considered to be the same "type of device" under this provision when they "do not differ significantly in purpose, design, materials, energy source,

[3] Although the FDCA refers to the authority of the Secretary of the Department Health and Human Services, the Secretary acts through the Commissioner of Food and Drugs. 21 U.S.C. § 393(d)(2); see also FDA Staff Manual Guide § 1410.10 (listing delegations of authority).

function, or any other feature related to safety and effectiveness, and for which similar regulatory controls are sufficient to provide reasonable assurance of safety and effectiveness" for all devices of that generic type. See 21 C.F.R. § 860.3(i). A "type of device" analysis is not the same as a "substantial equivalence" analysis. A "substantial equivalence" finding is narrower, such that a device may be of the same generic type, but still not be substantially equivalent to any other device within that type. See, e.g., 21 U.S.C. § 360c(f)(1)(A) (to qualify under this section, a device must be both within the same "type of device" and "substantially equivalent to another device within such type.").

The de novo reclassification provision was added to the FDCA by the Food and Drug Modernization Act of 1997, Pub. L. No. 105-115, 111 Stat. 2296. Congress observed that certain "lower risk devices were subjected to premarket approval" as Class III devices "because such devices were unique and found not to be substantially equivalent to a predicate device" legally on the market. S. Rep. No. 105-43, at 36 (1997). The manufacturers of these new types of devices were thus unable to take advantage of the less burdensome 510(k) process that was available to other lower risk devices because of the novelty of these devices and their intended uses. Congress therefore created the de novo provision to provide a streamlined reclassification process for these "unique" but "lower risk" devices. Id.

Before a device may be reclassified under the de novo reclassification provision, a manufacturer must first file a 510(k) submission and receive a determination from FDA that it is "a type of device that has not been previously classified under [the FDCA]." 21 U.S.C. § 360c(f)(2)(A); see also 21 C.F.R. § 860.3(i). Within 30 days of receiving this determination, a manufacturer may petition to have its device reclassified into Class I or II, explaining how the

imposition of general controls – and special controls for a Class II designation – are sufficient to provide a reasonable assurance of the safety and effectiveness of the device type. 21 U.S.C. § 360c(f)(2)(A).

FDA evaluates reclassification petitions under the de novo provision using the same substantive standard that it applies to petitions reviewed under 21 U.S.C. § 360c(f)(3). See S. Rep. No. 105-43, at 35 (noting that the de novo provision requires FDA "to classify devices based on the Act's risk-based classification criteria," which are equally applicable to 21 U.S.C. § 360c(f)(3) petitions). The procedures for reaching this decision are streamlined, however, as the de novo reclassification provision does not explicitly provide for the Commissioner to refer a petition to a panel for a recommendation, and the timeframe for reaching a decision on the petition is condensed. Rather than the 210 days provided under 21 U.S.C. § 360c(f)(3), the Commissioner must rule on a de novo reclassification petition within 60 days of submission. 21 U.S.C. § 360c(f)(2)(B)(i).

II. HPV INFECTION

HPV is the name for a group of approximately 80 different strains of a virus that infect skin. AR 280. HPV is one of the most common sexually transmitted diseases in the United States. Id. Many women who acquire HPV do not know that they have been infected because the disease often does not produce any visible signs or symptoms. Id. Most HPV infections resolve on their own without medical intervention, but some infections – those associated with so-called "high-risk" types of HPV – can persist and cause the cells lining the cervix to grow abnormally. Id. at 281-83. This abnormal growth may lead to the development of cervical cancer. Id. at 282. In fact, virtually all cancers of the cervix are associated with HPV infection.

Accordingly, persistent infection with certain high-risk types of HPV is considered the main risk factor in the development of cervical cancer. Id.

Pap tests have for many years been the primary tool used by doctors to screen women for cervical cancer because the tests can reveal changes in the structure of cervical cells, called "pre-cancerous" changes, that may be harbingers of cervical cancer. Id. at 283, 292. Pap test diagnoses are not always definitive, however. Id. at 283-84. A diagnosis of "atypical squamous cells of undetermined significance" ("ASCUS") is made where a Pap test indicates that cellular abnormalities are present, but the test results are inconclusive with respect to whether the changes are pre-cancerous. Id. at 283-84, 292-94. If a Pap test results in an ASCUS diagnosis, various additional medical procedures, such as colposcopy[4] and biopsy, may be used to visualize the cervix and obtain tissue in an attempt to determine whether there are cellular changes indicative of cervical disease, i.e., precancer or cancer. Id. at 283-84, 292-93. Because of the low sensitivity of these visual methods, they may fail to detect pre-cancerous or even cancerous changes in the cells of the cervix and must therefore be repeated at frequent intervals in hopes of detecting cervical cancer in its early stages. Id. at 284.

HPV DNA tests are laboratory assays that determine if the DNA associated with HPV is present in specimens obtained from patients and are typically performed using the same specimen collected from patients for their Pap tests. Id. at 283. HPV DNA tests recognize a subset of HPV types (the high-risk types), but do not distinguish between the many different high-risk

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[4] Colposcopy is a diagnostic procedure performed using a colposcope, which provides an illuminated, magnified view of the cervix and the tissues of the vagina and vulva, allowing the colposcopist to visually distinguish normal from abnormal appearing tissue and take directed biopsies for further examination. Id. at 284 n.13.

HPV types. Id. The process of genotyping, see discussion infra, may be used to further identify the particular high-risk HPV types present in a specimen. Because they are capable of detecting the presence of the high-risk HPV types associated with cervical cancer, the use of HPV DNA tests can improve the effectiveness of cervical cancer screening and permit women to be evaluated less frequently by the invasive visualization methods such as colposcopy and biopsy. Id. at 283-84. Thus, the published clinical guidelines for cervical cancer screening by medical professionals, which were developed by leading medical experts working with the American Society for Colposcopy and Cervical Pathology, now recommend that women with ASCUS Pap test results be tested for high-risk types of HPV using an in vitro[5] HPV DNA test. See id. at 292; Thomas C. Wright Jr. et al., 2006 Consensus Guidelines for the Management of Women with Abnormal Cervical Cancer Screening Tests ("Guidelines"), 197 Am. J. Obstetrics & Gynecology 346 (2007), AR 360-381. The Guidelines also recommend that women 30 years of age or older, even those whose Pap test diagnoses are normal, be tested for high-risk HPV because cervical cancer is more prevalent in older women. AR 374. FDA has approved two in vitro HPV DNA devices for this purpose, both of which were approved as Class III devices with approved PMAs. See AR 362 ("The appropriate use of these guidelines requires that laboratories use only HPV tests that have been analytically and clinically validated . . . , as documented by Food and Drug Administration approval.").

