The device to be substantially equivalent, in accordance with section 513(f)(1) of the FD&C Act (21 U.S.C. 360c(f)(1)), 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 FDA's regulations (21 CFR part 807).

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 must, within 60 days of receiving such a request, classify the device by written order. This classification will be the initial classification of the device type. Within 30 days after the issuance of an order classifying the device, FDA must publish a notice in the Federal Register announcing this classification (section 513(f)(2) of the FD&C Act).

In accordance with section 513(f)(1) of the FD&C Act, FDA issued an order on April 27, 2007, classifying the NeuroStar® TMS System for the treatment of major depressive disorder in patients who have failed to receive benefit from one antidepressant trial 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 May 23, 2007, Neurionetics, Inc., submitted a petition requesting classification, under section 513(f)(2) of the FD&C Act, of the NeuroStar® TMS System for the treatment of major depressive disorder in patients who have failed to receive benefit from one antidepressant trial. 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 513(a)(1) of the FD&C Act. 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 rTMS system can be classified into class II with the establishment of special controls. FDA believes that these special controls, in addition to general controls, are adequate to provide reasonable assurance of the safety and effectiveness of the device. Elsewhere in this issue of the Federal Register, FDA is announcing the availability of a guidance document entitled “Class II Special Controls Guidance Document: Repetitive Transcranial Magnetic Stimulation System,” which will serve as the special control for rTMS systems.

The device is assigned the generic name “Repetitive Transcranial Magnetic Stimulation System.” A repetitive transcranial magnetic stimulation system is an external device that delivers transcranial repetitive pulsed magnetic fields of sufficient magnitude to induce neural action potentials in the prefrontal cortex to treat the symptoms of major depressive disorder without inducing seizure in patients who have failed at least one antidepressant medication and are currently not on any antidepressant therapy. FDA has identified the risks to health associated with this type of device as follows:

- Failure to identify correct patient population;
- Ineffective treatment;
- Seizure;
- Scalp discomfort, scalp burn, or other adverse effects;
- Magnetic field effects on functioning of other medical devices;
- Adverse tissue reaction;
- Hazards associated with electrical equipment;
- Hazards caused by electromagnetic interference and electrostatic discharge hazards; and
- Hearing loss.

FDA believes that the class II special controls guidance document will aid in
mitigating the potential risks to health as described in table 1 of this document.

<table>
<thead>
<tr>
<th>Identified risk</th>
<th>Mitigation measures</th>
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<tbody>
<tr>
<td>Failure to identify correct patient population</td>
<td>Clinical testing.</td>
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<td>Ineffective treatment</td>
<td>Nonclinical analysis and testing.</td>
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<td></td>
<td>Software life cycle and risk management.</td>
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<td></td>
<td>Clinical testing.</td>
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<td></td>
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<td></td>
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<td>Nonclinical analysis and testing.</td>
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<tr>
<td>Magnetic field effects on functioning of other medical devices</td>
<td>Biocompatibility.</td>
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<tr>
<td>Adverse tissue reaction</td>
<td>Electrical equipment safety.</td>
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<td>Hazards associated with electrical equipment</td>
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<td>Hazards caused by electromagnetic interference and electrostatic discharge hazards</td>
<td>Electromagnetic compatibility.</td>
</tr>
<tr>
<td>Hearing loss</td>
<td>Labeling.</td>
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</tbody>
</table>

FDA believes that the special controls, in addition to general controls, address the risks to health identified previously in this document and provide reasonable assurances of the safety and effectiveness of the device type. Thus, on October 7, 2008, FDA issued an order to the petitioner classifying the device into class II. FDA is codifying this classification by adding § 882.5805.

Following the effective date of the final classification rule, manufacturers will need to address the issues covered in the special controls guidance. However, the manufacturer 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 requirement 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 that premarket notification is not necessary to provide reasonable assurance of the safety and effectiveness of the device and, therefore, the 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 rTMS system 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. Thus, 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, Executive Order 13563, the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (Pub. L. 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 final rule is not a significant regulatory action under 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 classification of this device into class II will relieve manufacturers of the cost of complying with the premarket approval requirements of section 515 of the FD&C 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 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 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. 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 from or in addition to” certain Federal requirements applicable to devices. 21 U.S.C. 360k. See Medtronic, Inc. v. Lohr, 518 U.S. 470 (1996); and Riegel v. Medtronic, Inc., 552 U.S. 312 (2008). The special controls established by this final rule 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).

V. How does this rule comply with the paperwork reduction Act of 1995?

FDA concludes that this final rule contains no new collections of information. Therefore, clearance by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501–3520) 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 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.


List of Subjects in 21 CFR Part 882

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 882 is amended as follows:

PART 882—NEUROLOGICAL DEVICES

§ 882.5805 Repetitive transcranial magnetic stimulation system.

(a) Identification. A repetitive transcranial magnetic stimulation system is an external device that delivers transcranial repetitive pulsed magnetic fields of sufficient magnitude to induce neural action potentials in the prefrontal cortex to treat the symptoms of major depressive disorder without inducing seizure in patients who have failed at least one antidepressant medication and are currently not on any antidepressant therapy.

(b) Classification. Class II (special controls). The special control is FDA’s “Class II Special Controls Guidance Document: Repetitive Transcranial Magnetic Stimulation System.” See § 882.1(e) for the availability of this guidance document.

Dated: July 20, 2011.

Nancy K. Stade,

Deputy Director for Policy, Center for Devices and Radiological Health.