09-1832-cv

IN THE UNITED STATES COURT OF APPEALS
FOR THE SECOND CIRCUIT

HIFI DNA TECH LLC,

Plaintiff-Appellant,

v.

UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES, et al.,

Defendants-Appellees,

BRIEF OF DEFENDANTS-APPELLEES

Of Counsel:

DAVID CADE
Acting General Counsel

MICHAEL M. LANDA
Acting Associate General Counsel
Food and Drug Division

ERIC M. BLUMBERG
Deputy Chief Counsel, Litigation

CLAUDIA J. ZUCKERMAN
Associate Chief Counsel
Food and Drug Division
U.S. Dep't of Health and Human Services
Office of General Counsel

TONY WEST
Assistant Attorney General

ANN M. RAVEL
Deputy Assistant Attorney General

EUGENE M. THIROLF
Director

LAUREN H. BELL
DRAKE CUTINI
Attorneys, Office of Consumer Litigation
U.S. Department of Justice
P.O. Box 386
Washington, D.C. 20044
202-353-1991
lauren.hash.bell@usdoj.gov

TABLE OF CONTENTS

TABLE OF AUTHORITIES

FEDERAL CASES

STATUTES

FEDERAL REGULATIONS

MISCELLANEOUS

Jurisdictional Statement

The United States District Court for the District of Connecticut exercised jurisdiction below pursuant to 28 U.S.C. § 1331. This Court has appellate jurisdiction under 28 U.S.C. § 1291, because this is an appeal from the district court's final judgment of dismissal, entered on March 31, 2009. JA 71.

Statement of the Issues

1. **Whether the district court properly affirmed FDA's denial of HiFi's petition to reclassify its medical device.**

2. **Whether HiFi waived its argument that the district court should have considered material evidence outside of the administrative record.**

3. **Assuming HiFi did not waive the issue, whether the district court should have considered evidence outside of the record.**

Statement of the Case

I. Nature of the Case, Course of Proceedings, and Disposition Below

This case involves a challenge by HiFi DNA Tech, LLC ("HiFi") to 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 regulatory standards than are Class III devices. HiFi's device is not currently on the market; HiFi has not attempted to have its device approved as a Class III device. It is automatically a Class III device by law, and it is HiFi's burden to demonstrate to the United States Food and Drug Administration ("FDA") that the device should be regulated as a Class II

device. HiFi submitted a petition seeking such reclassification, and FDA concluded that HiFi has not carried that burden.

HiFi's device is an in vitro diagnostic assay that HiFi intends to be used to detect the presence of Human Papillomavirus ("HPV"), an infection that may lead to cervical cancer. After a thorough review of HiFi's petition, FDA concluded that the device may not be reclassified at this time because there is not adequate 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.

The lawsuit underlying this appeal is a claim under the Administrative Procedure Act ("APA") challenging the scientific judgment of FDA in denying HiFi's petition for reclassification. Defendants filed a motion to dismiss, contending that the administrative record demonstrates that FDA carefully reviewed HiFi's reclassification petition and reasonably concluded, in an exercise of its scientific and technical expertise, that HiFi's device could not be reclassified into Class II because HiFi failed to establish a reasonable assurance of the safety and effectiveness of the HPV Device for its intended uses. The district court granted defendants' motion, and judgment was entered on March 31, 2009. This appeal followed.

II. 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 monitoring, 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, 343 (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 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 by its sponsor 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 and 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).

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).[1] If the Commissioner refers

[1] 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).

a petition to a panel, within 90 days from the date that a panel's recommendation is received 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 ground 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).

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" "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, because the de

novo reclassification provision does not explicitly require the Commissioner to refer a petition to a panel for a recommendation, and the time frame 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).

Statement of Facts

I. HiFi's Device

HiFi is the manufacturer of the Human Papillomavirus DNA Nested Polymerase Chain Reaction Detection Device[2] ("HPV Device"), which it maintains can "be used for detection of HPV DNA in clinical samples." AR 102.[3] HPV is the name for a group of approximately 80 different strains of a virus that infect skin. JA 22. 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

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[2] 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. JA 37 n.31.

[3] Citations in the form AR refer to the administrative record filed in the district court.

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 23-25. This abnormal growth may lead to the development of cervical cancer. Id. at 24. 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 24-25, 33-34. Pap test diagnoses are not always definitive, however. Id. at 24-26. A diagnosis of "atypical squamous cells of undetermined significance" ("ASCUS") is made when 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 24-25, 33-35. 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

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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

attempt to determine whether there are cellular changes indicative of cervical disease, i.e., precancer or cancer. Id. at 24-25, 33-34. 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 an effort to detect cervical cancer in its early stages. Id. at 25.

HPV DNA tests are laboratory assays that determine whether 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 25. HPV DNA tests recognize a subset of HPV types (the high-risk types), but do not distinguish between the many different high-risk HPV types. Id. The process of genotyping, see discussion infra at 14, may be used to further identify the particular high-risk HPV types present in a specimen. Because HPV DNA tests are capable of detecting the presence of the high-risk HPV types associated with cervical cancer, their use 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 25-26. Thus, the published clinical guidelines for cervical cancer screening by medical

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abnormal appearing tissue and take directed biopsies for further examination. Id. at JA 25 n.13.

professionals, which were developed by leading medical experts working with the American Society for Colposcopy and Cervical Pathology 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 2006 Consensus Guidelines for the Management of Women with Abnormal Cervical Cancer Screening Tests ("Guidelines"), AR 363-365. The Guidelines also recommend that high-risk HPV testing should be used to extend screening intervals in women 30 years of age or older who have normal cytology and negative high-risk HPV results. See 2006 Consensus Guidelines for the Management of Women with Abnormal Cervical Cancer Screening Tests ("Guidelines"), AR 373-375. At the time of FDA's decision on HiFi's petition, the Agency had approved two in vitro HPV DNA devices for this purpose, both of which were approved as Class III devices with approved PMAs.[6] See AR 362.

Plaintiff HiFi's HPV DNA device includes Polymerase Chain Reaction ("PCR") tubes, primer reagents, buffers, agarose gel powder, ethidium bromide,

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[5] "In vitro" means "in a glass" and refers to a test performed in a laboratory, as opposed to "in vivo," which refers to tests done in 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.").

[6] More recently FDA approved a third in vitro HPV DNA device as a Class III device.

and a molecular ruler. See JA 37. These components, along with general PCR equipment and accessories, are to "be used for preparation of sample materials . . . suitable for accurate HPV genotyping." JA 7 ¶ 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 JA 25, 34 n.25.

In its reclassification petition filed with FDA, HiFi discussed at length two intended uses for its device, which were considered by FDA in evaluating HiFi's reclassification petition. See JA 21, 55; AR 112, 124; see also 21 U.S.C. § 360c(a)(2) (stating that devices are classified by FDA based upon their intended use). 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.

HiFi's first intended use arises in situations when a Pap test has resulted in an ASCUS diagnosis, i.e., when 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 JA 34. 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 JA 25, 34. 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. at 25-26.

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. JA 31. 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. JA 31, 35; AR 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. JA 35; AR 374.

II. Regulatory History of HPV DNA Devices

At the time FDA denied HiFi's petition, the Agency had approved two in vitro HPV DNA devices. JA 27-30. 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; JA 28. The second device, the ViraType Human Papillomavirus DNA Typing Kit, manufactured by Digene Corporation, obtained premarket approval from FDA on March 11, 1991.[7] JA 28-29. 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

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[7] The third device, approved in March 2009 as a Class III device, is the Cervista™ HR, which is an HPV DNA test that, like the two other approved tests, detects high-risk HPV types. At the same time, FDA approved the Cervista™ HPV 16/18, which detects the two types of HPV (types 16 and 18) that cause the majority of cervical cancers among women in the United States. The Cervista™ HPV 16/18 is the first HPV DNA genotyping test approved by FDA and is to be used adjunctively with the Cervista™ HR test, and in combination with cervical cytology, to assess the presence or absence of high-risk HPV types 16 and 18 and to guide patient management.

Hybrid Capture Test").

III. HiFi's Attempts at Reclassification

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 JA 14 ¶ 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 its 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 JA 17 ¶ 26; AR 95.

On March 8, 2007, HiFi submitted a reclassification petition under 21 U.S.C. § 360c(f)(3), in a third attempt to reclassify its HPV Device into Class II. 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. HiFi sued FDA for unreasonable delay under the APA. HiFi DNA Tech, LLC v. HHS, No. 07–1511 (D. Conn. Oct. 12, 2007). Following FDA's denial of the reclassification petition in December 2007, HiFi voluntarily

dismissed that suit.

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. JA 55-68. 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. JA 63-68. 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. JA 38-29, 45-46, 64-66. For these reasons, HiFi failed to meet its burden of proving that its HPV Device meets the requirements for reclassification.

IV. The District Court Opinion

Defendants filed a Motion to Dismiss Plaintiff's Amended Complaint pursuant to Fed. R. Civ. P. 12(b)(6) on March 25, 2008. The district court granted Defendants' Motion to Dismiss and found that "FDA's 14-page denial of HiFi's petition clearly set[s] forth the basis for the FDA's determination." JA 83. The court noted that FDA's "'memo to the record'" 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 special controls." Id. Based on this "thorough review" of the evidence submitted by HiFi, the court held that FDA's denial of HiFi's petition was "not arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." Id.

Summary of Argument

The district court properly affirmed FDA's denial of HiFi's petition to reclassify is HPV Device. FDA fully considered HiFi's scientific arguments and reasonably concluded that HiFi had not met its burden of demonstrating that the HPV Device could be regulated as a Class II device. HiFi's attempt to avoid the more stringent regulation applied to Class III devices by having its device regulated as a Class II device was rejected by FDA, and FDA's decision should be affirmed by this Court.

FDA exercised its scientific discretion in this highly technical area and reasonably determined that HiFi's Device could not be reclassified from Class III to Class II. FDA's detailed Order demonstrates that the Agency thoroughly examined all of the scientific evidence and reasonably concluded that HiFi did not provide reasonable assurance of the safety and effectiveness of the Device. HiFi's allegations that FDA "failed to understand the science" are unavailing because FDA identified numerous inadequacies in the data submitted by HiFi, each of which supports FDA's decision to deny HiFi's petition. HiFi App. Br. at 25, 28.

HiFi argues that it was improper for the district court not to have considered evidence outside of the administrative record. However, HiFi waived this argument because HiFi never asked the district court to consider evidence outside the administrative record or to allow hearing or evidence outside the record to be taken.

Even if HiFi did not waive this issue, there is no basis for HiFi to supplement the record because under the APA judicial review is normally limited to the administrative record. Neither of HiFi's two reasons why the district court should have permitted supplementation of the record are supported by the facts or the law. HiFi's bald allegations of bad faith fail completely because there is no

evidence of bad faith. HiFi's attempt to reargue the science in an effort to supplement the record also fails. There is no legal basis for supplementing the record in this case.