[5] "In vitro" means "in a glass" and refers to a test performed in a laboratory, as opposed to "in vivo," which means within a living organism. See 21 C.F.R. § 201.119(a) (in vitro diagnostic products "are intended for use in the collection, preparation and examination of specimens taken from the human body.").

III. PLAINTIFF'S DEVICE

HiFi is the manufacturer of the Human Papillomavirus DNA Nested Polymerase Chain Reaction Detection Device ("HPV Device"), which it maintains can "be used for detection of HPV DNA in clinical samples." AR 102.[6] The device includes Polymerase Chain Reaction ("PCR") tubes, primer reagents, buffers, agarose gel powder, ethidium bromide, and a molecular ruler. See AR 295. These components, along with general PCR equipment and accessories, are to "be used for preparation of sample materials . . . suitable for accurate HPV genotyping." Am. Compl. ¶ 10; see also AR 112. Genotyping is the process of determining a portion of the genetic sequence (i.e., the specific order of the nucleotides in a DNA strand) of a particular organism. Genotyping can be used to determine which of the many types of HPV that infect humans are present in a particular specimen, and is useful in identifying whether an HPV infection is caused by a particular high-risk HPV type. See AR 283, 292 n.25.

In its reclassification petition, HiFi discusses at length the two intended uses it identifies for its device, which were considered by FDA in evaluating HiFi's reclassification petition. See AR 112, 124, 279, 491; see also 21 U.S.C. § 360c(a)(2) (stating that devices are classified by FDA based upon their intended use). To summarize, HiFi intends its HPV Device to be used along with genotyping to: (1) screen patients with ASCUS Pap test results to determine whether they should be referred for colposcopy; and (2) screen women 30 years and older, in conjunction with Pap testing, to guide patient management decisions. See AR 112, 124.

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[6] Polymerase Chain Reaction is a technique used to replicate a piece of DNA (the "DNA template") by means of an in vitro enzymatic procedure that sets in motion a chain reaction that replicates the DNA template exponentially. AR 295 n.31.

HiFi's first intended use arises in situations where a Pap test has resulted in an ASCUS diagnosis, i.e., where the results are inconclusive with respect to whether the cellular abnormalities detected by the Pap test are indicative of cervical disease. HiFi intends that its HPV Device will be used along with genotyping to detect whether any high-risk types of HPV are present. See AR 292. If this testing yields a positive HPV DNA test result, the patient will be referred immediately for further assessment, likely by colposcopy, to detect the presence of cervical disease. See AR 283, 292. By contrast, if the testing indicates that a patient is negative for high risk HPV types, the patient may be advised to wait for a year or more for further cervical cancer screening. Id.

HiFi's second intended use for its HPV Device is to screen women 30 years and older, in conjunction with Pap testing and genotyping, for high-risk types of HPV. AR 289. According to the professional Guidelines, which are referenced by HiFi in its second intended use statement, a woman 30 years or older who has a normal Pap test diagnosis but a positive HPV DNA test result should undergo another Pap test and HPV DNA test in one year. AR 289, 293, 374. By contrast, if this same woman had a negative HPV DNA test result, she would not undergo any additional cervical cancer screening for another three years. AR 293, 374.

IV. REGULATORY HISTORY OF HPV DNA DEVICES

FDA has approved two in vitro HPV DNA devices. AR 285-89. Both were post-amendments devices that were classified automatically by statute into Class III, and have since remained in Class III. Accordingly, before the devices could be marketed, their manufacturers were required to submit valid scientific evidence to FDA to provide a reasonable assurance of the safety and effectiveness of the devices. The first HPV DNA device to be granted premarket

approval by FDA was the ViraPap Human Papillomavirus DNA Detection Kit, manufactured by Life Technologies, Inc., which was approved on December 23, 1988. See AR 1, 286. The second device, the ViraType Human Papillomavirus DNA Typing Kit, manufactured by Digene Corporation, obtained premarket approval from FDA on March 11, 1991. AR 286-87. FDA approved a supplement to the PMA for this second device on March 31, 2003, to permit Digene to market the device for a new intended use. AR 287; see also 21 C.F.R. § 814.39 (evaluating PMA supplements for new intended uses under the same rigorous safety and effectiveness standards as those applied to original PMAs). The device marketed by Digene under this PMA supplement is the hc2 High-Risk HPV DNA Test using Hybrid Capture2 ("Digene Hybrid Capture Test").

Seeking to enter the market with its own HPV Device without having to first obtain premarket approval, HiFi filed a 510(k) submission with FDA on December 7, 2006. See Am. Compl. ¶ 17. Because the predicate device identified by HiFi in its 510(k) submission, the Digene Hybrid Capture Test, was itself a post-amendments Class III device with an approved PMA, HiFi could not demonstrate that its device was substantially equivalent to a predicate device that did not require premarket approval (e.g., a Class I or Class II device or a pre-amendments Class III device not yet subject to the requirement of PMA). See 21 U.S.C. §§ 360c(f)(1)(A), (i), 360e(b); 21 C.F.R. § 807.92(a)(3). Accordingly, by letter dated January 9, 2007, FDA rejected HiFi's 510(k) filing on the ground that the HPV Device remained in Class III because HiFi could not show substantial equivalence to a qualifying predicate device, but was of the same type as those that had been previously approved as Class III devices: "We have determined that your type of device is classified as a class III device by the approval order for the

VRAPAP [ViraPap] Human Papillomavirus DNA Detection Kit dated December 23, 1988." AR 20. "[T]he Act requires a class III device to have an approved PMA before it can be legally marketed, unless the device is reclassified." Id.

On January 19, 2007, HiFi submitted a petition to FDA, seeking to reclassify its HPV Device from Class III to Class II pursuant to the de novo reclassification provisions of 21 U.S.C. § 360c(f)(2). However, as FDA had indicated in its January 9, 2007, letter rejecting HiFi's 510(k) filing, HiFi's device was ineligible for de novo reclassification because only devices of "a type not previously classified under the Act" may be reclassified under the de novo provision, and HiFi's HPV Device is of the same "type of device" as the previously classified ViraPap HPV DNA Detection Kit. See 21 U.S.C. § 360c(f)(2)(A); AR 20. On February 27, 2007, Heather Rosecrans of FDA's Center for Devices and Radiological Health ("CDRH") reiterated this point to HiFi's President, Dr. Sin Hang Lee, in a telephone conversation. After that call, HiFi voluntarily withdrew its de novo reclassification petition. See Am. Compl. ¶¶ 26; AR 95.

