(44 U.S.C. 3501–3520). The collections of information in 21 CFR part 812 have been approved under OMB control number 0910–0078; the collections of information in 21 CFR part 807, subpart E have been approved under OMB control number 0910–0120; the collections of information in 21 CFR part 814, subpart B have been approved under OMB control number 0910–0231; and the collections of information under 21 CFR part 801 have been approved under OMB control number 0910–0485.

### XI. Proposed Effective Date

FDA is proposing that any final rule based on this proposal become effective on the date of its publication in the **Federal Register** or at a later date if stated in the final rule.

### XII. Comments

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**), either electronic or written comments regarding this document. It is only necessary to send one set of comments. It is no longer necessary to send two copies of mailed comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

### XIII. References

The following references have 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. (FDA has verified the Web site address, but FDA is not responsible for any subsequent changes to the Web site after this document publishes in the **Federal Register**.)

1. Geiger, Dale R, ''FY 2003 and 2004 Unit Costs for the Process of Medical Device Review,'' September 2005, *http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/Overview/MedicalDeviceUserFeeandModernizationActMDUFMA/umc109216.*

2. U.S. Department of Commerce, Bureau of Economic Analysis, National Income and Product Accounts Table 1.1.9, *http://www.bea.gov/national/nipaweb/SelectTable.asp*, accessed March 25, 2011.

### List of Subjects in 21 CFR Part 870

Medical devices.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 CFR part 870 be amended as follows:

## PART 870—CARDIOVASCULAR DEVICES

1. The authority citation for 21 CFR part 870 continues to read as follows:

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

2. Section 870.3680 is amended by revising paragraph (c) to read as follows:

**§ 870.3680 Cardiovascular permanent or temporary pacemaker electrode.**

* * * * *

(c) *Date PMA or notice of completion of PDP is required.* A PMA or notice of completion of a PDP is required to be filed with the Food and Drug Administration on or before [A DATE WILL BE ADDED 90 DAYS AFTER DATE OF PUBLICATION OF A FUTURE FINAL RULE IN THE **FEDERAL REGISTER**], for any permanent pacemaker electrode that was in commercial distribution before May 28, 1976, or that has, on or before [A DATE WILL BE ADDED 90 DAYS AFTER DATE OF PUBLICATION OF A FUTURE FINAL RULE IN THE **FEDERAL REGISTER**], been found to be substantially equivalent to any permanent pacemaker electrode that was in commercial distribution before May 28, 1976. Any other permanent pacemaker electrode shall have an approved PMA or declared completed PDP in effect before being placed in commercial distribution.

Dated: August 2, 2011.

**Nancy K. Stade,**

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

[FR Doc. 2011–19959 Filed 8–5–11; 8:45 am]

**BILLING CODE 4160–01–P**

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

### 21 CFR Part 882

**[Docket No. FDA–2011–N–0504]**

## Effective Date of Requirement for Premarket Approval for Cranial Electrotherapy Stimulator

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Proposed rule.

**SUMMARY:** The Food and Drug Administration (FDA) is proposing to require the filing of a premarket approval application (PMA) or a notice of completion of a product development protocol (PDP) for the Cranial Electrotherapy Stimulator. The Agency is also summarizing its proposed findings regarding the degree of risk of illness or injury designed to be eliminated or reduced by requiring this device to meet the statute's approval requirements and the benefits to the public from the use of the device. In addition, FDA is announcing the opportunity for interested persons to request that the Agency change the classification of the cranial electrotherapy stimulator based on new information. This action implements certain statutory requirements.

**DATES:** Submit either electronic or written comments by November 7, 2011. Submit requests for a change in classification by August 23, 2011. FDA intends that, if a final rule based on this proposed rule is issued, anyone who wishes to continue to market the device will need to submit a PMA within 90 days of the effective date of the final rule. Please see section XII of this document for the effective date of any final rule that may publish based on this proposal.

**ADDRESSES:** You may submit comments, identified by Docket No. FDA–2011–N–0504 by any of the following methods:

### Electronic Submissions

Submit electronic comments in the following ways:

- Federal eRulemaking Portal: *http://www.regulations.gov.* Follow the instructions for submitting comments.

### Written Submissions

Submit written submissions in the following ways:

- *Fax:* 301–827–6870.
- *Mail/Hand delivery/Courier (For paper, disk, or CD–ROM submissions):* Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

*Instructions:* All submissions received must include the Agency name and Docket No. FDA–2011–N–0504 for this rulemaking. All comments received may be posted without change to *http://www.regulations.gov,* including any personal information provided. For additional information on submitting comments, see the ''Comments'' heading of the **SUPPLEMENTARY INFORMATION** section of this document.

