



4160-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 866

[Docket No. FDA-2012-N-0165]

Medical Devices; Immunology and Microbiology Devices; Classification of Norovirus

Serological Reagents

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is classifying norovirus serological reagents into class II (special controls). The special control that will apply to these devices is the guidance document entitled "Class II Special Controls Guidance Document: Norovirus Serological Reagents." 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.

DATES: Effective Date: [INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER]. The classification was effective February 23, 2011.

FOR FURTHER INFORMATION CONTACT:

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SUPPLEMENTARY INFORMATION:

I. Legal Authority

In accordance with section 513(f)(1) of the Federal Food, Drug, and Cosmetic Act (FD&C 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 1976 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 FD&C Act, to a predicate device that does not require premarket approval. The Agency determines whether new devices are substantially equivalent to previous marketed 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 (21 CFR part 807) of FDA's regulations.

Section 513(f)(2) of the FD&C Act provides that any person who submits a premarket notification under section 510(k) of the FD&C 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), request FDA to classify the device under the criteria set forth in section 513(a)(1). 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 FD&C Act).

II. Classification

In accordance with section 513(f)(1) of the FD&C Act, FDA issued an order on February 14, 2011, classifying the RIDASCREEN® Norovirus 3rd Generation EIA 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 February 16, 2011, Lehnus and Associates Consulting, on behalf of R-Biopharm AG, submitted a petition requesting classification of the RIDASCREEN® Norovirus 3rd Generation EIA 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, 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 norovirus serological reagents, and this device type is identified as devices that consist of antigens and antisera used in serological tests to detect the presence of norovirus antigens in fecal samples. These devices aid in the diagnosis of

norovirus infection in the setting of an individual patient with symptoms of acute gastroenteritis when the individual patient is epidemiologically linked to other patients with symptoms of acute gastroenteritis and/or aid in the identification of norovirus as the etiology of an outbreak of acute gastroenteritis in the setting of epidemiologically linked patients with symptoms of acute gastroenteritis.

III. Risks to Health

FDA has identified the risks to health associated with this type of device as a false negative result and a false positive result. A false positive test result for an individual may lead to a potential delay in needed antibiotic treatment (when appropriate) and possibly less thorough laboratory evaluation for the true cause of illness; in the setting of an outbreak investigation, a false positive result may lead to unnecessary environmental interventions and/or significant patient restrictions. A false negative test result for an individual may lead to potentially unnecessary treatment for other causes of acute gastroenteritis, including possible antibiotic exposure; in the setting of an outbreak, a false negative result may lead to delay in recognizing the cause of the outbreak and additional spread of norovirus infection.

FDA has identified the following recommended mitigation measures to address these risks to health associated specifically with this type of device.

Table 1--Risks to Health and Recommended Mitigation Measures

Identified Risks	Recommended Mitigation Measures
A false positive test result for an individual may lead to a potential delay in needed antibiotic treatment (when appropriate) and possibly less thorough laboratory evaluation for the true cause of illness; in the setting of an outbreak investigation, a false positive result may lead to unnecessary environmental interventions and/or significant patient restrictions.	Performance Characteristics Labeling
A false negative test result for an individual may lead to potentially unnecessary treatment for other causes of acute gastroenteritis, including possible antibiotic exposure; in the setting of an outbreak, a false negative result may lead to delay in recognizing the cause of the outbreak and additional spread of norovirus infection.	Performance Characteristics Labeling

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. FDA believes that the special controls guidance document, in addition to general controls, addresses the risks to health identified previously and provides reasonable assurance of the safety and effectiveness of the device. Therefore, on February 23, 2011, FDA issued an order to the petitioner classifying the device into class II. FDA is codifying this device by adding § 866.3395.

IV. 510(k) Premarket Notification

Following the effective date of this final classification rule, any firm submitting a 510(k) premarket notification for a norovirus serological reagents 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 false negatives 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 norovirus serological reagents they intend to market.

V. Environmental Impact

The Agency has determined under 21 CFR 25.34(b) that this action is of 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, Executive Order 13563, the Regulatory Flexibility Act (Public Law 96-354) (5 U.S.C. 601-612), and the Unfunded Mandates Reform Act of 1995 (Public Law 104-4). Executive Orders 12866 and 13563 direct 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 proposed rule is not a significant regulatory action as defined by Executive Order 12866.

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 proposes to certify 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 \$136 million, using the most current (2010) Implicit Price Deflator for the Gross Domestic Product. FDA does not expect this proposed rule to result in any 1-year expenditure that would meet or exceed this amount.

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 "Class II Special Controls Guidance Document: Norovirus Serological Reagents." 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 R-Biopharm AG, c/o Lehnus and Associates, dated February 15, 2011.

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 866.3395 is added to subpart D to read as follows:

§ 866.3395 Norovirus serological reagents.

(a) Identification. Norovirus serological reagents are devices that consist of antigens and antisera used in serological tests to detect the presence of norovirus antigens in fecal samples. These devices aid in the diagnosis of norovirus infection in the setting of an individual patient

with symptoms of acute gastroenteritis when the individual patient is epidemiologically linked to other patients with symptoms of acute gastroenteritis and/or aid in the identification of norovirus as the etiology of an outbreak of acute gastroenteritis in the setting of epidemiologically linked patients with symptoms of acute gastroenteritis.

(b) Classification. Class II (special controls). The special control is FDA's guidance document entitled "Class II Special Controls Guidance Document: Norovirus Serological Reagents." See § 866.1(e) for the availability of this guidance document.

Dated: March 5, 2012.

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