On March 8, 2007, HiFi submitted a reclassification petition under 21 U.S.C. § 360c(f)(3), in another attempt to reclassify its HPV Device into Class II and thereby remove what HiFi characterized as "the regulatory roadblock" of PMA approval, which HiFi maintains serves "only to suffocate new technologies that may compete with the outdated inaccurate FDA-endorsed" HPV tests already approved and on the market. AR 109 (the petition is AR 96-163). FDA did not rule on HiFi's reclassification petition within the 210 days provided under 21 U.S.C. § 360c(f)(3), due to an error by FDA in assigning the official filing date.[7] HiFi sued FDA

[7] HiFi's reclassification petition was received by CDRH on March 9, 2007. The petition was then transferred for official filing to FDA's Division of Dockets Management, the agency's official repository for administrative proceedings, where it was not stamped as received until

for unreasonable delay under the APA. HiFi DNA Tech, LLC v. HHS, No. 07–1511 (D. Conn. Oct. 12, 2007). Following FDA's ruling on the reclassification petition in December 2007, HiFi voluntarily dismissed that suit.

V. THE FDA ORDER

On December 14, 2007, FDA issued a detailed, 14-page Order, in the form of a letter to HiFi's President, denying HiFi's petition for reclassification of the HPV Device from Class III to Class II. AR 491-501. As shown below, FDA evaluated all of the scientific evidence and determined that HiFi's device had not met the statutory criteria for a Class II device. Further, FDA considered the arguments raised by plaintiff and determined that they were without merit. Specifically, FDA determined that there were numerous inadequacies in the data submitted by HiFi, such that the HPV Device's basic performance characteristics, including its clinical sensitivity and specificity, cross-reactivity, and rate of false negative test results, could not be assessed. AR 297-307, 499-504. Even more fundamentally, FDA found that HiFi intends for its device to be used in conjunction with genotyping to confirm its positive test results, but HiFi did not submit any data demonstrating that an HPV genotyping test validated for diagnostic use with cervical cancer even exists. AR 296-308, 500-02. For these reasons, HiFi failed to meet its burden of proving that its HPV Device meets the requirements for reclassification.

May 22, 2007. CDRH relied upon this official filing date and believed that a response was not due until December 18, 2007, which would have been 210 days from the official filing date. The error was discovered only after HiFi filed its original lawsuit in October 2007. FDA ruled on HiFi's reclassification petition on December 14, 2007. AR 493.

VI. THE PRESENT LITIGATION

On January 11, 2008, HiFi filed suit against FDA, but did not properly serve the government with its complaint. HiFi filed an amended complaint on January 22, 2008, and served the government on January 24, 2008. In its amended complaint, HiFi alleges that FDA improperly denied its petition (Count One), and should have permitted plaintiff to obtain "de novo" review under 21 U.S.C. § 513(f)(2) (Count Two).

ARGUMENT

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 that special controls in combination with general controls would provide a reasonable assurance of the safety and effectiveness of the HPV Device for its intended uses. In reaching this determination, FDA properly employed its discretion under the FDCA to forgo referral of HiFi's petition to an expert panel because the evidence submitted by HiFi did not merit such consultation. Moreover, FDA's finding that the HPV Device was ineligible for de novo reclassification under 21 U.S.C. § 360c(f)(2) was fully in accord with the language and purpose of the FDCA.

I. STANDARD OF REVIEW

When reviewing agency action under the APA, "the district court sits as an appellate tribunal, not as a court authorized to determine in a trial-type proceeding whether the [agency's action] was factually flawed." Marshall County Health Care Auth., 988 F.2d at 1225. "[T]he

focal point for judicial review should be the administrative record already in existence. . . ." Camp v. Pitts, 411 U.S. 138, 142 (1973); see also Envtl. Def. Fund, Inc. v. Costle, 657 F.2d 275, 284 (D.C. Cir. 1981); 21 C.F.R. § 10.3(a) (stating that the administrative record consists of "the documents in the administrative file of a particular administrative action on which the Commissioner relies to support the action"). "Thus, the entire case on review is a question of law, and only a question of law." Marshall County Health Care Auth., 988 F.2d at 1226.

FDA's actions are subject to review under the APA and may be disturbed only if "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2)(A). "The arbitrary and capricious standard of review is narrow and particularly deferential." Envtl. Def. v. United States EPA, 369 F.3d 193, 201 (2d Cir. 2004) ("Envtl. Def."). Under this narrow standard of review, "[t]he court is not empowered to substitute its judgment for that of the agency" and may reverse the agency only where "there has been a clear error of judgment." Citizens to Preserve Overton Park, Inc. v. Volpe, 401 U.S. 402, 416 (1971); see also Henley v. FDA, 77 F.3d 616, 621 (2d Cir. 1996) ("[W]e might not have chosen the FDA's course had it been ours to chart. But that is hardly the point.").

A. Review of an Agency's Scientific Determination

A reviewing 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." Envtl. Def., 369 F.3d at 201; see also Motor Vehicle Mfrs. Ass'n of the United States, Inc. v. State Farm Mut. Auto. Ins. Co., 463 U.S. 29, 43 (1983). Courts are particularly deferential in reviewing an agency's determinations that are based on an evaluation of scientific

information within the agency's area of technical expertise. See Baltimore Gas & Elec. Co. v. Natural Res. Def. Council, Inc., 462 U.S. 87, 103 (1983) ("[A] reviewing court must remember that the [agency] is making predictions, within its area of special expertise, at the frontiers of science. When examining this kind of scientific determination, as opposed to simple findings of fact, a reviewing court must generally be at its most deferential.").

Courts have been particularly deferential to FDA with respect to issues pertaining to the classification of devices. In Contact Lens Mfrs. Ass'n. v. FDA, 766 F.2d 592 (D.C. Cir. 1985), the court upheld FDA's decision to withdraw its proposal to reclassify plaintiff's device to a less restrictive classification. The court recognized that the FDCA conferred "broad administrative discretion . . . upon the FDA" with respect to device classification. Id. at 594. Also, "in such matters generalist courts see through a glass darkly and should be especially reluctant to upset an expert agency's judgment. . . ." Id. at 600. In Gen. Med. Co., the court affirmed FDA's denial of plaintiff's request that its device be reclassified from Class III to Class I. The court noted "broad discretion" given to FDA "in implementing the definition of 'substantial equivalence,'" and that "the FDA was within its broad discretion in weighing unproven benefits against small but proven harms and finding the balance tilted towards a finding of a 'potential unreasonable risk of illness of injury.'" 770 F.2d 218, 221. In Ethicon, Inc. v. FDA., 762 F. Supp. 382 (D.D.C. 1991), plaintiff challenged FDA's decision to reclassify another manufacturer's device from a Class III to a Class II. The court stated: "Congress gave FDA sweeping discretion in determining the classification of devices and therefore in judging the safety and effectiveness of medical devices." Id. at 386. Also, "the Court does not weigh the evidence; it merely examines 'the record to see if there is evidence, which if accepted by the Secretary, supports the determination

of the agency.'" Id. at 389 (quoting in part Nat'l Soft Drink Ass'n v. Block, 721 F.2d 1348, 1354 (D.C. Cir. 1983)).

