UNITED STATES DISTRICT COURT

DISTRICT OF CONNECTICUT

CIVIL ACTION FILE NUMBER 3:08CV54AVC

HIFI DNA TECH, LLC PLAINTIFF, V. U.S. DEPT. OF HEALTH AND HUMAN SERVICES, U.S. FOOD AND DRUG ADMINISTRATION, MICHAEL O. LEAVITT In His Official Capacity As Secretary Of U.S. Health And Services, ANDREW VON ESCHENBACH In His Official Capacity As Commissioner Of The U.S. Food And Drug Administration DEFENDANTS.	:	**AMENDED COMPLAINT** JANUARY 22, 2008

Now comes HIFI DNA TECH, LLC, by its attorney Anthony J. Musto, and makes the following for its Amended Complaint.

INTRODUCTION

1. Plaintiff brings this action under the Administrative Procedure Act, 5 U.S.C. § 701, et. seq. for a review of the denial by Defendant Food and Drug Administration ("FDA") of Plaintiff's petition for reclassification of a human papillomavirus (HPV) Nested DNA polymerase chain reaction (PCR) Detection Device. Plaintiff requests that this Court (a) review and overturn the denial of the petition or, in the alternative,

(b) order defendants to review the device under 21 U.S.C. § 513(f)(2) for classification.

PARTIES, JURISDICTION & VENUE

2. Plaintiff is an entity duly formed under the laws of the State of Connecticut.

3. Defendant United States Department of Health and Human Services ("HHS") is a department of the United States.

4. Defendant Food and Drug Administration ("FDA") is an agency of HHS and an agency of the United States.

5. Defendant Michael O. Leavitt is the Secretary of HHS and is sued only in his official capacity.

6. Defendant Andrew von Eschenbach is the Commissioner of FDA and is sued only in his official capacity.

7. Venue is proper in this District under 28 U.S.C. Sec. 1391(e) as Plaintiff resides in this district.

8. Jurisdiction is founded upon the existence of a federal question and proper in this Court pursuant to 28 U.S.C. §1331 as arising under the laws of the United States and the Administrative Procedure Act codified as 5 U.S.C. § 701 et. sec. as a review of an administrative decision.

FACTUAL BACKGROUND

9. Plaintiff is a manufacturer of certain reagents for

making identical copies of DNA molecules in the test tube, generally known as primer-defined DNA PCR amplification.

10. Plaintiff intends to market a device for nested PCR amplification of HPV DNA intended to be used for preparation of sample materials ("the device") suitable for accurate HPV genotyping by direct automated DNA sequencing, a "spin-off" new technology of the national Human Genome Project. A simplified method for sample preparation provided by said device will facilitate technology transferring of the cutting-edge DNA sequencing technology into community hospital laboratories to improve patient care.

FIRST COUNT: The FDA Improperly Denied The Reclassification Petition Filed By The Plaintiff.

Paragraphs 1-10 are hereby incorporated herein by reference as if set forth at length.

11. On March 7, 2007 (after repeated obstruction and direction from FDA personnel as detailed in the second count, below) Plaintiff filed Reclassification Petition For Human Papillomavirus (HPV) DNA Nested Polymerase Chain Reaction (PCR) Detection ("the petition") pursuant to 21 U.S.C. § 360c(f)(1) with the FDA (attention: Ms. Heather Rosecrans), which petition was date-stamped on May 22, 2007 and posted on the FDA Dockets Management website under Docket No. 2007P-0210 for public

viewing on June 4, 2007.

12. On April 9, 2007 plaintiff sent a letter requesting to be informed of the names of the reviewers appointed to the classification review panel and of the date of the panel meeting so that he could attend the meeting to answer any questions raised by the panel.

13. After receiving no response from the FDA, the plaintiff brought suit in October of 2007 in this Court (case no. 3:07CV1511RNC) to compel the FDA to issue a decision, which suit was voluntarily withdrawn after the FDA issued a decision.

