DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 866

[Docket No. FDA–2011–N–0026]

Medical Devices; Immunology and Microbiology Devices; Classification of Ovarian Adnexal Mass Assessment Score Test System

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is classifying the ovarian adnexal mass assessment score test system into class II (special controls). The special control that will apply to these devices is the guidance document entitled "Guidance for Industry and FDA Staff; Class II Special Controls Guidance Document: Ovarian Adnexal Mass Assessment Score Test System." The Agency is classifying these devices into class II (special controls) because special controls, in addition to general controls, will provide a reasonable assurance of safety and effectiveness of these devices and there is sufficient information to establish special controls. Elsewhere in this issue of the **Federal Register**, FDA is announcing the availability of a guidance document that will serve as the special control for these devices.

DATES: *Effective Date:* April 22, 2011. The classification was effective September 11, 2009.

FOR FURTHER INFORMATION CONTACT: Donna Roscoe, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, rm. 5540, Silver Spring, MD 20993–0002, 301–796–6183.

SUPPLEMENTARY INFORMATION:

I. Legal Authority

The Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 301 *et seq.*), as amended by the Medical Device Amendments of 1976 (the 1976 amendments) (Pub. L. 94–295), the Safe Medical Devices Act of 1990 (the SMDA) (Pub. L. 101–629), and the Food and Drug Administration Modernization Act (the FDAMA) (Pub. L. 107–250) established a comprehensive system for the regulation of medical devices intended for human use. Section 513 of the FD&C Act (21 U.S.C. 360c) established three categories (classes) of devices, depending on the regulatory controls needed to provide reasonable assurance of their safety and effectiveness. The three categories of devices are class I (general controls), class II (special controls), and class III (premarket approval).

FDA refers to devices that were not in commercial distribution before May 28, 1976 (the date of enactment of the 1976 amendments), as postamendments devices. Postamendments devices are classified automatically by statute (section 513(f) of the FD&C Act into class III without any FDA rulemaking process. These devices remain in class III and require premarket approval, unless: (1) FDA reclassifies the device into class I or II; (2) FDA issues an order classifying the device into class I or class II in accordance with section 513(f)(2) of the FD&C Act; or (3) FDA issues an order finding the device to be substantially equivalent, under section 513(i), 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 FD&C Act (21 U.S.C. 360(k)) and part 807 of the regulations (21 CFR part 807).

A person may market a preamendments device that has been classified into class III through premarket notification procedures, without submission of a premarket approval application (PMA) until FDA issues a final regulation under section 515(b) of the FD&C Act (21 U.S.C. 360e(b)) requiring premarket approval.

Reclassification of postamendments devices is governed by section 513(f)(3) of the FD&C Act, formerly section 513(f)(2). This section provides that FDA may initiate the reclassification of a device classified into class III under section 513(f)(1) of the FD&C Act, or the manufacturer or importer of a device may petition the Secretary for the issuance of an order classifying the device in class I or class II. FDA's regulations in 21 CFR 860.134 set forth the procedures for the filing and review of a petition for reclassification of such class III devices. In order to change the classification of the device, it is necessary that the proposed new class have sufficient regulatory controls to provide reasonable assurance of the safety and effectiveness of the device for its intended use.

FDAMA added section 513(f)(2) to the FD&C Act which addresses classification of postamendments devices. Section 513(f)(2) of the FD&C Act provides that, upon receipt of a "not substantially equivalent" determination, a 510(k) applicant may request FDA to classify a postamendments device into class I or class II. Within 60 days from the date of such a written request, FDA must classify the device by written order. If FDA classifies the device into class I or II, the applicant has then received clearance to market the device and it can be used as a predicate device for other 510(k)s. It is expected that this process will be used for low risk devices. This process does not apply to devices that have been classified by regulation into class III—i.e., preamendments class III devices, or class III devices for which a PMA is appropriate.

II. Classification

In accordance with section 513(f)(1) of the FD&C Act, FDA issued an order on July 16, 2009, classifying the Vermillion, Inc. OVA1™ Test into 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 that was subsequently reclassified into class I or class II. On July 22, 2009, Vermillion, Inc., submitted a petition requesting classification of the OVA1™ Test under section 513(f)(2) of the FD&C Act. The manufacturer recommended that the device be classified into class II (Ref. 1).

In accordance with section 513(f)(2) of the FD&C Act, FDA reviewed the petition in order to classify the device under the criteria for classification set forth in section 513(a)(1). FDA classifies devices 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, the FDA determined that the device can be classified into class II with the establishment of special controls. FDA believes these special controls will provide reasonable assurance of the safety and effectiveness of the device.