B. Review of an Agency's Interpretation of Its Own Statute

"When a federal agency takes action under a particular statutory provision, [the courts] review the agency's interpretation of the statute under Chevron, U.S.A., Inc. v. Natural Res. Def. Council, Inc., 467 U.S. 837 (1984)." Envtl. Def., 369 F.3d at 201. Under the two-step Chevron analysis, the reviewing court must first "question whether Congress has directly spoken to the precise question at issue." Chevron, 467 U.S. at 842. To determine whether Congress has spoken to the precise question, courts apply "traditional tools of statutory interpretation – text, structure, purpose and legislative history." Consumer Elecs. Ass'n v. FCC, 347 F.3d 291, 297 (D.C. Cir. 2003) (citation and quotation marks omitted); see also Mizrahi v. Gonzales, 492 F.3d 156, 158 (2d Cir. 2007) (finding that these "interpretive clues" may be employed under Chevron step one in order to reveal Congressional intent). If the will of Congress can be clearly discerned, the "analysis ends . . . because both the agency and the courts 'must give effect to the unambiguously expressed intent of Congress.'" Envt. Def., 369 F.3d at 201 (quoting Chevron, 467 U.S. at 843).

Where a "statute is silent or ambiguous," however, "the court does not simply impose its own construction on the statute." Chevron, 467 U.S. at 843. Rather, the court proceeds to the second step of the Chevron analysis, under which "[c]ourts defer to statutory interpretations when (1) the agency is charged with implementing the statutory scheme, and (2) its interpretation is reasonable." Chauffeur's Training Sch., Inc. v. Spellings, 478 F.3d 117, 125 (2d Cir. 2007). If Congress has "explicitly or implicitly delegated authority to the agency to interpret ambiguities in

the statute . . . its construction of the statute will, if reasonable, be granted deference by the reviewing court." Envt. Def., 369 F.3d at 201 (citing United States v. Mead Corp., 533 U.S. 218 (2001)); see also Good Samaritan Hosp. Reg'l Med. Ctr. v. Shalala, 85 F.3d 1057, 1061-62 (2d Cir. 1996) (holding that "great deference must be accorded to the interpretation given the statute by the officers or agency charged with its administration") (citation and quotation marks omitted). Chevron deference is appropriate when "the interstitial nature of the legal question, the related expertise of the Agency, the importance of the question to administration of the statute, the complexity of that administration, and the careful consideration the Agency has given the question over a long period of time all indicate that Chevron provides the appropriate legal lens through which to view the legality of the Agency interpretation here at issue." Barnhart v. Walton, 535 U.S. 212, 222 (2002). Thus, deference is appropriate in the device reclassification context because of "the complexity of the statutory regime" and "FDA's expertise." See Mylan Laboratories, Inc. v. Thompson, 389 F.3d 1272, 1280 (D.C. Cir. 2004); see also Henley, 77 F.3d at 621 ("FDA possesses the requisite know-how to conduct such analyses, by sifting through the scientific evidence to determine the most accurate and up-to-date information regarding a particular drug, and how those data affect human usage.").

Such deference is particularly warranted when, as here, an "agency is empowered not only to construe its governing statute, but additionally to make safety judgments delegated to it by Congress." United States v. Algon Chem., Inc., 879 F.2d 1154, 1159 (3d Cir. 1989) (ruling that the party challenging FDA's statutory interpretation could "prevail only if it can show that the FDA's views about the need of public health are arbitrary and capricious") (citation and quotation marks omitted); see also Berlex Labs., Inc. v. FDA, 942 F. Supp. 19, 25 (D.D.C. 1996)

("FDA's policies and its interpretation of its own regulations will be paid special deference because of the breadth of Congress' delegation of authority to FDA and because of FDA's scientific expertise."). Thus, "FDA interpretations of the FDCA receive deference, as do its interpretations of its own regulations." Purepac Pharm. Co. v. TorPharm, Inc., 354 F.3d 877, 883 (D.C. Cir. 2004) (citation omitted).

II. FDA CORRECTLY DENIED PLAINTIFF'S PETITION BASED ON A THOROUGH EXAMINATION OF THE SCIENTIFIC EVIDENCE AND A PROPER APPLICATION OF THE STATUTORY STANDARDS

FDA's Order demonstrates that FDA thoroughly examined all of the scientific evidence, properly applied the law, and provided a reasoned explanation for its analysis. AR 491-504. Further, FDA reached its decision after conducting a careful evaluation of HiFi's petition for reclassification, including the more detailed data provided by HiFi in its earlier 510(k) submission, which HiFi had incorporated into its reclassification petition by reference. AR 493-94. FDA found that HiFi had failed to meet its burden of providing sufficient information, in the form of adequate, valid scientific evidence, "to establish special controls that, when combined with general controls, will provide reasonable assurance of the safety and effectiveness of the device." AR 494; see 21 U.S.C. § 360c(a)(1)(B). Accordingly, FDA denied HiFi's petition for reclassification.

In the first count of the amended complaint, HiFi challenges the scientific judgment of FDA in denying its petition for reclassification of the HPV Device from Class III to Class II. Am. Compl. ¶15 (alleging that FDA's "denial is not supported by medical science"). Because the HPV Device is automatically placed in Class III by operation of the statute, 21 U.S.C. § 360c(f)(1), HiFi, as the party seeking reclassification, "carries the burden of proving that the

device meets the requirements for reclassification set up by the [Medical Device] Amendments." Gen. Med. Co., 770 F.2d at 219; see also Contact Lens Mfrs. Ass'n, 766 F.2d at 599 ("We cannot fault the FDA's assignment of the burden of proof to those seeking to change the status quo."); Ethicon, 762 F. Supp. at 391 ("FDA need not specify which . . . tests will be appropriate because the proponent of a new product must do so."). To prevail on this claim, HiFi would need to establish that FDA "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 the product of agency expertise." Motor Vehicle Mfrs. Ass'n, 463 U.S. at 43.

The administrative record in this matter clearly reflects that FDA considered the evidence proffered by HiFi and reasonably concluded, in an exercise of its scientific expertise, that HiFi had not submitted sufficient information to permit a reclassification of the HPV Device. See Contact Lens Mfrs. Ass'n, 766 F.2d at 594 ("Congress itself was not positioned to determine the appropriate classification of every medical device . . . yet to be invented . . . . The legislators therefore charged the FDA with the task of implementing the Amendments, and thus of essaying judgments appropriate to ensure safe and effective medical devices without stifling innovative technology."); Ethicon, 762 F. Supp. at 386 ("Congress gave FDA sweeping discretion in determining the classification of devices . . . ."). Because FDA issued a detailed Order in which it carefully considered and properly denied HiFi's classification petition, HiFi failed to meet its burden. AR 491-504.