14. On December 14, 2007 the defendants issued a Reclassification Order on Docket No. 2007P-0210 denying the plaintiff's petition for reclassification ("the denial") and stating " by order in the form of this letter, FDA is denying your petition; your device remains in class III and is subject to pre-market approval requirements."

15. The denial is not supported by medical science or by applicable statutes. It should be declared invalid and void for the following reasons:

a. The reviewers of the petition did not follow established FDA procedures in making their decision of denial; specifically, to the best knowledge and belief of the Plaintiff, the FDA failed to forward the petition to the FDA Commissioner or to a classification panel for review.

b. The denial improperly compares the device to Digene's Hybrid Capture 2(hc2) High-Risk HPV DNA Test ("the Digene Test"), although the Digene Test uses a completely different scientific basis to determine the presence and type of HPV DNA, if any, present in a sample.

c. The denial results in the FDA's over-regulation of the device as a cancer test rather than as a test for a common virus, thus requiring unnecessary and costly PMA submission, in violation of the least burdensome provisions of the Food and Drug Administration Modernization Act of 1997 (as codified at 21 U.S.C. §360c(i)(1)(D) and 360c(a)(3)(D)(ii)) and at the expense of public interest.

d. The denial violated the non-biased implementation of the risk-based medical device classification provisions under 21 CFR § 860.3(c) in that other in vitro devices for the detection of infectious agents that may lead to chronic inflammation leading to cancer with human mortalities higher than that caused by cervical cancer, such as tests for H. Pylori (causing stomach inflammation), have been regulated as class I or II tests by the FDA without requiring PMA submissions. Such inconsistent and asymmetrical implement of the medical device statutes is not in the best interest of public health.

e. Although the portion of the denial based upon FDA's assertion that the device will be used to assess a woman's risk of developing cervical cancer and guide patient management decisions is erroneous, if it were correct, denying class II status is inconsistent with the FDA's decision regarding the classification of MammaPrint® (an in vitro device for the purpose of determining breast cancer prognosis).

f. The denial is based in part on the fact that the device was designated as Class III based upon the approval order for the VRAPAP Human Papillomavirus DNA Detection Kit dated December 23, 1988, although the FDA has refused to produce a copy of this December 23, 1988 approval order at the request of the Petitioner to show its statutory function as means for medical device classification.

g. The FDA erroneously found that Plaintiff did not provide adequate, scientific data as required by law.

h. The FDA's assertion that the device is of substantial importance in preventing impairment of human health is contrary to law, not supported by science, and contradicts other statements in the denial.

i. The FDA's allegation that the device presents a potential unreasonable risk of illness or injury is contrary to law, not supported by science, and contradicts other statements in the denial.

j. The FDA's allegation that the Plaintiff failed to perform any crossreactivity or interfering substances studies to show that results will not be affected by: (a) substances potentially present in cervical cytology specimens (such as contraceptives, personal hygiene products, etc); and/or (b) microorganisms other than the HPV strains targeted by the device, such as microorganisms that are normally found in the genital tract and any HPV genotypes that are not specifically targeted by the device test or state precisely which HPV strains are targeted by the device is erroneous in that it applies an incorrect scientific standard to the device.

k. The FDA's erroneously applied concepts of using clinical sensitivity and specificity, which are derived from the art of clinical judgment (i.e., judgment exercised by a doctor), to evaluate methods utilized by the device, are not appropriate to scientifically validate laboratory methodologies.

l. The FDA's declaration "FDA has not to date approved any HPV genotyping test for diagnostic use, however" stated as a basis in part for the denial reflects a failure of the FDA and should not be used as a tool or a policy for blocking new technology introduced for HPV genotyping.

m. The portion of the denial based upon the probe design is erroneous because the device does not use a probe; rather, the device uses a process known as PCR (polymerase chain

reaction) to replicate HPV DNA for automated DNA sequencing, a technology perfected in the work of the national Human Genome Project research.