Argument

I. FDA Denied HiFi's Petition Based on a Thorough Examination of the Scientific Evidence and a Proper Application of the Statutory Standard

A. Standard of Review

Review of the district court's grant of judgment is reviewed de novo. Chambers v. Time Warner, Inc., 282 F. 3d 147, 152 (2d Cir. 2002).

B. APA Review

FDA's actions in this case 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). Under this 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 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 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 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); Federal Power Comm'n v. Fla. Power & Light Co., 404 U.S. 453, 463 (1972); Henley, 77 F.3d at 620-21.

Courts have accorded a high level of deference to FDA with respect to issues pertaining to the classification of devices. In Contact Lens Manufacturers. 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 General Medical Co. v. FDA, 770 F.2d 214, 217 (D.C. Cir. 1985), the court affirmed FDA's denial of plaintiff's request that its device be reclassified from Class III to Class I. The court noted the "broad discretion" given to FDA "in implementing the definition of 'substantial equivalence,'" and that "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.'" Id. at 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 [FDA], 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)).

C. FDA Reasonably Concluded that HiFi Failed to Meet its Burden to Demonstrate that its Class III Device Could be Regulated in Class II

As explained above, as a matter of law, HiFi's HPV Device is automatically

classified as a Class III device. See 21 U.S.C. § 360c(f)(1). As a Class III device, it is subject to the most stringent regulatory controls under the FDCA to provide a reasonable assurance of its safety and effectiveness. See Buckman Co. v. Plaintiffs' Legal Comm., 531 U.S. at 343. HiFi's petition to have its HPV Device reclassified from Class III into Class II asserted that the device meets the statutory requirements for the less rigorous regulatory oversight afforded devices in Class II. In its Order, FDA explained the many ways in which HiFi failed to meet its burden to provide 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." JA 58; see 21 U.S.C. § 360c(a)(1)(B); 21 C.F.R. § 860.7.

FDA's Order demonstrates that the Agency thoroughly examined all of the scientific evidence, properly applied the law, and provided a reasoned explanation for its analysis. 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. JA 57-58. As discussed below, FDA identified numerous inadequacies in the data submitted by HiFi concerning the HPV Device's basic performance characteristics, including clinical sensitivity,

clinical specificity, cross-reactivity, reproducibility, and stability of the device's reagents. JA 39-49, 63-68.

More fundamentally, FDA found that HiFi's device is intended to be used in conjunction with genotyping to confirm positive test results, but HiFi did not submit any information demonstrating that there existed an HPV genotyping test that had been validated for diagnostic use with respect to cervical cancer. JA 38-39, 45-46, 64-66. Because there was no FDA-approved HPV genotyping test for diagnostic use, HiFi was required to submit information "to establish that there exists a clinically validated, safe and effective diagnostic HPV genotyping test – meaning an HPV genotyping test validated for diagnostic use in relation to cervical cancer, as [HiFi's] intended use statement requires." JA 64-65. HiFi's petition failed to contain such information. In fact, the genotyping method that HiFi actually used in conjunction with its device was dependent on articles that are labeled by their manufacturer for "'Research Use Only – Not for Use in Diagnostic Procedures.'" JA 39. On this basis alone, FDA could have denied HiFi's petition.

FDA also determined that HiFi did not provide evidence that the HPV Device is capable of generating results that have clinical significance, i.e., a showing that the device is clinically effective. JA 67. A showing of "clinical effectiveness is a prerequisite to providing reasonable assurance of the

effectiveness of the device for its intended use." JA 67. FDA cannot reclassify a device unless it finds that there is a reasonable assurance that the device is effective for its intended use(s). See 21 U.S.C. § 360c(a)(1)(B); 21 C.F.R. § 860.7(e)(1).

A determination of clinical effectiveness is based on a device's intended use. See 21 C.F.R. § 860.7(e)(1) (stating that devices are classified by FDA based upon their intended use). In its reclassification petition, HiFi discussed the two intended uses it identified for its device, which were both considered by FDA in evaluating HiFi's petition. See JA 21, 55. HiFi intends its HPV Device to be used along with genotyping to: (1) screen patients with ASCUS (atypical squamous cells of undetermined significance) Pap test results to determine whether the patients should be referred for colposcopy; and (2) screen women 30 years and older, in conjunction with Pap testing, to guide patient management decisions. Id. After careful analysis, FDA concluded that the intended uses for the HPV Device relate to the identification of a patient's HPV-infection status "to assess a woman's risk of developing cervical cancer where some risk is already suggested." JA 60; see JA 31-36, 60-62.

With respect to the first intended use of HiFi's device, FDA found that the HPV Device is intended to help physicians decide whether: (a) to have a patient

undergo colposcopy – an invasive procedure that could lead to biopsy to assess whether observed cervical abnormalities are precancerous or cancerous; or (b) to advise a patient to wait to be screened again later. JA 61. Regarding the second intended use, FDA found that the HPV Device is intended to guide physicians in making decisions for patients 30 years and older on the frequency and scope of the patient's screening for cervical abnormalities and possible malignancies. JA 61. In light of the device's intended uses, FDA determined that, to demonstrate clinical effectiveness, HiFi must provide data on the proportion of women with cervical precancer/cancer who have a positive test with the HPV Device ("clinical sensitivity") and the proportion of women without cervical precancer/cancer who test negative with the HPV Device ("clinical specificity"). JA 67.

FDA's Order explained that HiFi's purported clinical sensitivity study did not include information on the "cervical pathologic conditions of the study subjects." JA 64. As FDA described, without knowing whether the women were "positive or negative for cervical precancer or cancer," clinical sensitivity (also known as the true positive rate) could not be assessed. JA 64. The lack of data on cervical pathologic conditions also precluded an assessment of the rate of false negative test results – the proportion of individuals who in fact have cervical precancer/cancer, but who test negative with the HPV Device. JA 64. FDA

found that not having the false negative rate was "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." JA 64. As with clinical sensitivity, clinical specificity (also known as the true negative rate) cannot be assessed without knowing whether the women in the study are positive or negative for cervical precancer/cancer. JA 64. Because HiFi's petition did not reveal either the clinical sensitivity or clinical specificity of the device, FDA stated that it "cannot conclude that there is a reasonable assurance of the safety and effectiveness of the device for its intended use." JA 64.

Regarding another basic performance characteristic, cross-reactivity, FDA found that HiFi failed to establish, and indeed did not even conduct studies to assess, the cross-reactivity of its device. JA 63. 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. JA 63. Without such studies, the accuracy and reliability of the HPV Device cannot be ascertained. JA 63. FDA's Order fully addressed several other deficiencies in HiFi's petition and, as the administrative record demonstrates, FDA made reasoned determinations on each issue. See JA 63-68

D. HiFi's Arguments Do Not Establish that FDA's Denial of its Petition was Arbitrary and Capricious

In its opening brief on appeal, HiFi raises a series of challenges to FDA's denial of its petition. HiFi disputes FDA's scientific evaluation, claiming that the Agency "ignores the evidence presented as to safety and efficacy" of the HPV Device and "misapplies the standards regarding classification of devices." HiFi App. Br. at 22. Although HiFi seeks to have this Court second-guess FDA's judgment in determining the controls necessary for ensuring a device's safety and effectiveness, Congress has entrusted these regulatory judgments to FDA. FDA has particular scientific expertise, and has been given considerable deference, in the area of safety and effectiveness decisions regarding medical devices. See Ethicon, 762 F. Supp. at 386. HiFi has not shown (and is unable to show) that the Agency was arbitrary and capricious in reaching its conclusions.

1. HiFi's focus on polymerase chain reaction ("PCR") technology misunderstands the basis of FDA's decision

Although FDA determined that it could not reclassify the HPV Device in part because of the device's reliance on HPV genotyping, HiFi opines – under the Daubert standard – on the "efficacy and acceptance" of the PCR technology used in the HPV Device. HiFi App. Br. 23-24. Aside from the fact that PCR's admissibility in court based on Daubert has no bearing on the appropriate

regulatory controls for HiFi's device, the methodology of PCR technology is not at issue here. Nowhere in the administrative record does FDA state that it denied HiFi's reclassification petition because the HPV Device uses PCR technology. Therefore, HiFi's argument regarding PCR technology is a "straw man" and irrelevant.

2. HiFi cannot bypass the requirement of clinical effectiveness by minimizing the intended uses of its device

One of HiFi's principal arguments is that FDA "evaluated the device as a cancer test instead of a test for a virus" and, in so doing, the Agency incorrectly required evidence of the device's clinical effectiveness. HiFi App. Br. at 17. In making this argument, HiFi fails to acknowledge its own statements on the device's intended uses. See supra at 14. As evident in the record, FDA considered the fact that the HPV Device is not intended as a stand-alone diagnostic assay. See JA 35, 59. FDA found that, even though the device is intended to be used in conjunction with other tests, HiFi's stated intended uses make clear that the HPV Device is "associated with cancer screening and assessment of risk." JA 35. Specifically, FDA found that the device is "intended to inform the determination of risk" of cervical cancer, and is "intended to inform a critical threshold determination concerning patient management." JA 35; see JA

59-60. Based on these findings, FDA reasonably determined that HiFi must show the clinical effectiveness, including assessments of clinical sensitivity/specificity, of the HPV Device, and that HiFi failed to do so.

3. HiFi cannot rely on the use of an unapproved HPV genotyping procedure with its device to generate clinically effective results, and the device, on its own, is incapable of producing such results

For the reason repeatedly noted, HiFi's reliance on HPV genotyping cannot serve to establish the clinical effectiveness of the HPV Device. JA 39, 45, 64-66. According to HiFi, the HPV Device by itself, without the genotyping step, provides a "preliminary identification of HPV," by "amplify[ing] DNA that is presumptively HPV." HiFi App. Br. at 25, 28. HiFi acknowledges that the HPV Device does not distinguish between high-risk and low-risk types of HPV (id. at 11), which means that the device cannot independently produce results that have clinical significance.

When it reviewed HiFi's reclassification petition, FDA determined that, to the extent that the HPV Device was detecting numerous low-risk types of HPV, which are not associated with precancer or cancer, the HPV Device would be "analytically too sensitive to be clinically useful, resulting in false positive results that may lead many women to unnecessarily undergo further uncomfortable

screening and potentially invasive procedures such as colposcopy and biopsy." JA 48; see id. at 62 n.9 (according to published clinical guidelines – which were referenced in HiFi's intended use statement – for cervical cancer screening by medical professionals, "'[t]esting for low-risk (nononcogenic) HPV types has no role in the evaluation of women with abnormal cervical cytological results'"). By indiscriminately detecting both types (high- and low-risk) of HPV, the HPV Device does not provide results that have clinical significance for its intended uses. See JA 47-48 (noting that the "majority of HPV infections are clinically insignificant"). Therefore, HiFi's device could not meet the required showing of effectiveness.