A. Plaintiff's Supporting Data Are Inadequate To Support Reclassification

After reviewing HiFi's reclassification petition, which included descriptions of the studies and tests conducted by HiFi as well as published articles on the general topics of HPV and cervical cancer, FDA determined that the supporting data submitted by HiFi were insufficient to support a reclassification of the HPV Device. AR 297-301, 307-08, 499-501; see also 21 C.F.R. § 860.123(a)(6) (requiring a reclassification petition to include a "full statement of the reasons, together with supporting data," in the form of valid, scientific evidence, to explain "how the proposed classification will provide reasonable assurance of the safety and effectiveness of the device").

Among the numerous, fundamental inadequacies in the data submitted by HiFi were that HiFi had: failed to perform any cross-reactivity studies; not established the clinical sensitivity or clinical specificity of its device; failed to show that the device would perform consistently under a variety of laboratory conditions; and not demonstrated the stability of the device's reagents. AR 499-501. FDA also observed that the study descriptions given by HiFi made it clear that its device must be used in conjunction with HPV genotyping in order to confirm positive HPV DNA test results, but that "FDA has not to date approved any HPV genotyping test for diagnostic use," and HiFi had not "submitted any evidence to establish that . . . [an] HPV genotyping test validated for diagnostic use in relation to cervical cancer" even exists. AR 500-501. In fact, the genotyping method that HiFi purports to have used in conjunction with its device is dependent upon articles that are labeled by their manufacturer for "Research Use Only – Not for Use in Diagnostic Procedures." AR 297.

HiFi maintains that "FDA erroneously found that Plaintiff did not provide adequate, scientific data as required by law." Am. Compl. ¶ 15(g). HiFi, however, offers only two specific examples in response to the numerous inadequacies noted by FDA. Neither of the arguments is persuasive. First, HiFi alleges that FDA applied "an incorrect scientific standard" in requiring it to provide data from cross-reactivity studies. Id. at ¶ 15(j). As FDA explained in its Order, however, such studies are critical to assure that substances and microorganisms normally found in the genital tract do not interfere with the device's detection of the HPV strains it targets. AR 499. Without such studies, the accuracy and reliability of the HPV Device cannot be ascertained. Id.

Second, HiFi maintains that FDA erred in requiring evidence of its device's clinical sensitivity and specificity because these concepts "are not appropriate to scientifically validate laboratory methodologies." Am. Compl. ¶ 15(k). However, FDA's findings regarding sensitivity and specificity pertain to the inadequacy of plaintiff's studies, AR 499-501, and thus point to the lack of data supporting the safety and effectiveness of the device whether it is used in the laboratory or used clinically. In addition, HiFi's intended use statements make plain that the results from its device are meant to be used outside of the laboratory to assist medical professionals to make clinical decisions when screening women for cervical cancer. See AR 102 (stating that the HPV Device is "intended to be used for detection of HPV DNA in clinical samples"). Studies demonstrating that the device is capable of accurately informing these clinical decisions are necessary in order to determine that the device is safe and effective for its intended use. AR 500. "There are many reasons why a device of your type . . . may not be clinically effective (with patients) even if it were shown to be effective in the laboratory (with

specimens)." AR 503; see also 21 C.F.R. § 860.7(e)(1) ("There is a reasonable assurance that a device is effective when it can be determined, based on valid scientific evidence, that in a significant portion of the target population, the use of the device for its intended uses . . . will provide clinically significant results.").

Clinical data is also necessary in order to demonstrate that the HPV Device can accurately distinguish the relevant HPV types from among a large number of genetically similar HPV types. The presence of specific HPV types are detected in the laboratory through the use of small segments of DNA (or other nucleic acid) called "probes," which bond to the targeted HPV types due to complementary association (i.e., a sequence of probe DNA that inversely "matches" a sequence of HPV DNA from a particular, targeted HPV type). Because the high-risk HPV types meant to be detected by HiFi's HPV Device are so genetically similar, the probes designed to detect these types may cross-react or compete with non-targeted DNA sequences (including low-risk HPV types) and produce inaccurate results. In order to correct for this difficulty in assessing analytical performance in the laboratory, specific clinical data showing that the device is capable of correctly identifying women at risk for cervical disease is necessary to evaluate the specific probe combinations used by the HPV Device and establish that the device is safe and effective for its intended use.

HiFi contends that FDA's determination based on "the probe design is erroneous because the device does not use a probe; rather, the device uses a process known as PCR (polymerase chain reaction) to replicate HPV DNA for automated DNA sequencing. . . ." Am. Compl. ¶ 15(m). FDA's general definition of the term "probe," see AR 306, 504, was intended to encompass the "primers" that are used by HiFi's HPV Device (i.e., the method by which unique

DNA sequences are chosen to recognize specific DNA targets for the purpose of replicating the targets by PCR). AR 306. FDA's analysis of the need for clinical data to support probe design is equally applicable to HiFi's device. AR 504. Without this data, the safety and effectiveness of the HPV Device cannot be determined.

Complex 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. See Contact Lens Mfrs. Ass'n, 766 F.2d at 599-600 (holding, in the context of a device reclassification matter, that a court "should be especially reluctant to upset an expert agency's judgment that a party has failed to adduce sufficient scientific proof of safety and effectiveness"). Even if HiFi had come forward with enough evidence to demonstrate that a scientific disagreement existed with respect to these determinations, it could not show that FDA has failed to consider "the relevant factors" or made "a clear error of judgment" in concluding that HiFi failed to meet its burden of providing sufficient information, in the form of adequate, valid scientific evidence, to support reclassification of the HPV Device. Citizens to Preserve Overton Park, Inc., 401 U.S. at 416; see also Ethicon, 762 F. Supp. at 389 ("the Court does not weigh the evidence; it merely examines 'the record to see if there is evidence, which . . . supports the determination of the agency'") (quoting Nat'l Soft Drink Ass'n, 721 F.2d at 1354). This Court should therefore defer to FDA's reasonable scientific judgment that HiFi failed to present sufficient data to support reclassification of the HPV Device.

B. Special Controls Do Not Provide a Reasonable Assurance of the Safety and Effectiveness of the Plaintiff's Device

Although the lack of supporting data, by itself, justifies FDA's decision to deny the reclassification petition, FDA found additional inadequacies in the petition. FDA reviewed the special controls proposed by HiFi and determined that they were insufficient to provide a reasonable assurance of the safety and effectiveness of the HPV Device. Although FDA had no objection to several of the warnings for the proposed labeling and promotional materials offered by HiFi as special controls, FDA found that these warnings by themselves could not provide a reasonable assurance of the safety and effectiveness of HiFi's device because there was inadequate evidence to establish that, even when used in accordance with the warnings, the device produces accurate, reliable, and consistent results. AR 501-02. In addition, FDA observed that several of the special controls proposed by HiFi incorporated genotyping. Because genotyping has not been shown to be clinically validated for cervical cancer screening (as explained above), HiFi's reliance upon genotyping as a special control does not provide a reasonable assurance of the safety and effectiveness of the HPV Device. Id. at 502.

