DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 866

[Docket No. 2007N–0136]

Medical Devices; Immunology and Microbiology Devices; Classification of Gene Expression Profiling Test System for Breast Cancer Prognosis

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is classifying gene expression profiling test systems for breast cancer prognosis into class II (special controls). The special control that will apply to the device is the guidance document entitled ''Class II Special Controls Guidance Document: Gene Expression Profiling Test System for Breast Cancer Prognosis.'' The agency is classifying the device into class II (special controls) in order to provide a reasonable assurance of safety and effectiveness of the device. Elsewhere in this issue of the **Federal Register**, FDA is announcing the availability of the guidance document that will serve as the special control for this device.

DATES: This final rule is effective June 8, 2007. The classification was effective February 6, 2007.

FOR FURTHER INFORMATION CONTACT: Reena Philip, Center for Devices and Radiological Health (HFZ–440), Food and Drug Administration, 2098 Gaither Rd., Rockville, MD 20850, 240–276–1286.

SUPPLEMENTARY INFORMATION:

I. What Is the Background of This Rulemaking?

In accordance with section 513(f)(1) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 360c(f)(1)), devices that were not in commercial distribution before May 28, 1976, the date of enactment of the Medical Device Amendments of 1976 (the amendments), generally referred to as postamendments devices, are classified automatically by statute into class III without any FDA rulemaking process. These devices remain in class III and require premarket approval, unless and until the device is classified or reclassified into class I or II, or FDA issues an order finding the device to be substantially equivalent, in accordance with section 513(i) of the act, to a predicate device that does not require premarket approval. The agency determines whether new devices are substantially equivalent to predicate devices by means of premarket notification procedures in section 510(k) of the act (21 U.S.C. 360(k)) and part 807 (21 CFR part 807) of FDA's regulations.

Section 513(f)(2) of the act provides that any person who submits a premarket notification under section 510(k) of the act for a device that has not previously been classified may, within 30 days after receiving an order classifying the device in class III under section 513(f)(1) of the act, request FDA to classify the device under the criteria set forth in section 513(a)(1) of the act. FDA shall, within 60 days of receiving such a request, classify the device by written order. This classification shall be the initial classification of the device. Within 30 days after the issuance of an order classifying the device, FDA must publish a notice in the **Federal Register** announcing such classification (section 513(f)(2) of the act).

In accordance with section 513(f)(1) of the act, FDA issued an order on January 19, 2007, classifying the Agendia BV, MAMMAPRINT as class III, because it was not substantially equivalent to a device that was introduced or delivered for introduction into interstate commerce for commercial distribution before May 28, 1976, or a device which was subsequently reclassified into class I or class II. Agendia BV submitted a petition dated January 22, 2007, requesting classification of the MAMMAPRINT under section 513(f)(2) of the act. FDA filed the petition on January 30, 2007. The manufacturer recommended that the device be classified into class II.

In accordance with section 513(f)(2) of the act, FDA reviewed the petition in order to classify the device under the criteria for classification set forth in section 513(a)(1) of the act. Devices are to be classified into class II if general controls, by themselves, are insufficient to provide reasonable assurance of safety and effectiveness, but there is sufficient information to establish special controls to provide reasonable assurance of the safety and effectiveness of the device for its intended use. After review of the information submitted in the petition, FDA determined that the Agendia BV, MAMMAPRINT can be classified in class II with the establishment of special controls. FDA believes these special controls, in addition to general controls, will provide reasonable assurance of safety and effectiveness of the device.

The device is assigned the generic name ''gene expression profiling test system for breast cancer prognosis.'' It is identified as a device that measures the ribonucleic acid (RNA) expression level of multiple genes and combines this information to yield a signature (pattern or classifier or index) to aid in prognosis of previously diagnosed breast cancer.

A gene expression profiling test system for breast cancer prognosis is intended to provide prognostic information to aid in clinical evaluation of breast cancer patients. Failure of this device to perform as indicated may lead to erroneous test results. False positive results will misclassify the patient into a higher risk group and false negative results will misclassify the patient into a lower risk group. Misclassification of cancer recurrence risk may lead to incorrect prognosis with attendant psychological distress, inaccurate counseling, and suboptimal patient care.

FDA believes the class II special controls guidance document will aid in mitigating potential risks by providing recommendations on labeling and validation of performance characteristics. The guidance document also provides information on how to meet premarket (510(k)) submission requirements for the device. FDA believes that following the class II special controls guidance document generally addresses the risks to health identified in the previous paragraph. Therefore, on February 6, 2007, FDA issued an order to the petitioner classifying the device into class II. FDA is codifying this classification by adding § 866.6040.

Following the effective date of this final classification rule, any firm submitting a 510(k) premarket notification for a gene expression profiling test system for breast cancer prognosis will need to address the issues covered in the special controls guidance. However, the firm need only show that its device meets the recommendations of the guidance, or in some other way provides equivalent assurance of safety and effectiveness.