n. The portion of the denial based upon sampling methodology is erroneous because sampling methodology as described in the denial is not applicable to the PCR specimen amplification methodology.

o. The portion of the denial based upon combination of HPV genotypes is erroneous because the device simply replicates HPV DNA for DNA sequencing and does not perform HPV genotyping or any evaluation of the relative risks or appropriate treatment thereof.

p. The FDA's assertion that the device is intended for use in evaluating cancer risk is erroneous in that the device is simply a test for a virus DNA and does not dictate any clinical judgment.

q. The denial is inconsistent with prior FDA approvals in that FDA Commissioner and the Secretary of HHS knew or should have known that FDA has reviewed and approved a type-specific vaccine, Gardasil®, to prevent the infection caused by 4 genotypes of potentially carcinogenic HPV using PCR-based HPV DNA detection and genotyping methods similar to the device to support clinical safety and effectiveness of the genotype-specific vaccine on human subjects.

r. The portion of the denial based upon the asserted lack of clinical sensitivity and clinical specificity data is inconsistent with the prior approval of similar HPV DNA PCR-based amplification methodology for confirming the clinical safety and effectiveness of Gardasil® without such evaluation by clinical sensitivity and clinical specificity data, and the denial provides no reason as to why a method is scientifically acceptable for drug or vaccine evaluation with the results utilized to support clinical safety and effectiveness of the drug or vaccine, but not acceptable for preparing material for clinical tests in monitoring vaccine safety in patients.

s. Because injection of the genotype-specific vaccine, Gardasil®, into women who are already PCR-positive and sero-positive for vaccine-relevant HPV types at the time of vaccination is not only ineffective, but may even inadvertently enhance the risk of developing high-grade precancerous intraepithelial lesions by 44.6% in the recipients, and the denial discourages competitive introduction of a PCR-based HPV DNA device for accurate HPV genotyping methodologies that may be useful for monitoring a safe usage of the type-specific vaccination against HPV infections for each individuals among sexually active young women, the denial is not in the best interest of the consumers.

t. The portion of the denial based upon the alleged insufficiency of special controls is erroneous as contrary to accepted science.

SECOND COUNT: The FDA Should Have Permitted Plaintiff To Obtain "De Novo" Review Under The Less-Burdensome Provisions Of 21 U.S.C. 360(f)(1).

Paragraphs 1-15 of the First Count are hereby incorporated herein by reference as if set forth at length.

16. On October 30, 2006 Plaintiff, through its representative, Dr. Sin Hang Lee, wrote in a letter including a supportive pre-publication scientific manuscript to seek FDA advice and guidance to introduce the device into the U.S. market by means of pre-market notification procedures under 21 U.S.C. § 360(k) and Part 807 of the FDA regulations, 21 C.F.R. § 807.

17. Without a response or an objection from the FDA, the plaintiff followed the published FDA regulation of in vitro diagnostic devices and submitted a pre-market notification for the device on December 7, 2006 and a Summary of Comparison with the Digene Test as a predicate in Table Format for the convenience of the FDA reviewers.

18. The plaintiff received a decision letter dated January 9, 2007 from the FDA, stating "We have reviewed your Section 510(k) pre-market notification…." and "We have determined that your type of device is classified as a class III device by the

approval order for the VRAPAP Human Papillomavirus DNA Detection Kit dated December 23, 1988".

19. Plaintiff has requested, but never received, a copy of the FDA approval order for the VRAPAP Human Papillomavirus DNA Detection Kit dated December 23, 1988, and has been otherwise unable to locate said order, although, upon knowledge and belief said order relates to the approval of the Digene Test discussed below.

20. A telephone call and an email dated January 18, 2007 from the Plaintiff to Dr. Uwe Scherf of OIVD requested for a copy of the FDA approval order for the VRAPAP Human Papillomavirus DNA Detection Kit dated December 23, 1988 to no avail. Dr. Scherf only stated that device has been classified as a cancer test and therefore must go through PMA submission, referring to an OIVD regulatory policy letter dated March 18, 2004 signed by Dr. Steven Gutman: tests "intended for use in identifying and typing HPV infection to stratify women at risk for cervical cancer have been assigned to class III, requiring submission and approval of PMAs".