The device is assigned the generic name ovarian adnexal mass assessment score test system, and it is identified as a device that measures one or more proteins in serum or plasma. It yields a single result for the likelihood that an adnexal pelvic mass in a woman, for whom surgery is planned, is malignant. The test is for adjunctive use, in the context of a negative primary clinical and radiological evaluation, to augment the identification of patients whose gynecologic surgery requires oncology expertise and resources.

III. Risks to Health

FDA has identified the risks to health associated with this type of device as a false negative result, a false positive result, and off-label use as a screening test, stand-alone diagnostic test, or as a test to determine whether or not to proceed with surgery. Failure of the system to perform as indicated could lead to inaccurate risk assessment and improper management of patients with ovarian malignancies. Specifically, a falsely low ovarian adnexal mass score could result in a determination that the patient may not have ovarian malignancy, which could lead to less than optimal surgical expertise and resources. A falsely high ovarian adnexal mass score could result in a determination that the patient may have ovarian malignancy which could lead to inappropriate surgical decisions and unnecessary patient anxiety. Off-label use of the test, including use of test results as a stand-alone diagnostic without consideration of other diagnostic testing and clinical assessment, could also pose a risk for morbidity and mortality due to non-referral for oncologic evaluation and treatment.

FDA believes that the special controls guidance document, in addition to general controls, addresses the risks to health identified above and provides reasonable assurance of the safety and effectiveness of the device. Therefore, on September 11, 2009, FDA issued an order to the petitioner classifying the device into class II. FDA is codifying this device by adding § 866.6050.

IV. 510(k) Premarket Notification

Following the effective date of this final classification rule, any firm submitting a 510(k) premarket notification for ovarian adnexal mass assessment score test system 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 FD&C Act provides that FDA may exempt a class II device from the premarket notification requirements under section 510(k), 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, FDA has determined because of the risks of false positives and negatives and off label use that premarket notification is necessary to provide reasonable assurance of the safety and effectiveness of the device and, therefore, this type of device is not exempt from premarket notification requirements. 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 ovarian adnexal mass assessment score test system they intend to market.

V. Environmental Impact

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.

VI. Analysis of Impacts

FDA has examined the impacts of the final rule under Executive Order 12866 and the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (Pub. L. 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 this rule is deregulatory and imposes no new burdens, the Agency certifies that the final rule will not have a significant economic 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 $135 million, using the most current (2009) 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.

A. Background

An ovarian adnexal mass assessment test system is a device that measures one or more proteins in serum or plasma to yield a single result for the likelihood that an adnexal pelvic mass in a woman for whom surgery is planned is malignant. Such a test would identify women who would benefit from referral to a gynecological oncologist, despite negative results from other clinical and radiographic tests for ovarian cancer.

The ovarian adnexal mass assessment test system device is currently classified into class III, the highest level of regulatory oversight. The device was initially placed in this classification automatically because there was no predicate device to which it could be found substantially equivalent. Manufacturers of ovarian adnexal mass assessment test systems, as makers of class III devices, bear all costs associated with premarket approval, including the cost of submitting the premarket approval application (PMA) and payment of user fees. The costs associated with the submission of the PMA are substantial, potentially reaching $1,000,000.

We are aware of a single manufacturer producing a single product affected by this device classification. The manufacturer submitted a request for Evaluation of Automatic Class III Designation, recommending classification into class II. Placing this device in a classification with less burdensome regulatory requirements affects the current manufacturer and potentially affects others, encouraging future entry into this market.

In response to the manufacturer request, FDA is classifying ovarian adnexal mass assessment test system devices into class II. Based on the experience of FDA reviewers, the Agency concludes that the ovarian adnexal mass assessment test system device would not be safe and effective under general controls. FDA has therefore chosen special controls to address the specific risks of false positives, false negatives, and off-label use. These special controls in addition to the application of general controls would be consistent with the principle of applying the least degree of regulatory control necessary to provide reasonable assurance of safety and effectiveness. The application of this intermediate level of regulatory oversight would be consistent with the treatment of other devices with similar risk profiles.

The special controls recommend a black box warning to reduce the risks of off-label use. The Agency is separately

proposing to require the application of the black box warning to labeling and advertising through notice and comment rulemaking. For the purposes of this analysis, we assume that this final rule will establish special controls with a reference to a black box warning regarding off-label use, but the analysis of the impact of the addition of the warning to the product label will be included in a separate rulemaking.