4. Hi-Fi's comparison study does not demonstrate that its device is clinically effective

According to HiFi, its HPV Device is reliable because it produces results that are more accurate than results generated by the FDA-approved Digene HC2 device. HiFi App. Br. at 11-12, 26-27. Among the problems with HiFi's analysis is that HiFi did not, in fact, compare the "HPV Device" with the "Digene HC2." Rather, as HiFi concedes, it compared the Digene HC2 against the HPV Device "used together with DNA sequencing," which is not part of HiFi's device. Id. at 11. In addition, HiFi incorrectly positions its HPV Device as the reference test.

Because no independent verification of HiFi's results is possible without the data that HiFi failed to provide to FDA, and because the clinical performance of the approved Digene HC2 has been successfully established, the Digene HC2 must be treated as the reference in a comparison study. There is no scientific basis for HiFi to insist that the HPV Device's positive test results are correct and the negative results of the Digene HC2 are incorrect.

Moreover, even if HiFi's statement regarding the comparative accuracy of the HPV Device were true (which it is not), it would not establish whether HiFi's device is clinically effective because the clinical data needed to make such a determination – the cervical pathologic conditions of the patients providing the samples tested – were not available. JA 40. Finally, the Digene HC2 is approved by FDA as a Class III device; therefore, it does not follow that HiFi's comparison could support its request to lower the HPV Device's classification to Class II.

5. HiFi's remaining arguments are unavailing

HiFi's contention that "[c]ross reactivity does not exist in genotyping" overlooks the potential for cross-reactivity to interfere with the performance of the HPV Device. There are factors that could affect the ability of the HPV Device to detect HPV infections. As FDA explained, cross-reactivity may occur with "microorganisms other than the HPV strains targeted by the assay." JA 42 n.37.

And, as HiFi admits, "there is a chance that some other types of DNA may be amplified" by the HPV Device. HiFi App. Br. at 28. Nevertheless, HiFi failed to perform any studies to evaluate the potential impact of cross-reactivity on the HPV Device's performance.

HiFi also contends that FDA has subjected other devices to less burdensome regulatory oversight as Class I and II devices, and that this inconsistency militates in favor of reclassifying its HPV Device. HiFi App. Br. at 16. One of the devices HiFi identifies, a test for detecting the bacterium Helicobacter pylori ("H. pylori") in the stomach, was cited by HiFi in its reclassification petition. Id. at 16, 18; see JA 51. 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. JA 51 ("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. . . .").

Finally, HiFi asserts that FDA used the word "probe" rather than "primer" in describing one of the many inadequacies in the reclassification petition and, therefore, that "portion of the denial . . . is erroneous." HiFi App. Br. at 16. Based on definitions of "probe" and "primer" located on internet sites, HiFi stresses that a probe identifies, whereas a primer replicates, DNA. Id. at 20. The distinction is without a difference here. First, HiFi appears to be concerned that the choice of words indicates the Agency was unaware that the HPV Device uses PCR technology. See HiFi App. Br. at 16. This concern is unjustified – it was readily apparent to FDA that HiFi's device is based on PCR technology. See, e.g., JA 50 (containing FDAss explanation that the HPV detection method used by the HPV Device is "PCR amplification"). Moreover, the semantic argument cannot cure the two fundamental flaws in HiFi's petition: (1) the lack of data to demonstrate the clinical effectiveness of HiFi's device; and (2) the reliance on an unapproved HPV genotyping test to confirm positive results.

E. FDA's Determination that HiFi Did Not Provide Adequate, Valid Scientific Evidence to Support the Reclassification of its Device is Entitled to Deference and Should be Upheld

HiFi's attempt to avoid the more stringent regulation applied to Class III devices by having its device regulated as a Class II device was rejected by FDA. Complex scientific judgments such as these, regarding the quantity 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. 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. This Court should uphold FDA's reasonable scientific judgment that HiFi failed to present sufficient data to support reclassification of the HPV Device.

II. There is No Basis for Considering Evidence Outside of the Administrative Record

A. Standard of Review

A district court's determination of a request to consider evidence outside the administrative record is reviewed under an abuse of discretion standard. Nat'l Audubon Soc. v. Hoffman, 132 F.3d 7, 16 (2d Cir. 1997).

B. HiFi Waived its Argument that the Administrative Record Should Have Been Supplemented by the District Court

HiFi now claims that the district court should have "allowed some hearing and evidence outside the record to be taken." HiFi App. Br. at 14. However, HiFi did not make a request to the district court to have a hearing or supplement the administrative record. The only conceivable claim that HiFi could make that it raised this issue below is that HiFi attached an Exhibit to its response to Defendant's Motion to Dismiss that contained extra-record evidence. See Pl.'s Resp. to Mot. to Dismiss, Ex. A. However, HiFi did not make any argument to the district court regarding this Exhibit. Id. In an abundance of caution, Defendants responded to HiFi's Exhibit and argued that consideration of the evidence was improper, because under the APA, judicial review is limited to the administrative record that was before the agency. Defs.'s Reply at 1, n.1. The district court did not receive any request from HiFi to consider the Exhibit and made no ruling on

whether it considered the supplemental Exhibit. JA 72-83. Having never raised this argument in the district court, the argument is waived. "It is a well-established general rule that an appellate court will not consider an issue raised for the first time on appeal." Allianz Ins. Co. v. Lerner, 416 F.3d 109, 114 (2d Cir. 2005) (internal quotation marks and citations omitted). See also Coon ex rel. Coon v. Willet Dairy, 536 F.3d 171, 172 (2d Cir. 2008) (failure to properly raise claim before district court waived on appeal); Anthony v. City of New York, 339 F.3d 129, 136 n.3 (2d Cir. 2003).

C. HiFi Has Demonstrated No Circumstances Supporting Supplementation of the Record

Even if HiFi did not waive the issue, it cannot supplement the administrative record. "Generally, a court reviewing an agency decision is confined to the administrative record compiled by that agency when it made the decision." Nat'l Audubon Soc'y, 132 F.3d at 14 (citing Fla. Power & Light Co. v. Lorion, 470 U.S. 729, 743-44 (1985)). "[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).

HiFi alleges two bases for supplementing the administrative record. First, HiFi makes unsupported allegations of bad faith. HiFi App. Br. at 14. ("[F]acts outside the administrative record were necessary . . . to evaluate the apparent improper behavior on the part of the agency decision makers."). "FDA has shown an unwillingness to deal fairly with Plaintiff," according to HiFi, because the Agency: (a) did not rule on HiFi's initial petition for reevaluation of Class III status; (b) delayed in ruling on the petition it eventually denied; (c) did not "allow any comment by or ask any questions of Plaintiff during the petition process"; and (d) "focus[ed] on cancer." Id. at 21-22. None of these allegations of bad faith has merit.

To supplement an administrative record based on "bad faith" claims, plaintiffs must make "a strong showing of bad faith or improper behavior." Citizens to Preserve Overton Park v. Volpe, 401 U.S. at 420. See also Nat'l Nutritional Foods Ass'n. v. FDA, 491 F.2d 1141, 1145 (2d Cir. 1974), cert. denied, 419 U.S. 874 (1974); Sierra Club v. Robertson, 784 F.Supp. 593, 601 (W.D. Ark. 1991). Supplementation of the record on this basis is not warranted because HiFi has made no showing of bad faith or improper behavior on the part of FDA.

First, FDA did not rule on HiFi's initial petition seeking an evaluation of the

automatic Class III designation, called "de novo reclassification," because the Agency found that HiFi's device does not meet the criteria for this method of review. See 21 U.S.C. § 360c(f)(2)(A) (stating that only devices of a type not previously classified under the statute may be reclassified under the de novo reclassification provision); AR 20 (finding that HiFi's device is of the same type of device as a previously classified HPV DNA device). But even if FDA were to have conducted a review of HiFi's initial petition for de novo reclassification, it would have made no difference in the outcome. HiFi's device is required to meet the *same* risk-based classification criteria that FDA found the device failed to meet in reviewing the reclassification petition that was subsequently submitted. Either way, therefore, HiFi's device is considered a Class III device. See 21 U.S.C. § 360c(f)(2)(A) (containing, in the de novo reclassification provision, a cross-reference to the established criteria for regulating the three classes of devices).

Second, the short delay in ruling on HiFi's reclassification petition was the result of a clerical error in assigning an official date of receipt to the petition. JA 31 n.17. 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 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, 280 days after the petition was filed. AR 494.

The one case HiFi cites to show that the delay here is evidence of bad faith is easily distinguishable. In Tummino v. Torti, 603 F. Supp. 2d 519, 544 (E.D.N.Y. 2009), the court identified several issues, such as a five-year response time and significant departures from typical agency procedures, that contributed to its determination of bad faith. In comparison, a delay of less than three months in HiFi's situation, particularly for the reason explained, provides no support for a finding of bad faith. Cf. HiFi DNA Tech, LLC v. HHS, No. 07–1511 (D. Conn. Oct. 12, 2007) (upon FDA's December 2007 ruling on HiFi's reclassification petition, HiFi voluntarily dismissed its suit against FDA for unreasonable delay under the APA).

Third, although HiFi alleges unfairness because FDA did not "allow any comment by or ask any questions of Plaintiff during the petition process," it does not cite to any authority for the assertion that it was entitled to make comments, or to receive questions, while FDA was reviewing its petition. Nor can it do so. It

was HiFi's burden to provide 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." JA 58; see 21 U.S.C. § 360c(a)(1)(B); 21 C.F.R. § 860.7. Because HiFi did not provide sufficient information to meet that burden, FDA denied the petition. HiFi's failure in this regard does not create obligations for FDA or require FDA to undertake procedures that are not required by law or regulations. See Vermont Yankee Nuclear Power Corp., v. NRDC, Inc., 435 U.S. 519, 544 (1978) ("agencies should be free to fashion their own rules of procedure.").

Fourth and finally, HiFi's assertion that FDA's "focus on cancer" is evidence of improper behavior is simply a re-casting of its challenge to FDA's scientific determination, an issue that is fully addressed above.

HiFi also alleges that extra-record evidence is necessary to clarify the scientific issues. Specifically, HiFi states that "facts outside the administrative record were necessary to review the agency's decision to explain and clarify the technical matter involved in the agency action." HiFi App. Br. at 14. It appears that HiFi is arguing that, because "FDA's denial of its petition was arbitrary and capricious" and "the product of misapplied science," it should be allowed to supplement the record. HiFi App. Br. at 15. HiFi fundamentally misunderstands

legal principles underlying record review and cites no cases to support its assertion that the record should be supplemented for the reasons it advances. In limited cases, supplementation of the record "may be necessary when the record does not support the agency action, when the agency has not considered all relevant factors, or when the reviewing court simply cannot evaluate the challenged action on the basis of the record before it." Nat'l Audubon Soc'y, 132 F.3d at 14 (citing Fla. Power, 470 U.S. at 743-44). None of these circumstances exists here. In the present case, the record more than adequately supports FDA's action. HiFi has attempted to reargue the science as a basis for supplementing the record, but the record fully supports FDA's action. There is no basis for a finding that FDA has not considered all the relevant factors. HiFi disagrees with FDA's scientific determinations, but this disagreement is not a basis for one of the very rare instances in which record supplementation is appropriate. For these reasons, HiFi's claims that the district court erred in not considering evidence outside the administrative record must fail.