21. Pursuant to 21 U.S.C. § 360c(f)(2), on January 18, 2007 plaintiff submitted a Request for Evaluation of Automatic Class III Designation of the device under 21 U.S.C. § 360c(f)(2), also known as de novo review.

22. Plaintiff claimed as a statutory basis for the de novo

review that there should have been a "not substantially equivalent" determination by the FDA between the device and the Digene Test although the latter device was quoted as a predicate for the 21 U.S.C. § 360(k) submission as a formality as required according to the OIVD regulations.

23. Plaintiff summarized the similarities and differences between the device and the Digene Test in table format as an attachment to the original submission showing eight differences for the FDA's attention including but not limited to:

a. that the device is based on target DNA PCR amplification, a technology developed within the past 20 years and after approval of the Digene Test, while the Digene Test, approved in 1988, depends upon signal amplification to increase its sensitivity, and

b. that the device provides materials suitable for accurate genotyping by direct automated DNA sequencing, but itself does not perform HPV genotyping whereas the Digene Test detects a group of 13 "high-risk" HPV types, but cannot offer specific HPV genotyping information or be modified for a specific genotyping determination.

24. The FDA failed to review the petition for de novo review together with all accompanying data in order to determine the proper statutory procedure for classification of the device.

25. On January 22, 2006 and on February 21, 2007,

plaintiff wrote to the Director of Division of Microbiology Devices, Office of In Vitro Diagnostic Device Evaluation and Safety, Center for Devices and Radiological Health (CDRH), FDA and the CDRH Ombudsman respectively, urging the FDA not to use non-statutory regulatory block to prevent de novo review of the device.

26. On February 27, 2007 Ms. Heather Rosecrans of the Office of Device Evaluation, CDRH telephoned to advise Dr. Sin Hang Lee to withdraw the Petition for Evaluation of Automatic Class III Designation under de novo review and to send her a fax letter as soon as possible, and re-submit a petition for reclassification for the device instead under 21 U.S.C. § 360c(f)(1), in order to facilitate the review process, arguing that otherwise the original petition would not be reviewed for years.

27. Plaintiff reluctantly, and after repeated obstruction and direction from FDA personnel, filed the petition for reclassification that is the subject of the first count of this Amended Complaint.

28. Thereafter, Plaintiff sent another two letters on March 23, 2007 and April 2, 2007 respectively to the CDRH Ombudsman, requesting a mediation which might lead to a less burdensome review of the submission by the means of the de novo process rather than the longer, more burdensome 21 U.S.C. §

360c(f)(1) reclassification process, which might require the attention of the FDA Commissioner and a classification panel.

29. Based on review of the differences between the device and the Digene Test, and after proper review, the FDA should have found that the two devices were "not substantially equivalent" and permitted the device to be evaluated under the less burdensome provisions of de novo review found in 21 U.S.C. § 360c(f)(2).

REQUEST FOR RELIEF

WHEREFORE, Plaintiff requests that this Court:

1. Review and reverse the denial of the petition, or, in the alternative,

2. Declare the denial invalid and void, and order defendants to conduct an unbiased review of the device under 21 U.S.C. § 513(f)(2) for classification, and

3. Order such other relief as the Court sees fit.

THE PLAINTIFF
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BY: _____

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Certificate of Service

I hereby certify that on the above date, a copy of the foregoing motion to dismiss, memorandum in support, and attachments was filed electronically and served by mail on anyone unable to accept electronic filing. Notice of this filing will be sent by e-mail to all parties by operation of the court's electronic filing system or by mail to anyone unable to accept electronic filing as indicated on the Notice of Electronic Filing. Parties may access this filing through the court's CM/ECF System.

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