B. Costs of the Final Rule

This final rule is deregulatory. Device manufacturers currently subject to class III requirements will be subject to the less burdensome requirements for makers of class II devices. Through this classification, manufacturers of ovarian adnexal mass assessment test system devices will be relieved of the obligation to submit a PMA prior to marketing. The cost of submitting a PMA can reach $1,000,000, plus user fees of an additional $217,787 in FY 2010, increasing to $256,384 in 2012. This device classification will substantially reduce an existing burden on manufacturers of ovarian adnexal mass assessment test system devices. Considering the cost of submitting a PMA plus the relevant user fees, the reduction could be $1,000,000 per device.

The Regulatory Flexibility Act requires Agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. Classification of the affected device into class II after it had automatically been placed in class III will relieve manufacturers of the cost of complying with the premarket approval requirements of section 515 of the FD&C Act. Because of the reduced burden, the Agency does not believe that this final rule will have a significant economic impact on a substantial number of small entities.

VII. Federalism

FDA has analyzed this final rule in accordance with the principles set forth in Executive Order 13132. Section 4(a) of the Executive Order requires Agencies to "construe * * * a Federal statute to preempt State law only where the statute contains an express preemption provision or there is some other clear evidence that the Congress intended preemption of State law, or where the exercise of State authority conflicts with the exercise of Federal authority under the Federal statute." Federal law includes an express preemption provision that preempts certain state requirements "different or in addition to" certain federal requirements applicable to devices. 21 U.S.C. 360k; *See Medtronic* v. *Lohr,* 518 U.S. 470 (1996); *Riegel* v. *Medtronic, Inc.,* 552 U.S. 312 (2008). The special controls established by this rulemaking create "requirements" to address each identified risk to health presented by these specific medical devices under 21 U.S.C. 360k, even though product sponsors may have flexibility in how they meet those requirements. Cf. *Papike* v. *Tambrands, Inc.,* 107 F.3d 737, 740–42 (9th Cir. 1997).

VIII. Paperwork Reduction Act of 1995

This final rule establishes as special controls a guidance document that refers to previously approved collections of information found in other FDA regulations. These collections of information are subject to review by the Office of Management and Budget under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520). Elsewhere in this issue of the **Federal Register**, FDA is publishing a notice announcing the availability of the guidance document entitled "Guidance for Industry and FDA Staff; Class II Special Controls Guidance Document: Ovarian Adnexal Mass Assessment Score Test System." The notice contains an analysis of the paperwork burden for the guidance.

IX. References

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 Vermillion, Inc., for reclassification of the OVA1™ Test submitted July 22, 2009.

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 866.6050 is added to subpart G to read as follows:

§ 866.6050 Ovarian adnexal mass assessment score test system.

(a) *Identification.* An ovarian/adnexal mass assessment test system is a device that measures one or more proteins in serum or plasma. It yields a single result for the likelihood that an adnexal pelvic mass in a woman, for whom surgery is planned, is malignant. The test is for adjunctive use, in the context of a negative primary clinical and radiological evaluation, to augment the identification of patients whose gynecologic surgery requires oncology expertise and resources.

(b) *Classification.* Class II (special controls). The special control for this device is FDA's guidance document entitled "Class II Special Controls Guidance Document: Ovarian Adnexal Mass Assessment Score Test System." For the availability of this guidance document, *see* § 866.1(e).

Dated: March 16, 2011.

Leslie Kux,

Acting Assistant Commissioner for Policy.

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DEPARTMENT OF HOMELAND SECURITY

Coast Guard

33 CFR Part 117

[Docket No. USCG–2011–0100]

RIN 1625–AA09

Drawbridge Operation Regulation; Buffalo Bayou, Mile 4.3, Houston, Harris County, TX

AGENCY: Coast Guard, DHS.

ACTION: Final rule.

SUMMARY: The Coast Guard is removing the existing drawbridge operation regulation for the drawbridge across Buffalo Bayou, mile 4.3, Houston, Harris County, Texas. The bridge was replaced with a fixed bridge in 1991 and the operating regulation is no longer applicable or necessary.

DATES: This rule is effective March 23, 2011.

ADDRESSES: Documents indicated in this preamble as being available in the docket, are part of docket USCG–2011–0100 and are available by going to *http://www.regulations.gov,* inserting USCG–2011–0100 in the "Keyword" box, and then clicking "Search." This material is also available for inspection or copying at the Docket Management Facility (M–30), U.S. Department of Transportation, West Building Ground