Conclusion

For the foregoing reasons, the district court's decision should be affirmed.

Respectfully submitted,

TONY WEST
Assistant Attorney General

ANN M. RAVEL
Deputy Assistant Attorney General

EUGENE M. THIROLF
Director

LAUREN H. BELL
DRAKE CUTINI
Attorneys, Office of
Consumer Litigation
U.S. Department of Justice
P.O. Box 386
Washington, D.C. 20044
202-353-1991
lauren.hash.bell@usdoj.gov

Of Counsel:

DAVID CADE
Acting General Counsel

MICHAEL M. LANDA
Acting Associate General Counsel
Food and Drug Division

ERIC M. BLUMBERG
Deputy Chief Counsel, Litigation

CLAUDIA J. ZUCKERMAN
Associate Chief Counsel
Food and Drug Division
U.S. Dep't of Health and Human
Services
Office of General Counsel
5600 Fishers Lane
Rockville, MD 20857
301-827-3676

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STATUTORY ADDENDUM

STATUTORY ADDENDUM

Effective:[See Text Amendments]

United States Code Annotated Currentness
Title 5. Government Organization and Employees (Refs & Annos)
Part I. The Agencies Generally
Chapter 7. Judicial Review (Refs & Annos)
§ 706. Scope of review

To the extent necessary to decision and when presented, the reviewing court shall decide all relevant questions of law, interpret constitutional and statutory provisions, and determine the meaning or applicability of the terms of an agency action. The reviewing court shall--

(1) compel agency action unlawfully withheld or unreasonably delayed; and

(2) hold unlawful and set aside agency action, findings, and conclusions found to be--

(A) arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law;

(B) contrary to constitutional right, power, privilege, or immunity;

(C) in excess of statutory jurisdiction, authority, or limitations, or short of statutory right;

(D) without observance of procedure required by law;

(E) unsupported by substantial evidence in a case subject to sections 556 and 557 of this title or otherwise reviewed on the record of an agency hearing provided by statute; or

(F) unwarranted by the facts to the extent that the facts are subject to trial de novo by the reviewing court.

In making the foregoing determinations, the court shall review the whole record or those parts of it cited by a party, and due account shall be taken of the rule of prejudicial error.

CREDIT(S)

(Pub.L. 89-554, Sept. 6, 1966, 80 Stat. 393.)

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END OF DOCUMENT

Effective: October 26, 2002

United States Code Annotated Currentness
Title 21. Food and Drugs (Refs & Annos)
Chapter 9. Federal Food, Drug, and Cosmetic Act (Refs & Annos)
Subchapter V. Drugs and Devices
Part A. Drugs and Devices (Refs & Annos)
§ 360c. Classification of devices intended for human use

(a) Classes of devices

(1) There are established the following classes of devices intended for human use:

(A) Class I, General Controls.--

(i) A device for which the controls authorized by or under section 351, 352, 360, 360f, 360h, 360i, or 360j of this title or any combination of such sections are sufficient to provide reasonable assurance of the safety and effectiveness of the device.

(ii) A device for which insufficient information exists to determine that the controls referred to in clause (i) are sufficient to provide reasonable assurance of the safety and effectiveness of the device or to establish special controls to provide such assurance, but because it--

(I) is not 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, and

(II) does not present a potential unreasonable risk of illness or injury,

is to be regulated by the controls referred to in clause (i).

(B) Class II, Special Controls.--

A device which cannot be classified as a class I device because the general controls by themselves are insufficient to provide reasonable assurance of the safety and effectiveness of the device, and for which there is sufficient information to establish special controls to provide such assurance, including the promulgation of performance standards, postmarket surveillance, patient registries, development and dissemination of guidelines (including guidelines for the submission of clinical data in premarket notification submissions in accordance with section 360(k) of this title), recommendations, and other appropriate actions as the Secretary deems ne-

cessary to provide such assurance. For a device that is purported or represented to be for a use in supporting or sustaining human life, the Secretary shall examine and identify the special controls, if any, that are necessary to provide adequate assurance of safety and effectiveness and describe how such controls provide such assurance.

(C) Class III, Premarket Approval.--

A device which because--

(i) it (I) cannot be classified as a class I device because insufficient information exists to determine that the application of general controls are sufficient to provide reasonable assurance of the safety and effectiveness of the device, and (II) cannot be classified as a class II device because insufficient information exists to determine that the special controls described in subparagraph (B) would provide reasonable assurance of its safety and effectiveness, and

(ii)(I) is 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

(II) presents a potential unreasonable risk of illness or injury,

is to be subject, in accordance with section 360e of this title, to premarket approval to provide reasonable assurance of its safety and effectiveness.

If there is not sufficient information to establish a performance standard for a device to provide reasonable assurance of its safety and effectiveness, the Secretary may conduct such activities as may be necessary to develop or obtain such information.

(2) For purposes of this section and sections 360d and 360e of this title, the safety and effectiveness of a device are to be determined--

(A) with respect to the persons for whose use the device is represented or intended,

(B) with respect to the conditions of use prescribed, recommended, or suggested in the labeling of the device, and

(C) weighing any probable benefit to health from the use of the device against any probable risk of injury or illness from such use.

(3)(A) Except as authorized by subparagraph (B), the effectiveness of a device is, for purposes of this section and sections 360d and 360e of this title, to be determined, in accordance with regulations promulgated by the

Secretary, on the basis of well-controlled investigations, including 1 or more clinical investigations where appropriate, by experts qualified by training and experience to evaluate the effectiveness of the device, from which investigations it can fairly and responsibly be concluded by qualified experts that the device will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling of the device.

(B) If the Secretary determines that there exists valid scientific evidence (other than evidence derived from investigations described in subparagraph (A))--

(i) which is sufficient to determine the effectiveness of a device, and

(ii) from which it can fairly and responsibly be concluded by qualified experts that the device will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling of the device,

then, for purposes of this section and sections 360d and 360e of this title, the Secretary may authorize the effectiveness of the device to be determined on the basis of such evidence.

(C) In making a determination of a reasonable assurance of the effectiveness of a device for which an application under section 360e of this title has been submitted, the Secretary shall consider whether the extent of data that otherwise would be required for approval of the application with respect to effectiveness can be reduced through reliance on postmarket controls.

(D)(i) The Secretary, upon the written request of any person intending to submit an application under section 360e of this title, shall meet with such person to determine the type of valid scientific evidence (within the meaning of subparagraphs (A) and (B)) that will be necessary to demonstrate for purposes of approval of an application the effectiveness of a device for the conditions of use proposed by such person. The written request shall include a detailed description of the device, a detailed description of the proposed conditions of use of the device, a proposed plan for determining whether there is a reasonable assurance of effectiveness, and, if available, information regarding the expected performance from the device. Within 30 days after such meeting, the Secretary shall specify in writing the type of valid scientific evidence that will provide a reasonable assurance that a device is effective under the conditions of use proposed by such person.

(ii) Any clinical data, including one or more well-controlled investigations, specified in writing by the Secretary for demonstrating a reasonable assurance of device effectiveness shall be specified as result of a determination by the Secretary that such data are necessary to establish device effectiveness. The Secretary shall consider, in consultation with the applicant, the least burdensome appropriate means of evaluating device effectiveness that would have a reasonable likelihood of resulting in approval.

(iii) The determination of the Secretary with respect to the specification of valid scientific evidence under clauses (i) and (ii) shall be binding upon the Secretary, unless such determination by the Secretary could be con-

trary to the public health.

(b) Classification panels

(1) For purposes of--

(A) determining which devices intended for human use should be subject to the requirements of general controls, performance standards, or premarket approval, and

(B) providing notice to the manufacturers and importers of such devices to enable them to prepare for the application of such requirements to devices manufactured or imported by them,

the Secretary shall classify all such devices (other than devices classified by subsection (f) of this section) into the classes established by subsection (a) of this section. For the purpose of securing recommendations with respect to the classification of devices, the Secretary shall establish panels of experts or use panels of experts established before May 28, 1976, or both. Section 14 of the Federal Advisory Committee Act shall not apply to the duration of a panel established under this paragraph.

(2) The Secretary shall appoint to each panel established under paragraph (1) persons who are qualified by training and experience to evaluate the safety and effectiveness of the devices to be referred to the panel and who, to the extent feasible, possess skill in the use of, or experience in the development, manufacture, or utilization of, such devices. The Secretary shall make appointments to each panel so that each panel shall consist of members with adequately diversified expertise in such fields as clinical and administrative medicine, engineering, biological and physical sciences, and other related professions. In addition, each panel shall include as nonvoting members a representative of consumer interests and a representative of interests of the device manufacturing industry. Scientific, trade, and consumer organizations shall be afforded an opportunity to nominate individuals for appointment to the panels. No individual who is in the regular full-time employ of the United States and engaged in the administration of this chapter may be a member of any panel. The Secretary shall designate one of the members of each panel to serve as chairman thereof.

(3) Panel members (other than officers or employees of the United States), while attending meetings or conferences of a panel or otherwise engaged in its business, shall be entitled to receive compensation at rates to be fixed by the Secretary, but not at rates exceeding the daily equivalent of the rate in effect for grade GS-18 of the General Schedule, for each day so engaged, including traveltime; and while so serving away from their homes or regular places of business each member may be allowed travel expenses (including per diem in lieu of subsistence) as authorized by section 5703 of Title 5, for persons in the Government service employed intermittently.

(4) The Secretary shall furnish each panel with adequate clerical and other necessary assistance.

(5) Classification panels covering each type of device shall be scheduled to meet at such times as may be appropriate for the Secretary to meet applicable statutory deadlines.

(6)(A) Any person whose device is specifically the subject of review by a classification panel shall have--

(i) the same access to data and information submitted to a classification panel (except for data and information that are not available for public disclosure under section 552 of Title 5) as the Secretary;

(ii) the opportunity to submit, for review by a classification panel, information that is based on the data or information provided in the application submitted under section 360e of this title by the person, which information shall be submitted to the Secretary for prompt transmittal to the classification panel; and

(iii) the same opportunity as the Secretary to participate in meetings of the panel.

(B) Any meetings of a classification panel shall provide adequate time for initial presentations and for response to any differing views by persons whose devices are specifically the subject of a classification panel review, and shall encourage free and open participation by all interested persons.

(7) After receiving from a classification panel the conclusions and recommendations of the panel on a matter that the panel has reviewed, the Secretary shall review the conclusions and recommendations, shall make a final decision on the matter in accordance with section 360e(d)(2) of this title, and shall notify the affected persons of the decision in writing and, if the decision differs from the conclusions and recommendations of the panel, shall include the reasons for the difference.