HiFi alleges that FDA's "denial based upon the alleged insufficiency of special controls is erroneous as contrary to accepted science." Am. Compl. ¶ 15(t). Specifically, HiFi argues that the fact that "'FDA has not to date approved any HPV genotyping test for diagnostic use' . . . reflects a failure of FDA and should not be used as a tool or a policy for blocking new technology introduced for HPV genotyping." Id. at ¶ 15(l) (quoting the Order). Even if there were any merit to HiFi's strange contention that FDA is responsible for the non-existence of an approved genotyping test that HiFi relies upon as a special control, this would not alter the statutory

standard applicable to HiFi's reclassification petition. FDA is only permitted to reclassify the HPV Device into Class II if special controls can be established that provide a reasonable assurance of the safety and effectiveness of the device. 21 U.S.C. § 360c(a)(1)(B). HiFi provides no justification for its untenable position that FDA could find genotyping to be an appropriate special control when there is no evidence that an approved HPV genotyping test for this purpose even exists. Thus, FDA reasonably concluded that HiFi has not provided sufficient evidence to establish special controls that are sufficient to provide a reasonable assurance of the safety and effectiveness of its device. AR 502; see also 21 U.S.C. § 360c(a)(1)(B)-(C), (f)(3)(C).

C. Plaintiff's Device Fits the Statutory Definition of a Class III Device

In an effort to provide a thorough response to HiFi's reclassification petition, FDA also addressed additional arguments raised by HiFi regarding whether the HPV Device has the characteristics of a Class III device. However, as FDA explained in its Order, these findings were not the basis for the agency's denial of HiFi's requested reclassification into Class II. AR 495 n.4. HiFi's device was automatically designated Class III by operation of law. 21 U.S.C. § 360c(f)(1). It can be reclassified into Class II even if it is for "a use which is of substantial importance in preventing impairment of human health" and "presents a potential unreasonable risk of illness or injury" (both of which are characteristics of a Class III device), so long as "special controls could be established that would provide a reasonable assurance of the safety and effectiveness of [HiFi's] device." AR 495 n.4. HiFi failed to show, however, that such special controls could be established. FDA's findings with respect to whether the HPV Device has the characteristics of a Class III device are essentially agency dicta; nevertheless, if the Court were to

consider these findings, FDA's conclusion that the HPV Device has the characteristics of a Class III device was reasonable and appropriate.

1. Plaintiff's Device Is of Substantial Importance In Preventing Impairment of Human Health

FDA concluded that the HPV Device is of "substantial importance in preventing impairment of human health" after observing that both of the intended uses identified by HiFi "relate to identifying HPV infection status in order to . . . . guide patient management decisions that can themselves lead to more definitive diagnosis and treatment of cervical cancer." AR 496. In fact, HiFi's second intended use statement explicitly references the professional Guidelines for cervical cancer screening. AR 491, 497. These Guidelines provide that if a woman 30 years or older with a normal Pap test diagnosis tests positive for high-risk HPV types using an approved HPV DNA device, she should undergo additional cervical cancer screening in one year, whereas the same woman testing negative would not be tested for another three years. AR 374, 497-98. Because HiFi's device is "intended to help physicians make a potentially significant decision: whether to immediately refer patients to . . . intervention, or to advise patients to wait and be screened again later," FDA determined that HiFi's device "is of substantial importance in preventing impairment of human health." AR 497; 21 U.S.C. § 360c(a)(1)(C)(ii)(I).

HiFi contends that FDA reached this conclusion because FDA mistakenly believed that HiFi's device was "a cancer test rather than . . . a test for a common virus." Am. Compl. ¶ 15(c); see also ¶¶ 15(h) & (p) (insisting "that the device is simply a test for virus DNA and does not dictate any clinical judgment"). As is clear from its Order, however, FDA specifically considered this contention in evaluating HiFi's reclassification petition. FDA found that the

purported utility of the HPV Device is that it detects HPV DNA, which will in turn "guide patient management decisions" by influencing a physician's decision whether to immediately refer a patient for further cervical cancer screening or advise the patient to wait and be tested again later. AR 495-98. HiFi's own intended use statements, the second of which states that the information from the HPV Device "together with the . . . professional guidelines, may be used to guide patient management," confirms the accuracy of FDA's finding. AR 112, 491. As the administrative record makes clear, FDA properly concluded that the HPV Device is of "substantial importance in preventing impairment of human health." AR 496-98; 21 U.S.C. § 360c(a)(1)(C)(ii)(I).

2. Plaintiff's Device Presents a Potential Unreasonable Risk of Illness or Injury

FDA also determined that the HPV Device "presents a potential unreasonable risk of illness or injury because its rate of false negative results was not known." AR 496. A false negative test result, when the patient has pre-cancerous cellular changes or cancer but receives a negative HPV DNA test result, may "lead to delays in timely diagnosis and treatment, allowing an undetected condition to worsen and potentially increasing morbidity and mortality from cervical cancer." AR 498; see also id. at 500. Despite the obvious potential harms from false negative test results, FDA found that HiFi had "neither established the risk of false negative tests results for your device . . . nor shown that this risk is reasonable." AR 498.

In one study description submitted by HiFi, "Sensitivity in Detection of HPV DNA in Clinical Samples, Compared to FDA-Approved Device," HiFi explicitly stated that it had not collected information on the "cervical pathologic conditions" of the study subjects (i.e., whether

the subjects being tested actually had precancer or cancer) because these "conditions were not the subjects of the study." AR 142. Without such information, however, FDA cannot assess the device's rate of false negative test results. AR 500. FDA found this evidentiary failing to be "particularly troubling" because "one of the greatest risks posed by this device is the risk of delivering false negative test results, as these results may lead to delays in timely diagnosis and treatment of cervical cancer." Id. This evidentiary failing led FDA to conclude that the HPV Device "presents a potential unreasonable risk of illness or injury." AR 496, 498; see H.R. Rep. No. 853, 94th Cong., 2d Sess., at 36 (1976) ("The fact that a device is being marketed without sufficient testing is an adequate basis for the Secretary's conclusion that the device presents a potential unreasonable risk to health.").