Section 510(m) of the act provides that FDA may exempt a class II device from the premarket notification requirements under section 510(k) of the act, if FDA determines that premarket notification is not necessary to provide reasonable assurance of the safety and effectiveness of the device. For this type of device, however, FDA has determined that premarket review of the system's key performance characteristics, test methodology, labeling, and other requirements as outlined in § 807.87, will provide reasonable assurance that acceptable levels of performance for both safety and effectiveness will be addressed before marketing clearance. Thus,

persons who intend to market this type of device must submit to FDA a premarket notification, prior to marketing the device, which contains information about the gene expression profiling test system for breast cancer prognosis they intend to market.

II. What Is the Environmental Impact of This Rule?

The agency has determined under 21 CFR 25.34(b) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

III. What Is the Economic Impact of This Rule?

FDA has examined the impacts of the final rule under Executive Order 12866, the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (Public Law 104–4). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). The agency believes that this final rule is not a significant regulatory action under the Executive Order.

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because classification of these devices into class II will relieve manufacturers of the device of the cost of complying with the premarket approval requirements of section 515 of the act (21 U.S.C. 360e), and may permit small potential competitors to enter the marketplace by lowering their costs, the agency certifies that the final rule will not have a significant impact on a substantial number of small entities.

Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that agencies prepare a written statement, which includes an assessment of anticipated costs and benefits, before proposing ''any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any one year.'' The current threshold after adjustment for inflation is $122 million, using the most current (2005) Implicit Price Deflator for the Gross Domestic Product. FDA does not expect this final rule to result in any 1-year expenditure that would meet or exceed this amount.

IV. Does This Final Rule Have Federalism Implications?

FDA has analyzed this final rule in accordance with the principles set forth in Executive Order 13132. FDA has determined that the rule does not contain policies that have substantial direct effects on the States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government. Accordingly, the agency has concluded that the rule does not contain policies that have federalism implications as defined in the Executive Order and, consequently, a federalism summary impact statement is not required.

V. How Does This Rule Comply With the Paperwork Reduction Act of 1995?

This final rule contains no collections of information. Therefore, clearance by the Office of Management and Budget under the Paperwork Reduction Act of 1995 is not required.

VI. What References Are on Display?

The following reference has been placed on display in the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852, and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. Petition from Agendia BV, dated January 22, 2007.

List of Subjects in 21 CFR Part 866

Biologics, Laboratories, Medical devices.

■ Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 866 is amended as follows:

PART 866—IMMUNOLOGY AND MICROBIOLOGY DEVICES

■ 1. The authority citation for 21 CFR part 866 continues to read as follows:

Authority: 21 U.S.C. 351, 360, 360c, 360e, 360j, 371.

■ 2. Section 866.6040 is added to subpart G to read as follows:

§ 866.6040 Gene expression profiling test system for breast cancer prognosis.

(a) *Identification.* A gene expression profiling test system for breast cancer prognosis is a device that measures the ribonucleic acid (RNA) expression level of multiple genes and combines this information to yield a signature (pattern or classifier or index) to aid in prognosis of previously diagnosed breast cancer.

(b) *Classification.* Class II (special controls). The special control is FDA's guidance document entitled ''Class II Special Controls Guidance Document: Gene Expression Profiling Test System for Breast Cancer Prognosis.'' See § 866.1(e) for the availability of this guidance document.

Dated: May 1, 2007.

Linda S. Kahan,

Deputy Director, Center for Devices and Radiological Health.

[FR Doc. E7–8871 Filed 5–8–07; 8:45 am]

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DEPARTMENT OF THE INTERIOR

Office of Surface Mining Reclamation and Enforcement

30 CFR Part 935

[OH–251–FOR]

Ohio Regulatory Program

AGENCY: Office of Surface Mining Reclamation and Enforcement, Interior.

ACTION: Final rule; approval of amendment.

SUMMARY: We are approving an amendment to the Ohio regulatory program (the ''Ohio program'') under the Surface Mining Control and Reclamation Act of 1977 (SMCRA or the Act). This amendment is intended to remove certain Conflict of Interest provisions from the approved Ohio program that were previously approved by OSM but have not been promulgated by Ohio through their rulemaking process.

EFFECTIVE DATE: May 9, 2007.

FOR FURTHER INFORMATION CONTACT: Mr. George Rieger, Chief, Pittsburgh Field Division, Telephone: (717) 782–4036. E-mail: *grieger@osmre.gov*.

SUPPLEMENTARY INFORMATION:

I. Background on the Ohio Program

Section 503(a) of the Act permits a State to assume primacy for the regulation of surface coal mining and reclamation operations on non-Federal and non-Indian lands within its borders by demonstrating that its program includes, among other things, ''a State