(8) A classification panel under this subsection shall not be subject to the annual chartering and annual report requirements of the Federal Advisory Committee Act.

(c) Classification panel organization and operation

(1) The Secretary shall organize the panels according to the various fields of clinical medicine and fundamental sciences in which devices intended for human use are used. The Secretary shall refer a device to be classified under this section to an appropriate panel established or authorized to be used under subsection (b) of this section for its review and for its recommendation respecting the classification of the device. The Secretary shall by regulation prescribe the procedure to be followed by the panels in making their reviews and recommendations. In making their reviews of devices, the panels, to the maximum extent practicable, shall provide an opportunity for interested persons to submit data and views on the classification of the devices.

(2)(A) Upon completion of a panel's review of a device referred to it under paragraph (1), the panel shall, subject to subparagraphs (B) and (C), submit to the Secretary its recommendation for the classification of the device. Any such recommendation shall (i) contain (I) a summary of the reasons for the recommendation, (II) a summary of the data upon which the recommendation is based, and (III) an identification of the risks to health (if any) presented by the device with respect to which the recommendation is made, and (ii) to the extent practicable, include a recommendation for the assignment of a priority for the application of the requirements of section 360d or 360e of this title to a device recommended to be classified in class II or class III.

(B) A recommendation of a panel for the classification of a device in class I shall include a recommendation as to whether the device should be exempted from the requirements of section 360, 360i, or 360j(f) of this title.

(C) In the case of a device which has been referred under paragraph (1) to a panel, and which--

(i) is intended to be implanted in the human body or is purported or represented to be for a use in supporting or sustaining human life, and

(ii)(I) has been introduced or delivered for introduction into interstate commerce for commercial distribution before May 28, 1976, or

(II) is within a type of device which was so introduced or delivered before such date and is substantially equivalent to another device within that type,

such panel shall recommend to the Secretary that the device be classified in class III unless the panel determines that classification of the device in such class is not necessary to provide reasonable assurance of its safety and effectiveness. If a panel does not recommend that such a device be classified in class III, it shall in its recommendation to the Secretary for the classification of the device set forth the reasons for not recommending classification of the device in such class.

(3) The panels shall submit to the Secretary within one year of the date funds are first appropriated for the implementation of this section their recommendations respecting all devices of a type introduced or delivered for introduction into interstate commerce for commercial distribution before May 28, 1976.

(d) Panel recommendation; publication; priorities

(1) Upon receipt of a recommendation from a panel respecting a device, the Secretary shall publish in the Federal Register the panel's recommendation and a proposed regulation classifying such device and shall provide interested persons an opportunity to submit comments on such recommendation and the proposed regulation. After reviewing such comments, the Secretary shall, subject to paragraph (2), by regulation classify such device.

(2)(A) A regulation under paragraph (1) classifying a device in class I shall prescribe which, if any, of the requirements of section 360, 360i, or 360j(f) of this title shall not apply to the device. A regulation which makes a requirement of section 360, 360i, or 360j(f) of this title inapplicable to a device shall be accompanied by a statement of the reasons of the Secretary for making such requirement inapplicable.

(B) A device described in subsection (c)(2)(C) of this section shall be classified in class III unless the Secretary determines that classification of the device in such class is not necessary to provide reasonable assurance of its safety and effectiveness. A proposed regulation under paragraph (1) classifying such a device in a class other than class III shall be accompanied by a full statement of the reasons of the Secretary (and supporting documentation and data) for not classifying such device in such class and an identification of the risks to health (if any)

presented by such device.

(3) In the case of devices classified in class II and devices classified under this subsection in class III and described in section 360e(b)(1) of this title the Secretary may establish priorities which, in his discretion, shall be used in applying sections 360d and 360e of this title, as appropriate, to such devices.

(e) Classification changes

(1) Based on new information respecting a device, the Secretary may, upon his own initiative or upon petition of an interested person, by regulation (A) change such device's classification, and (B) revoke, because of the change in classification, any regulation or requirement in effect under section 360d or 360e of this title with respect to such device. In the promulgation of such a regulation respecting a device's classification, the Secretary may secure from the panel to which the device was last referred pursuant to subsection (c) of this section a recommendation respecting the proposed change in the device's classification and shall publish in the Federal Register any recommendation submitted to the Secretary by the panel respecting such change. A regulation under this subsection changing the classification of a device from class III to class II may provide that such classification shall not take effect until the effective date of a performance standard established under section 360d of this title for such device.

(2) By regulation promulgated under paragraph (1), the Secretary may change the classification of a device from class III--

(A) to class II if the Secretary determines that special controls would provide reasonable assurance of the safety and effectiveness of the device and that general controls would not provide reasonable assurance of the safety and effectiveness of the device, or

(B) to class I if the Secretary determines that general controls would provide reasonable assurance of the safety and effectiveness of the device.

(f) Initial classification and reclassification of certain devices

(1) Any device intended for human use which was not introduced or delivered for introduction into interstate commerce for commercial distribution before May 28, 1976, is classified in class III unless--

(A) the device--

(i) is within a type of device (I) which was introduced or delivered for introduction into interstate commerce for commercial distribution before such date and which is to be classified pursuant to subsection (b) of this section, or (II) which was not so introduced or delivered before such date and has been classified in class I or II, and

(ii) is substantially equivalent to another device within such type, or

(B) the Secretary in response to a petition submitted under paragraph (3) has classified such device in class I or II.

A device classified in class III under this paragraph shall be classified in that class until the effective date of an order of the Secretary under paragraph (2) or (3) classifying the device in class I or II.

(2)(A) Any person who submits a report under section 360(k) of this title for a type of device that has not been previously classified under this chapter, and that is classified into class III under paragraph (1), may request, within 30 days after receiving written notice of such a classification, the Secretary to classify the device under the criteria set forth in subparagraphs (A) through (C) of subsection (a)(1) of this section. The person may, in the request, recommend to the Secretary a classification for the device. Any such request shall describe the device and provide detailed information and reasons for the recommended classification.

(B)(i) Not later than 60 days after the date of the submission of the request under subparagraph (A), the Secretary shall by written order classify the device involved. Such classification shall be the initial classification of the device for purposes of paragraph (1) and any device classified under this paragraph shall be a predicate device for determining substantial equivalence under paragraph (1).

(ii) A device that remains in class III under this subparagraph shall be deemed to be adulterated within the meaning of section 351(f)(1)(B) of this title until approved under section 360e of this title or exempted from such approval under section 360j(g) of this title.

(C) Within 30 days after the issuance of an order classifying a device under this paragraph, the Secretary shall publish a notice in the Federal Register announcing such classification.

(3)(A) The Secretary may initiate the reclassification of a device classified into class III under paragraph (1) of this subsection or the manufacturer or importer of a device classified under paragraph (1) may petition the Secretary (in such form and manner as he shall prescribe) for the issuance of an order classifying the device in class I or class II. Within thirty days of the filing of such a petition, the Secretary shall notify the petitioner of any deficiencies in the petition which prevent the Secretary from making a decision on the petition.

(B)(i) Upon determining that a petition does not contain any deficiency which prevents the Secretary from making a decision on the petition, the Secretary may for good cause shown refer the petition to an appropriate panel established or authorized to be used under subsection (b) of this section. A panel to which such a petition has been referred shall not later than ninety days after the referral of the petition make a recommendation to the Secretary respecting approval or denial of the petition. Any such recommendation shall contain (I) a summary of the reasons for the recommendation, (II) a summary of the data upon which the recommendation is based, and (III) an identification of the risks to health (if any) presented by the device with respect to which the petition was filed. In the case of a petition for a device which is intended to be implanted in the human body or which is pur-

ported or represented to be for a use in supporting or sustaining human life, the panel shall recommend that the petition be denied unless the panel determines that the classification in class III of the device is not necessary to provide reasonable assurance of its safety and effectiveness. If the panel recommends that such petition be approved, it shall in its recommendation to the Secretary set forth its reasons for such recommendation.

(ii) The requirements of paragraphs (1) and (2) of subsection (c) of this section (relating to opportunities for submission of data and views and recommendations respecting priorities and exemptions from sections 360, 360i, and 360j(f) of this title) shall apply with respect to consideration by panels of petitions submitted under subparagraph (A).

(C)(i) Within ninety days from the date the Secretary receives the recommendation of a panel respecting a petition (but not later than 210 days after the filing of such petition) the Secretary shall by order deny or approve the petition. If the Secretary approves the petition, the Secretary shall order the classification of the device into class I or class II in accordance with the criteria prescribed by subsection (a)(1)(A) or (a)(1)(B) of this section. In the case of a petition for a device which is intended to be implanted in the human body or which is purported or represented to be for a use in supporting or sustaining human life, the Secretary shall deny the petition unless the Secretary determines that the classification in class III of the device is not necessary to provide reasonable assurance of its safety and effectiveness. An order approving such petition shall be accompanied by a full statement of the reasons of the Secretary (and supporting documentation and data) for approving the petition and an identification of the risks to health (if any) presented by the device to which such order applies.

(ii) The requirements of paragraphs (1) and (2)(A) of subsection (d) of this section (relating to publication of recommendations, opportunity for submission of comments, and exemption from sections 360, 360i, and 360j(f) of this title) shall apply with respect to action by the Secretary on petitions submitted under subparagraph (A).

(4) If a manufacturer reports to the Secretary under section 360(k) of this title that a device is substantially equivalent to another device--

(A) which the Secretary has classified as a class III device under subsection (b) of this section,

(B) which was introduced or delivered for introduction into interstate commerce for commercial distribution before December 1, 1990, and

(C) for which no final regulation requiring premarket approval has been promulgated under section 360e(b) of this title,

the manufacturer shall certify to the Secretary that the manufacturer has conducted a reasonable search of all information known or otherwise available to the manufacturer respecting such other device and has included in the report under section 360(k) of this title a summary of and a citation to all adverse safety and effectiveness data respecting such other device and respecting the device for which the section 360(k) report is being made and which has not been submitted to the Secretary under section 360i of this title. The Secretary may require the

manufacturer to submit the adverse safety and effectiveness data described in the report.

(5) The Secretary may not withhold a determination of the initial classification of a device under paragraph (1) because of a failure to comply with any provision of this chapter unrelated to a substantial equivalence decision, including a finding that the facility in which the device is manufactured is not in compliance with good manufacturing requirements as set forth in regulations of the Secretary under section 360j(f) of this title (other than a finding that there is a substantial likelihood that the failure to comply with such regulations will potentially present a serious risk to human health).

(g) Information

Within sixty days of the receipt of a written request of any person for information respecting the class in which a device has been classified or the requirements applicable to a device under this chapter, the Secretary shall provide such person a written statement of the classification (if any) of such device and the requirements of this chapter applicable to the device.