HiFi alleges that "FDA's allegation that the device presents an unreasonable risk of illness or injury is contrary to law [and] not supported by science." Am. Compl. ¶ 15(i). However, HiFi fails to allege facts sufficient to show that FDA wrongly concluded that the device's unknown rate of false negatives presents an unreasonable risk of illness or injury. In its Order denying HiFi's reclassification petition, FDA clearly stated that its basis for its conclusion that the HPV Device "presents an unreasonable risk" was the fact that HiFi had "neither established the risk of false negative test results . . . nor shown that this risk is reasonable." AR 498. Because HiFi does not dispute this finding, it cannot prevail on its claim that FDA's conclusion is unreasonable.

D. FDA's Decision is Consistent With the Policy Objectives of the FDCA

FDA's Order is also well-grounded in the public health objectives of the FDCA. HiFi advances two policy arguments in support of its reclassification petition, but it cannot show that

the interests purportedly served by reclassifying its HPV Device outweigh FDA's obligation to protect the public from medical devices not shown to be safe and effective.

First, HiFi contends that FDA has subjected "other in vitro devices for the detection of . . . cancer" to less burdensome regulatory oversight as Class I and II devices and that this inconsistency militates in favor of reclassifying its HPV Device. Am. Compl. ¶ 15(d), see also ¶¶ 15(e), (q). One group of devices cited by HiFi tests for the bacterium Helicobacter pylori ("H. pylori") in the stomach (this was also raised by HiFi in its reclassification petition). Id. ¶ 15(d); AR 115-16 . In considering this argument, FDA found that HiFi had mischaracterized the intended uses of these devices, as they "are not expressly intended for use in cancer screening," and that, in any event, HiFi could not meet its burden of providing adequate scientific data for its device through argument by analogy to another device. AR 309 ("That other, unrelated devices may be classified in class I does not mitigate or relieve petitioner's burden of proving that the proposed classification will provide a reasonable assurance of the safety and effectiveness of this device. . . ."); see also Contact Lens Mfrs. Ass'n, 766 F.2d at 594 (rejecting claims that a device, a soft contact lens, had "suffered disparate treatment in relation to other medical devices (indeed, other contact lenses). . . ."); Ethicon, 762 F. Supp at 387 (rejecting an argument that the factors from another case were controlling "because, simply put, it concerned a different device. The agency's characterization of a generic class or type of device is fact-specific. . . .").

Second, HiFi argues that FDA's denial of its petition should be overturned because it "discourages competitive introduction of a PCR-based HPV DNA device" and is therefore "not in the best interest of the consumers." Am. Compl. ¶15(s). In enacting the MDA, however, "Congress's primary concern was to prevent the marketing of devices not both safe and

effective." Gen. Med. Co., 770 F.2d at 222; see also Medtronic, 518 U.S. at 474. In so doing, Congress relegated all new devices to Class III, thereby knowingly imposing upon them the "costly and time-consuming process" of premarket approval. Contact Lens Mfrs. Ass'n, 766 F.2d at 594. To date, two in vitro HPV DNA devices have received FDA premarket approval. AR 285-88. Even if HiFi were correct that FDA's denial of its reclassification petition discourages marketplace competition, FDA must construe the statute that it administers "to effectuate the overriding purpose of protecting the public health." Gen. Med. Co., 770 F.2d at 218 (citing United States v. An Article of Drug . . . Bacto-Unidisk, 394 U.S. 784, 798 (1969)).

Because Congress instructed FDA, above all other concerns, to protect the public from medical devices not shown to be safe and effective, HiFi cannot succeed in having its device reclassified simply by arguing that other dissimilar devices are subject to less stringent regulatory controls. FDA reasonably concluded, based on its scientific expertise, that HiFi failed to meet its burden of establishing the criteria for reclassification. HiFi cannot show that FDA's scientific judgment was arbitrary or capricious under the APA. The decision of the FDA must be upheld. See Henley, 77 F.3d at 621; Contact Lens Mfrs. Ass'n, 766 F.2d at 603 (upholding FDA's refusal to reclassify a device in light of "the difficulty of the assignment Congress entrusted to the agency, and the respect we owe to the FDA's expert judgment").

E. FDA'S Determination That Panel Review of Plaintiff's Petition Was Not Necessary is Consistent With the Statute

HiFi also alleges that FDA "did not follow established FDA procedures in making their decision of denial" in that "FDA failed to forward the petition to the FDA Commissioner[8] or to a classification panel for review." Am. Compl. ¶ 15(a).[9] Here, Congress explicitly granted the Commissioner the discretion to decide whether panel referral is warranted. HiFi sought reclassification of its HPV Device pursuant to 21 U.S.C. § 360c(f)(3), which states that "the Secretary may for good cause shown refer the petition to an appropriate panel. . . ."

This discretionary language was added to the FDCA by the Safe Medical Device Act of 1990, which struck from the statute the words "the Secretary shall" refer the petition to an appropriate panel and replaced them with "the Secretary may for good cause shown" refer the petition to an appropriate panel. Pub. L. 101-629 § 18, 104 Stat. 4511, 4528 (Nov. 28, 1990). The House Report states that in amending the FDCA, the "requirement that FDA shall refer petitions for classifying new devices in class I and class II to a classification panel is made discretionary." H. Rep. 101-808, at 32 (Oct. 5, 1990).

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[8] The Commissioner's authority to rule on reclassification petitions is delegated to the Director of the Office of In Vitro Diagnostic Device Evaluation and Safety in CDRH. See FDA Staff Manual Guide § 1410.405, available at http://www.fda.gov/smg/vol2/1410/1410_405.html.

[9] Elsewhere in its Amended Complaint, HiFi appears to concede that referral to a panel under 21 U.S.C. § 360c(f)(3) is discretionary. In arguing that it was disadvantaged by FDA's failure to review its petition under the de novo provision, 21 U.S.C. § 360c(f)(2), HiFi objects to FDA's use of the "longer, more burdensome 21 U.S.C. § 360c(f)(1) [sic] reclassification process, which might require the attention of the FDA Commissioner and a classification panel." Am. Compl. ¶ 28 (emphasis added).

When this much discretion is given to an agency, the agency's exercise of its discretion on this particular topic is not subject to judicial review. The APA provides that judicial review is available except to the extent that "agency action is committed to agency discretion by law." 5 U.S.C. § 701(a)(2). In determining whether agency action is committed to agency discretion, the appropriate inquiry is whether "statutes are drawn in such broad terms that in a given case there is no law to apply." Citizens to Preserve Overton Park, 401 U.S. at 410. This is what Congress intended in the APA: "Where laws are so broadly drawn that agencies have large discretion, the situation cannot be remedied by an administrative procedure act but must be treated by the revision of statutes conferring administrative powers." Administrative Procedure Act, Legislative History, H.R. Rep. 1980, 79th Cong. 2d Sess. 275 (1946). When matters are committed to agency discretion, they are not to be reviewed at all, even for an abuse of discretion. Heckler v. Chaney, 470 U.S. 821, 830 (1985); see also Lincoln v. Vigil, 508 U.S. 182, 191 (1993). In a case remarkably similar to the instant case, the Second Circuit, citing Heckler and Lincoln, concluded that courts lack jurisdiction to review Board of Immigration "members' decisions to decide cases without referral to three-member panels" when the relevant regulation provides "that a BIA member 'may' refer a case to a three-member panel in certain circumstances – not that he 'must' do so – and provides no guidance concerning when such reference is appropriate, making it even more difficult for a Court of Appeals to review." Kambolli v. Gonzales, 449 F.3d 454, 463 (2d Cir. 2006).