(h) Definitions

For purposes of this section and sections 351, 360, 360d, 360e, 360f, 360i, and 360j of this title

(1) a reference to "general controls" is a reference to the controls authorized by or under sections 351, 352, 360, 360f, 360h, 360i, and 360j of this title,

(2) a reference to "class I", "class II", or "class III" is a reference to a class of medical devices described in subparagraph (A), (B), or (C) of subsection (a)(1) of this section, and

(3) a reference to a "panel under section 360c of this title" is a reference to a panel established or authorized to be used under this section.

(i) Substantial equivalence

(1)(A) For purposes of determinations of substantial equivalence under subsection (f) of this section and section 360j(l) of this title, the term "substantially equivalent" or "substantial equivalence" means, with respect to a device being compared to a predicate device, that the device has the same intended use as the predicate device and that the Secretary by order has found that the device--

(i) has the same technological characteristics as the predicate device, or

(ii) (I) has different technological characteristics and the information submitted that the device is substantially equivalent to the predicate device contains information, including appropriate clinical or scientific data if deemed necessary by the Secretary or a person accredited under section 360m of this title, that demonstrates

that the device is as safe and effective as a legally marketed device, and (II) does not raise different questions of safety and effectiveness than the predicate device.

(B) For purposes of subparagraph (A), the term "different technological characteristics" means, with respect to a device being compared to a predicate device, that there is a significant change in the materials, design, energy source, or other features of the device from those of the predicate device.

(C) To facilitate reviews of reports submitted to the Secretary under section 360(k) of this title, the Secretary shall consider the extent to which reliance on postmarket controls may expedite the classification of devices under subsection (f)(1) of this section.

(D) Whenever the Secretary requests information to demonstrate that devices with differing technological characteristics are substantially equivalent, the Secretary shall only request information that is necessary to making substantial equivalence determinations. In making such request, the Secretary shall consider the least burdensome means of demonstrating substantial equivalence and request information accordingly.

(E)(i) Any determination by the Secretary of the intended use of a device shall be based upon the proposed labeling submitted in a report for the device under section 360(k) of this title. However, when determining that a device can be found substantially equivalent to a legally marketed device, the director of the organizational unit responsible for regulating devices (in this subparagraph referred to as the "Director") may require a statement in labeling that provides appropriate information regarding a use of the device not identified in the proposed labeling if, after providing an opportunity for consultation with the person who submitted such report, the Director determines and states in writing--

(I) that there is a reasonable likelihood that the device will be used for an intended use not identified in the proposed labeling for the device; and

(II) that such use could cause harm.

(ii) Such determination shall--

(I) be provided to the person who submitted the report within 10 days from the date of the notification of the Director's concerns regarding the proposed labeling;

(II) specify the limitations on the use of the device not included in the proposed labeling; and

(III) find the device substantially equivalent if the requirements of subparagraph (A) are met and if the labeling for such device conforms to the limitations specified in subclause (II).

(iii) The responsibilities of the Director under this subparagraph may not be delegated.

(iv) Repealed. Pub.L. 107-250, Title II, § 208, Oct. 26, 2002, 116 Stat. 1613

(F) Not later than 270 days after November 21, 1997, the Secretary shall issue guidance specifying the general principles that the Secretary will consider in determining when a specific intended use of a device is not reasonably included within a general use of such device for purposes of a determination of substantial equivalence under subsection (f) of this section or section 360j(l) of this title.

(2) A device may not be found to be substantially equivalent to a predicate device that has been removed from the market at the initiative of the Secretary or that has been determined to be misbranded or adulterated by a judicial order.

(3)(A) As part of a submission under section 360(k) of this title respecting a device, the person required to file a premarket notification under such section shall provide an adequate summary of any information respecting safety and effectiveness or state that such information will be made available upon request by any person.

(B) Any summary under subparagraph (A) respecting a device shall contain detailed information regarding data concerning adverse health effects and shall be made available to the public by the Secretary within 30 days of the issuance of a determination that such device is substantially equivalent to another device.

CREDIT(S)

(June 25, 1938, c. 675, § 513, as added May 28, 1976, Pub.L. 94-295, § 2, 90 Stat. 540, and amended Nov. 28, 1990, Pub.L. 101-629, §§ 4(a), 5(a), (b), (c)(1), (c)(3), 12(a), 18(a), 104 Stat. 4515, 4517, 4518, 4523, 4528; June 16, 1992, Pub.L. 102-300, § 6(e), 106 Stat. 240; Aug. 13, 1993, Pub.L. 103-80, § 3(s), 107 Stat. 778; Nov. 21, 1997, Pub.L. 105-115, Title II, §§ 205(a), (b), 206(b), (c), 207, 208, 217, 111 Stat. 2336, 2337, 2339, 2340, 2350; Oct. 26, 2002, Pub.L. 107-250, Title II, § 208, 116 Stat. 1613.)

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Title 21. Food and Drugs (Refs & Annos)
Chapter 9. Federal Food, Drug, and Cosmetic Act (Refs & Annos)
Subchapter V. Drugs and Devices
Part A. Drugs and Devices (Refs & Annos)
→ **§ 360e. Premarket approval**

(a) General requirement

A class III device--

(1) which is subject to a regulation promulgated under subsection (b) of this section; or

(2) which is a class III device because of section 360c(f) of this title,

is required to have, unless exempt under section 360j(g) of this title, an approval under this section of an application for premarket approval or, as applicable, an approval under subsection (c)(2) of this section of a report seeking premarket approval.

(b) Regulation to require premarket approval

(1) In the case of a class III device which--

(A) was introduced or delivered for introduction into interstate commerce for commercial distribution before May 28, 1976; or

(B) is (i) of a type so introduced or delivered, and (ii) is substantially equivalent to another device within that type,

the Secretary shall by regulation, promulgated in accordance with this subsection, require that such device have an approval under this section of an application for premarket approval.

(2)(A) A proceeding for the promulgation of a regulation under paragraph (1) respecting a device shall be initiated by the publication in the Federal Register of a notice of proposed rulemaking. Such notice shall contain--

(i) the proposed regulation;

(ii) proposed findings with respect to the degree of risk of illness or injury designed to be eliminated or reduced by requiring the device to have an approved application for premarket approval and the benefit to the public from use of the device;

(iii) opportunity for the submission of comments on the proposed regulation and the proposed findings; and

(iv) opportunity to request a change in the classification of the device based on new information relevant to the classification of the device.

(B) If, within fifteen days after publication of a notice under subparagraph (A), the Secretary receives a request for a change in the classification of a device, he shall, within sixty days of the publication of such notice and after consultation with the appropriate panel under section 360c of this title, by order published in the Federal Register, either deny the request for change in classification or give notice of his intent to initiate such a change under section 360c(e) of this title.

(3) After the expiration of the period for comment on a proposed regulation and proposed findings published under paragraph (2) and after consideration of comments submitted on such proposed regulation and findings, the Secretary shall (A) promulgate such regulation and publish in the Federal Register findings on the matters referred to in paragraph (2)(A)(ii), or (B) publish a notice terminating the proceeding for the promulgation of the regulation together with the reasons for such termination. If a notice of termination is published, the Secretary shall (unless such notice is issued because the device is a banned device under section 360f of this title) initiate a proceeding under section 360c(e) of this title to reclassify the device subject to the proceeding terminated by such notice.

(4) The Secretary, upon his own initiative or upon petition of an interested person, may by regulation amend or revoke any regulation promulgated under this subsection. A regulation to amend or revoke a regulation under this subsection shall be promulgated in accordance with the requirements prescribed by this subsection for the promulgation of the regulation to be amended or revoked.

(c) Application for premarket approval

(1) Any person may file with the Secretary an application for premarket approval for a class III device. Such an application for a device shall contain--

(A) full reports of all information, published or known to or which should reasonably be known to the applicant, concerning investigations which have been made to show whether or not such device is safe and effective;

(B) a full statement of the components, ingredients, and properties and of the principle or principles of operation, of such device;

(C) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and, when relevant, packing and installation of, such device;

(D) an identifying reference to any performance standard under section 360d of this title which would be applicable to any aspect of such device if it were a class II device, and either adequate information to show that such aspect of such device fully meets such performance standard or adequate information to justify any deviation from such standard;

(E) such samples of such device and of components thereof as the Secretary may reasonably require, except that where the submission of such samples is impracticable or unduly burdensome, the requirement of this subparagraph may be met by the submission of complete information concerning the location of one or more such devices readily available for examination and testing;

(F) specimens of the labeling proposed to be used for such device;

(G) the certification required under section 282(j)(5)(B) of Title 42 (which shall not be considered an element of such application); and

(H) such other information relevant to the subject matter of the application as the Secretary, with the concurrence of the appropriate panel under section 360c of this title, may require.

(2)(A) Any person may file with the Secretary a report seeking premarket approval for a class III device referred to in subsection (a) of this section that is a reprocessed single-use device. Such a report shall contain the following:

(i) The device name, including both the trade or proprietary name and the common or usual name.

(ii) The establishment registration number of the owner or operator submitting the report.

(iii) Actions taken to comply with performance standards under section 360d of this title.

(iv) Proposed labels, labeling, and advertising sufficient to describe the device, its intended use, and directions for use.

(v) Full reports of all information, published or known to or which should be reasonably known to the applicant, concerning investigations which have been made to show whether or not the device is safe or effective.

(vi) A description of the device's components, ingredients, and properties.

(vii) A full description of the methods used in, and the facilities and controls used for, the reprocessing and packing of the device.

(viii) Such samples of the device that the Secretary may reasonably require.

(ix) A financial certification or disclosure statement or both, as required by part 54 of title 21, Code of Federal Regulations.

(x) A statement that the applicant believes to the best of the applicant's knowledge that all data and information submitted to the Secretary are truthful and accurate and that no material fact has been omitted in the report.

(xi) Any additional data and information, including information of the type required in paragraph (1) for an application under such paragraph, that the Secretary determines is necessary to determine whether there is reasonable assurance of safety and effectiveness for the reprocessed device.

(xii) Validation data described in section 360(o)(1)(A) of this title that demonstrates that the reasonable assurance of the safety or effectiveness of the device will remain after the maximum number of times the device is reprocessed as intended by the person submitting such report.

(B) In the case of a class III device referred to in subsection (a) of this section that is a reprocessed single-use device:

(i) Subparagraph (A) of this paragraph applies in lieu of paragraph (1).

(ii) Subject to clause (i), the provisions of this section apply to a report under subparagraph (A) to the same extent and in the same manner as such provisions apply to an application under paragraph (1).

(iii) Each reference in other sections of this chapter to an application under this section, other than such a reference in section 379i or 379j of this title, shall be considered to be a reference to a report under subparagraph (A).

(iv) Each reference in other sections of this chapter to a device for which an application under this section has been approved, or has been denied, suspended, or withdrawn, other than such a reference in section 379i or 379j of this title, shall be considered to be a reference to a device for which a report under subparagraph (A) has been approved, or has been denied, suspended, or withdrawn, respectively.

(3) Upon receipt of an application meeting the requirements set forth in paragraph (1), the Secretary--

(A) may on the Secretary's own initiative, or

(B) shall, upon the request of an applicant unless the Secretary finds that the information in the application which would be reviewed by a panel substantially duplicates information which has previously been reviewed by a panel appointed under section 360c of this title,

refer such application to the appropriate panel under section 360c of this title for study and for submission (within such period as he may establish) of a report and recommendation respecting approval of the application, together with all underlying data and the reasons or basis for the recommendation. Where appropriate, the Secretary shall ensure that such panel includes, or consults with, one or more pediatric experts.

(4)(A) Prior to the submission of an application under this subsection, the Secretary shall accept and review any portion of the application that the applicant and the Secretary agree is complete, ready, and appropriate for review, except that such requirement does not apply, and the Secretary has discretion whether to accept and review such portion, during any period in which, under section 379j(g) of this title, the Secretary does not have the authority to collect fees under section 379j(a) of this title.

(B) Each portion of a submission reviewed under subparagraph (A) and found acceptable by the Secretary shall not be further reviewed after receipt of an application that satisfies the requirements of paragraph (1), unless a significant issue of safety or effectiveness provides the Secretary reason to review such accepted portion.

(C) Whenever the Secretary determines that a portion of a submission under subparagraph (A) is unacceptable, the Secretary shall, in writing, provide to the applicant a description of any deficiencies in such portion and identify the information that is required to correct these deficiencies, unless the applicant is no longer pursuing the application.

(d) Action on application for premarket approval

(1)(A) As promptly as possible, but in no event later than one hundred and eighty days after the receipt of an application under subsection (c) of this section (except as provided in section 360j(l)(3)(D)(ii) of this title or unless, in accordance with subparagraph (B)(i), an additional period as agreed upon by the Secretary and the applicant), the Secretary, after considering the report and recommendation submitted under paragraph (2) of such subsection, shall--

(i) issue an order approving the application if he finds that none of the grounds for denying approval specified in paragraph (2) of this subsection applies; or

(ii) deny approval of the application if he finds (and sets forth the basis for such finding as part of or accompanying such denial) that one or more grounds for denial specified in paragraph (2) of this subsection apply.

In making the determination whether to approve or deny the application, the Secretary shall rely on the condi-

tions of use included in the proposed labeling as the basis for determining whether or not there is a reasonable assurance of safety and effectiveness, if the proposed labeling is neither false nor misleading. In determining whether or not such labeling is false or misleading, the Secretary shall fairly evaluate all material facts pertinent to the proposed labeling.

(B)(i) The Secretary may not enter into an agreement to extend the period in which to take action with respect to an application submitted for a device subject to a regulation promulgated under subsection (b) of this section unless he finds that the continued availability of the device is necessary for the public health.

(ii) An order approving an application for a device may require as a condition to such approval that the sale and distribution of the device be restricted but only to the extent that the sale and distribution of a device may be restricted under a regulation under section 360j(e) of this title.

(iii) The Secretary shall accept and review statistically valid and reliable data and any other information from investigations conducted under the authority of regulations required by section 360j(g) of this title to make a determination of whether there is a reasonable assurance of safety and effectiveness of a device subject to a pending application under this section if--

(I) the data or information is derived from investigations of an earlier version of the device, the device has been modified during or after the investigations (but prior to submission of an application under subsection (c) of this section) and such a modification of the device does not constitute a significant change in the design or in the basic principles of operation of the device that would invalidate the data or information; or

(II) the data or information relates to a device approved under this section, is available for use under this chapter, and is relevant to the design and intended use of the device for which the application is pending.

(2) The Secretary shall deny approval of an application for a device if, upon the basis of the information submitted to the Secretary as part of the application and any other information before him with respect to such device, the Secretary finds that--

(A) there is a lack of a showing of reasonable assurance that such device is safe under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof;

(B) there is a lack of a showing of reasonable assurance that the device is effective under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof;

(C) the methods used in, or the facilities or controls used for, the manufacture, processing, packing, or installation of such device do not conform to the requirements of section 360j(f) of this title;

(D) based on a fair evaluation of all material facts, the proposed labeling is false or misleading in any particu-

lar; or

(E) such device is not shown to conform in all respects to a performance standard in effect under section 360d of this title compliance with which is a condition to approval of the application and there is a lack of adequate information to justify the deviation from such standard.

Any denial of an application shall, insofar as the Secretary determines to be practicable, be accompanied by a statement informing the applicant of the measures required to place such application in approvable form (which measures may include further research by the applicant in accordance with one or more protocols prescribed by the Secretary).

(3)(A)(i) The Secretary shall, upon the written request of an applicant, meet with the applicant, not later than 100 days after the receipt of an application that has been filed as complete under subsection (c) of this section, to discuss the review status of the application.

(ii) The Secretary shall, in writing and prior to the meeting, provide to the applicant a description of any deficiencies in the application that, at that point, have been identified by the Secretary based on an interim review of the entire application and identify the information that is required to correct those deficiencies.

(iii) The Secretary shall notify the applicant promptly of--

(I) any additional deficiency identified in the application, or

(II) any additional information required to achieve completion of the review and final action on the application,

that was not described as a deficiency in the written description provided by the Secretary under clause (ii).

(B) The Secretary and the applicant may, by mutual consent, establish a different schedule for a meeting required under this paragraph.

(4) An applicant whose application has been denied approval may, by petition filed on or before the thirtieth day after the date upon which he receives notice of such denial, obtain review thereof in accordance with either paragraph (1) or (2) of subsection (g) of this section, and any interested person may obtain review, in accordance with paragraph (1) or (2) of subsection (g) of this section, of an order of the Secretary approving an application.

(5) In order to provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating human diseases or conditions, the Secretary shall provide review priority for devices--

(A) representing breakthrough technologies,

(B) for which no approved alternatives exist,

(C) which offer significant advantages over existing approved alternatives, or

(D) the availability of which is in the best interest of the patients.

(6)(A)(i) A supplemental application shall be required for any change to a device subject to an approved application under this subsection that affects safety or effectiveness, unless such change is a modification in a manufacturing procedure or method of manufacturing and the holder of the approved application submits a written notice to the Secretary that describes in detail the change, summarizes the data or information supporting the change, and informs the Secretary that the change has been made under the requirements of section 360j(f) of this title.

(ii) The holder of an approved application who submits a notice under clause (i) with respect to a manufacturing change of a device may distribute the device 30 days after the date on which the Secretary receives the notice, unless the Secretary within such 30-day period notifies the holder that the notice is not adequate and describes such further information or action that is required for acceptance of such change. If the Secretary notifies the holder that a supplemental application is required, the Secretary shall review the supplement within 135 days after the receipt of the supplement. The time used by the Secretary to review the notice of the manufacturing change shall be deducted from the 135-day review period if the notice meets appropriate content requirements for premarket approval supplements.

(B)(i) Subject to clause (ii), in reviewing a supplement to an approved application, for an incremental change to the design of a device that affects safety or effectiveness, the Secretary shall approve such supplement if--

(I) nonclinical data demonstrate that the design modification creates the intended additional capacity, function, or performance of the device; and

(II) clinical data from the approved application and any supplement to the approved application provide a reasonable assurance of safety and effectiveness for the changed device.

(ii) The Secretary may require, when necessary, additional clinical data to evaluate the design modification of the device to provide a reasonable assurance of safety and effectiveness.

(e) Withdrawal and temporary suspension of approval of application

(1) The Secretary shall, upon obtaining, where appropriate, advice on scientific matters from a panel or panels under section 360c of this title, and after due notice and opportunity for informal hearing to the holder of an approved application for a device, issue an order withdrawing approval of the application if the Secretary finds--

(A) that such device is unsafe or ineffective under the conditions of use prescribed, recommended, or suggested in the labeling thereof;

(B) on the basis of new information before him with respect to such device, evaluated together with the evidence available to him when the application was approved, that there is a lack of a showing of reasonable assurance that the device is safe or effective under the conditions of use prescribed, recommended, or suggested in the labeling thereof;

(C) that the application contained or was accompanied by an untrue statement of a material fact;

(D) that the applicant (i) has failed to establish a system for maintaining records, or has repeatedly or deliberately failed to maintain records or to make reports, required by an applicable regulation under section 360i(a) of this title, (ii) has refused to permit access to, or copying or verification of, such records as required by section 374 of this title, or (iii) has not complied with the requirements of section 360 of this title;

(E) on the basis of new information before him with respect to such device, evaluated together with the evidence before him when the application was approved, that the methods used in, or the facilities and controls used for, the manufacture, processing, packing, or installation of such device do not conform with the requirements of section 360j(f) of this title and were not brought into conformity with such requirements within a reasonable time after receipt of written notice from the Secretary of nonconformity;

(F) on the basis of new information before him, evaluated together with the evidence before him when the application was approved, that the labeling of such device, based on a fair evaluation of all material facts, is false or misleading in any particular and was not corrected within a reasonable time after receipt of written notice from the Secretary of such fact; or

(G) on the basis of new information before him, evaluated together with the evidence before him when the application was approved, that such device is not shown to conform in all respects to a performance standard which is in effect under section 360d of this title compliance with which was a condition to approval of the application and that there is a lack of adequate information to justify the deviation from such standard.

(2) The holder of an application subject to an order issued under paragraph (1) withdrawing approval of the application may, by petition filed on or before the thirtieth day after the date upon which he receives notice of such withdrawal, obtain review thereof in accordance with either paragraph (1) or (2) of subsection (g) of this section.

(3) If, after providing an opportunity for an informal hearing, the Secretary determines there is reasonable probability that the continuation of distribution of a device under an approved application would cause serious, adverse health consequences or death, the Secretary shall by order temporarily suspend the approval of the application approved under this section. If the Secretary issues such an order, the Secretary shall proceed expeditiously under paragraph (1) to withdraw such application.

(f) Product development protocol

(1) In the case of a class III device which is required to have an approval of an application submitted under subsection (c) of this section, such device shall be considered as having such an approval if a notice of completion of testing conducted in accordance with a product development protocol approved under paragraph (4) has been declared completed under paragraph (6).

(2) Any person may submit to the Secretary a proposed product development protocol with respect to a device. Such a protocol shall be accompanied by data supporting it. If, within thirty days of the receipt of such a protocol, the Secretary determines that it appears to be appropriate to apply the requirements of this subsection to the device with respect to which the protocol is submitted, the Secretary--

(A) may, at the initiative of the Secretary, refer the proposed protocol to the appropriate panel under section 360c of this title for its recommendation respecting approval of the protocol; or

(B) shall so refer such protocol upon the request of the submitter, unless the Secretary finds that the proposed protocol and accompanying data which would be reviewed by such panel substantially duplicate a product development protocol and accompanying data which have previously been reviewed by such a panel.