Even if FDA's action on this issue were reviewed, however, it should be upheld because plaintiff's petition is so lacking in merit that plaintiff has not shown "good cause" such that its petition should have been referred to a panel. See AR 491-504. This decision should be

afforded deference because of "the broad administrative discretion Congress conferred upon the FDA" to implement the FDCA's medical device provisions. Contact Lens Mfrs. Ass'n, 766 F.2d at 594; see also Gen. Med. Co., 770 F.2d at 218, 221; Ethicon, 762 F.Supp. at 386. FDA's decision, which comports with both the plain language of the statute and its statutory and legislative history, is reasonable, within its discretion, and should be upheld.

III. FDA'S DETERMINATION THAT PLAINTIFF'S DEVICE WAS NOT ELIGIBLE FOR DE NOVO RECLASSIFICATION UNDER 21 U.S.C. § 360c(f)(2) IS CONSISTENT WITH THE STATUTE AND CONGRESSIONAL INTENT

In the Second Count of its Amended Complaint, HiFi alleges that "FDA should have . . . permitted the device to be evaluated under the less burdensome provisions of de novo review found in 21 U.S.C. § 360c(f)(2)." Am. Compl. ¶ 29; see also id. ¶¶ 15(b), (f).[10] HiFi has waived this argument, however, because it voluntarily withdrew its de novo reclassification petition and refiled for reclassification pursuant to 21 U.S.C. § 360c(f)(3). See AR 95. Had HiFi wished to pursue reclassification under the de novo provision, it should have waited the statutorily prescribed 60 days and permitted FDA to issue an order on the de novo petition. 21 U.S.C. § 360c(f)(2)(B)(i) ("Not later than 60 days after the date of the submission of the request . . . , the Secretary shall by written order classify the device."). See Wrenn v. Sec'y, Dep't of Veterans Affairs, 918 F.2d 1073, 1078 (2d Cir. 1990) (ruling that "a claimant who initiates the administrative process must pursue that process to a final agency decision").

[10] Although the caption to HiFi's Second Count states that HiFi was entitled to review of its petition under the "'de novo' . . . provisions of 21 U.S.C. § 360(f)(1)," the prayer for relief and paragraphs 1, 21, and 29 reference 21 U.S.C. § 360c(f)(2), which is the correct citation to the de novo reclassification provision.

Even if HiFi had not waived this argument, its claim would still fail because it cannot demonstrate that FDA's interpretation of the statute is unreasonable. See Chevron, 467 U.S. at 843; Good Samaritan Hosp. Reg'l Med. Ctr., 85 F.3d at 1062. As discussed above, the de novo route is permitted only for "a type of device that has not been previously classified. . . ." 21 U.S.C. § 360c(f)(2)(A). As also discussed above, when FDA initially rejected HiFi's 510(k) filing, it did so on the ground that it was of a type of device that had been previously classified as a Class III device, not a Class I or II device: "We have determined that your type of device is classified as a class III device by the approval order for the VRAPAP Human Papillomavirus DNA Detection Kit dated December 23, 1988."[11] AR 20. This is the same reason that the de novo provision is inapplicable; i.e., plaintiff's device is not "a type of device that has not been previously classified. . . ." 21 U.S.C. § 360c(f)(2)(A).[12]

The HiFi HPV Device and the ViraPap Human Papillomavirus DNA Detection Kit are both HPV DNA tests that are intended to aid in the diagnosis of sexually transmitted HPV infections and serve as an adjunct to Pap tests in the identification of women at increased risk of developing cervical cancer. AR 112, 286, 289. As such, they are the same type of device. See 21 C.F.R. § 860.3(i) (devices are the same "generic type of device" when they "do not differ significantly in purpose, design, materials, energy source, function, or any other feature related to safety and effectiveness").

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[11] The December 23, 1988, approval order for the ViraPap Human Papillomavirus DNA Detection Kit, which HiFi argues that FDA refused to produce, Am. Compl. ¶¶ 15(f), 19, is included in the administrative record. AR 1-5.

[12] Contrary to plaintiff's argument, Am. Compl. ¶ 29, FDA did not find "substantial equivalence" between the two devices, only that they are of the same type.

HiFi also contends that FDA erred in comparing its device to the Digene HyBrid Capture Test, which HiFi maintains "uses a completely different scientific basis to determine the presence and type of HPV DNA if any, present in a sample." Am. Compl ¶ 15(b). FDA's determination that the HPV Device was ineligible for de novo review was premised on a finding that HiFi's device, in light of its intended uses, was the same type of device as the first-approved HPV DNA test, the ViraPap Human Papillomavirus DNA Detection Kit. AR 20. FDA did not reference Digene's HyBrid Capture Test in determining that HiFi's type of device had already been classified as Class III and was thus ineligible for de novo review. In any event, HiFi's two intended use statements for its HPV Device are identical to those for Digene's HyBrid Capture Test, but for the addition of language regarding genotyping. AR 112, 287-89. HiFi's reliance on genotyping is highly problematic, as explained above, and does not make HiFi's device a different type of device than the existing HPV DNA tests.

FDA's finding that HiFi's device and the ViraPap were the same generic type of device is a factual determination squarely within its area of expertise and, as such, merits substantial deference. See Ethicon, 762 F. Supp. at 387 ("The agency's characterization of a generic class or type of device is fact-specific."). Similarly, FDA's determination that devices of the same general type may not be reclassified pursuant to the de novo reclassification provision is a reasonable interpretation of the statute the agency is charged with implementing. See Gen. Med. Co., 770 F.2d at 218, 221 ("FDA has broad discretion in implementing" the device amendments).

CONCLUSION

For the foregoing reasons, Plaintiff's complaint should be dismissed pursuant to Federal Rule of Civil Procedure 12(b)(6).

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March 24, 2008

Certificate of Service

I hereby certify that on March 24, 2008, a motion to dismiss, memorandum in support, attachment, and notice of manual filing were filed by the government defendants electronically and served by mail on anyone unable to accept electronic filing. Notice of this filing will be sent by e-mail to all parties by operation of the court's electronic filing system or by mail to anyone unable to accept electronic filing as indicated on the Notice of Electronic Filing. Parties may access this filing through the court's CM/ECF System.

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