(3) A proposed product development protocol for a device may be approved only if--

(A) the Secretary determines that it is appropriate to apply the requirements of this subsection to the device in lieu of the requirement of approval of an application submitted under subsection (c) of this section; and

(B) the Secretary determines that the proposed protocol provides--

(i) a description of the device and the changes which may be made in the device,

(ii) a description of the preclinical trials (if any) of the device and a specification of (I) the results from such trials to be required before the commencement of clinical trials of the device, and (II) any permissible variations in preclinical trials and the results therefrom,

(iii) a description of the clinical trials (if any) of the device and a specification of (I) the results from such trials to be required before the filing of a notice of completion of the requirements of the protocol, and (II) any permissible variations in such trials and the results therefrom,

(iv) a description of the methods to be used in, and the facilities and controls to be used for, the manufacture, processing, and, when relevant, packing and installation of the device,

(v) an identifying reference to any performance standard under section 360d of this title to be applicable to

any aspect of such device,

(vi) if appropriate, specimens of the labeling proposed to be used for such device,

(vii) such other information relevant to the subject matter of the protocol as the Secretary, with the concurrence of the appropriate panel or panels under section 360c of this title, may require, and

(viii) a requirement for submission of progress reports and, when completed, records of the trials conducted under the protocol which records are adequate to show compliance with the protocol.

(4) The Secretary shall approve or disapprove a proposed product development protocol submitted under paragraph (2) within one hundred and twenty days of its receipt unless an additional period is agreed upon by the Secretary and the person who submitted the protocol. Approval of a protocol or denial of approval of a protocol is final agency action subject to judicial review under chapter 7 of Title 5.

(5) At any time after a product development protocol for a device has been approved pursuant to paragraph (4), the person for whom the protocol was approved may submit a notice of completion--

(A) stating (i) his determination that the requirements of the protocol have been fulfilled and that, to the best of his knowledge, there is no reason bearing on safety or effectiveness why the notice of completion should not become effective, and (ii) the data and other information upon which such determination was made, and

(B) setting forth the results of the trials required by the protocol and all the information required by subsection (c)(1) of this section.

(6)(A) The Secretary may, after providing the person who has an approved protocol and opportunity for an informal hearing and at any time prior to receipt of notice of completion of such protocol, issue a final order to revoke such protocol if he finds that--

(i) such person has failed substantially to comply with the requirements of the protocol,

(ii) the results of the trials obtained under the protocol differ so substantially from the results required by the protocol that further trials cannot be justified, or

(iii) the results of the trials conducted under the protocol or available new information do not demonstrate that the device tested under the protocol does not present an unreasonable risk to health and safety.

(B) After the receipt of a notice of completion of an approved protocol the Secretary shall, within the ninety-day period beginning on the date such notice is received, by order either declare the protocol completed or declare it

not completed. An order declaring a protocol not completed may take effect only after the Secretary has provided the person who has the protocol opportunity for an informal hearing on the order. Such an order may be issued only if the Secretary finds--

(i) such person has failed substantially to comply with the requirements of the protocol,

(ii) the results of the trials obtained under the protocol differ substantially from the results required by the protocol, or

(iii) there is a lack of a showing of reasonable assurance of the safety and effectiveness of the device under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof.

(C) A final order issued under subparagraph (A) or (B) shall be in writing and shall contain the reasons to support the conclusions thereof.

(7) At any time after a notice of completion has become effective, the Secretary may issue an order (after due notice and opportunity for an informal hearing to the person for whom the notice is effective) revoking the approval of a device provided by a notice of completion which has become effective as provided in subparagraph (B) if he finds that any of the grounds listed in subparagraphs (A) through (G) of subsection (e)(1) of this section apply. Each reference in such subparagraphs to an application shall be considered for purposes of this paragraph as a reference to a protocol and the notice of completion of such protocol, and each reference to the time when an application was approved shall be considered for purposes of this paragraph as a reference to the time when a notice of completion took effect.

(8) A person who has an approved protocol subject to an order issued under paragraph (6)(A) revoking such protocol, a person who has an approved protocol with respect to which an order under paragraph (6)(B) was issued declaring that the protocol had not been completed, or a person subject to an order issued under paragraph (7) revoking the approval of a device may, by petition filed on or before the thirtieth day after the date upon which he receives notice of such order, obtain review thereof in accordance with either paragraph (1) or (2) of subsection (g) of this section.

(g) Review

(1) Upon petition for review of--

(A) an order under subsection (d) of this section approving or denying approval of an application or an order under subsection (e) of this section withdrawing approval of an application, or

(B) an order under subsection (f)(6)(A) of this section revoking an approved protocol, under subsection (f)(6)(B) of this section declaring that an approved protocol has not been completed, or under subsection (f)(7) of this section revoking the approval of a device,

the Secretary shall, unless he finds the petition to be without good cause or unless a petition for review of such order has been submitted under paragraph (2), hold a hearing, in accordance with section 554 of Title 5, on the order. The panel or panels which considered the application, protocol, or device subject to such order shall designate a member to appear and testify at any such hearing upon request of the Secretary, the petitioner, or the officer conducting the hearing, but this requirement does not preclude any other member of the panel or panels from appearing and testifying at any such hearing. Upon completion of such hearing and after considering the record established in such hearing, the Secretary shall issue an order either affirming the order subject to the hearing or reversing such order and, as appropriate, approving or denying approval of the application, reinstating the application's approval, approving the protocol, or placing in effect a notice of completion.

(2)(A) Upon petition for review of--

(i) an order under subsection (d) of this section approving or denying approval of an application or an order under subsection (e) of this section withdrawing approval of an application, or

(ii) an order under subsection (f)(6)(A) of this section revoking an approved protocol, under subsection (f)(6)(B) of this section declaring that an approved protocol has not been completed, or under subsection (f)(7) of this section revoking the approval of a device,

the Secretary shall refer the application or protocol subject to the order and the basis for the order to an advisory committee of experts established pursuant to subparagraph (B) for a report and recommendation with respect to the order. The advisory committee shall, after independent study of the data and information furnished to it by the Secretary and other data and information before it, submit to the Secretary a report and recommendation, together with all underlying data and information and a statement of the reasons or basis for the recommendation. A copy of such report shall be promptly supplied by the Secretary to any person who petitioned for such referral to the advisory committee.

(B) The Secretary shall establish advisory committees (which may not be panels under section 360c of this title) to receive referrals under subparagraph (A). The Secretary shall appoint as members of any such advisory committee persons qualified in the subject matter to be referred to the committee and of appropriately diversified professional backgrounds, except that the Secretary may not appoint to such a committee any individual who is in the regular full-time employ of the United States and engaged in the administration of this chapter. Members of an advisory committee (other than officers or employees of the United States), while attending conferences or meetings of their committee or otherwise serving at the request of the Secretary, shall be entitled to receive compensation at rates to be fixed by the Secretary, which rates may not exceed the daily equivalent for grade GS-18 of the General Schedule for each day (including traveltime) they are so engaged; and while so serving away from their homes or regular places of business each member may be allowed travel expenses, including per diem in lieu of subsistence, as authorized by section 5703 of Title 5 for persons in the Government service employed intermittently. The Secretary shall designate the chairman of an advisory committee from its members. The Secretary shall furnish each advisory committee with clerical and other assistance, and shall by regulation prescribe the procedures to be followed by each such committee in acting on referrals made under subparagraph (A).

(C) The Secretary shall make public the report and recommendation made by an advisory committee with respect to an application and shall by order, stating the reasons therefor, either affirm the order referred to the advisory committee or reverse such order and, if appropriate, approve or deny approval of the application, reinstate the application's approval, approve the protocol, or place in effect a notice of completion.

(h) Service of orders

Orders of the Secretary under this section shall be served (1) in person by any officer or employee of the department designated by the Secretary, or (2) by mailing the order by registered mail or certified mail addressed to the applicant at his last known address in the records of the Secretary.

(i) Revision

(1) Before December 1, 1995, the Secretary shall by order require manufacturers of devices, which were introduced or delivered for introduction into interstate commerce for commercial distribution before May 28, 1976, and which are subject to revision of classification under paragraph (2), to submit to the Secretary a summary of and citation to any information known or otherwise available to the manufacturer respecting such devices, including adverse safety or effectiveness information which has not been submitted under section 360i of this title. The Secretary may require the manufacturer to submit the adverse safety or effectiveness data for which a summary and citation were submitted, if such data are available to the manufacturer.

(2) After the issuance of an order under paragraph (1) but before December 1, 1995, the Secretary shall publish a regulation in the Federal Register for each device--

(A) which the Secretary has classified as a class III device, and

(B) for which no final regulation has been promulgated under subsection (b) of this section,

revising the classification of the device so that the device is classified into class I or class II, unless the regulation requires the device to remain in class III. In determining whether to revise the classification of a device or to require a device to remain in class III, the Secretary shall apply the criteria set forth in section 360c(a) of this title. Before the publication of a regulation requiring a device to remain in class III or revising its classification, the Secretary shall publish a proposed regulation respecting the classification of a device under this paragraph and provide reasonable opportunity for the submission of comments on any such regulation. No regulation requiring a device to remain in class III or revising its classification may take effect before the expiration of 90 days from the date of its publication in the Federal Register as a proposed regulation.

(3) The Secretary shall, as promptly as is reasonably achievable, but not later than 12 months after the effective date of the regulation requiring a device to remain in class III, establish a schedule for the promulgation of a subsection (b) of this section regulation for each device which is subject to the regulation requiring the device to remain in class III.

CREDIT(S)

(June 25, 1938, c. 675, § 515, as added May 28, 1976, Pub.L. 94-295, § 2, 90 Stat. 552, and amended Nov. 28, 1990, Pub.L. 101-629, §§ 4(b)(1), 9(a), 18(c), 104 Stat. 4515, 4521, 4528; Aug. 13, 1993, Pub.L. 103-80, § 3(t), 107 Stat. 778; Nov. 21, 1997, Pub.L. 105-115, Title II, §§ 201(b), 202, 205(c), 209(b), 216(b), 111 Stat. 2334, 2338, 2341, 2349; Oct. 26, 2002, Pub.L. 107-250, Title II, §§ 209, 210, Title III, § 302(c), 116 Stat. 1613, 1614, 1618; Apr. 1, 2004, Pub.L. 108-214, § 2(d)(1), 118 Stat. 576; Sept. 27, 2007, Pub.L. 110-85, Title VIII, § 801(b)(3)(D), 121 Stat. 921.)

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(s) Lauren N. Bell

Attorney for Appellee

Dated: September 23, 2009

CERTIFICATE OF SERVICE

I hereby certify that I caused the Appellees' Brief to be served on this 23rd day of September, 2009, upon the following by electronic mail and by Federal Express Overnight:

Anthony J. Musto
2 Sherman Court
Fairfield, CT 06824
203-259-4488
attymusto@sbcglobal.net

Lauren Bell

Lauren Bell