*Docket:* For access to the docket to read background documents or comments received, go to *http://www.regulations.gov* and insert the docket number, found in brackets in the heading of this document, into the ''Search'' box and follow the prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

**FOR FURTHER INFORMATION CONTACT:** Timothy Marjenin, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, rm. 2258, Silver Spring, MD 20993–0002, 301–796–6502, e-mail: *timothy.marjenin@fda.hhs.gov.*

**SUPPLEMENTARY INFORMATION:**

## I. Background—Regulatory Authorities

The Federal Food, Drug, and Cosmetic Act (the FD&C Act), as amended by the Medical Device Amendments of 1976 (the 1976 amendments) (Pub. L. 94–295), the Safe Medical Devices Act of 1990 (SMDA) (Pub. L. 101–629), and the Food and Drug Administration Modernization Act of 1997 (FDAMA) (Pub. L. 105–115), the Medical Device User Fee and Modernization Act of 2002 (MDUFMA) (Pub. L. 107–250), the Medical Devices Technical Corrections Act (Pub. L. 108–214), and the Food and Drug Administration Amendments Act of 2007 (Pub. L. 110–85), among other amendments, establish 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, reflecting 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).

Under section 513 of the FD&C Act, devices that were in commercial distribution before the enactment of the 1976 amendments, May 28, 1976 (generally referred to as preamendments devices), are classified after FDA has: (1) Received a recommendation from a device classification panel (an FDA advisory committee); (2) published the panel's recommendation for comment, along with a proposed regulation classifying the device; and (3) published a final regulation classifying the device. FDA has classified most preamendments devices under these procedures.

Devices that were not in commercial distribution prior to May 28, 1976 (generally referred to as postamendments devices) are automatically classified by section 513(f) of the FD&C Act into class III without any FDA rulemaking process. Those devices remain in class III and require premarket approval unless, and until, the device is 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 predicate devices by means of premarket notification procedures in section 510(k) of the FD&C Act (21 U.S.C. 360(k)) and 21 CFR part 807.

A preamendments device that has been classified into class III may be marketed by means of premarket notification procedures (510(k) process) without submission of a 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. Section 515(b)(1) of the FD&C Act establishes the requirement that a preamendments device that FDA has classified into class III is subject to premarket approval. A preamendments class III device may be commercially distributed without an approved PMA or a notice of completion of a PDP until 90 days after FDA issues a final rule requiring premarket approval for the device, or 30 months after final classification of the device under section 513 of the FD&C Act, whichever is later. Also, a preamendments device subject to the rulemaking procedure under section 515(b) of the FD&C Act is not required to have an approved investigational device exemption (IDE) (see part 812 (21 CFR part 812)) contemporaneous with its interstate distribution until the date identified by FDA in the final rule requiring the submission of a PMA for the device. At that time, an IDE is required only if a PMA has not been submitted or a PDP completed.

Section 515(b)(2)(A) of the FD&C Act provides that a proceeding to issue a final rule to require premarket approval shall be initiated by publication of a notice of proposed rulemaking containing: (1) The regulation; (2) proposed findings with respect to the degree of risk of illness or injury designed to be eliminated or reduced by requiring the device to have an approved PMA or a declared completed PDP and the benefit to the public from the use of the device; (3) an opportunity for the submission of comments on the proposed rule and the proposed findings; and (4) an opportunity to request a change in the classification of the device based on new information relevant to the classification of the device.

Section 515(b)(2)(B) of the FD&C Act provides that if FDA receives a request for a change in the classification of the device within 15 days of the publication of the notice, FDA shall, within 60 days of the publication of the notice, consult with the appropriate FDA advisory committee and publish a notice denying the request for change in reclassification or announcing its intent to initiate a proceeding to reclassify the device under section 513(e) of the FD&C Act. Section 515(b)(3) of the FD&C Act provides that FDA shall, after the close of the comment period on the proposed rule and consideration of any comments received, issue a final rule to require premarket approval or publish a document terminating the proceeding together with the reasons for such termination. If FDA terminates the proceeding, FDA is required to initiate reclassification of the device under section 513(e) of the FD&C Act, unless the reason for termination is that the device is a banned device under section 516 of the FD&C Act (21 U.S.C. 360f).

When a proposed rule to require premarket approval for a preamendments device is finalized, section 501(f)(2)(B) of the FD&C Act (21 U.S.C. 351(f)(2)(B)) requires that a PMA or notice of completion of a PDP for any such device be filed within 90 days of the date of issuance of the final rule or 30 months after the final classification of the device under section 513 of the FD&C Act, whichever is later. If a PMA or notice of completion of a PDP is not filed by the later of the two dates, commercial distribution of the device is required to cease since the device would be deemed adulterated under section 501(f) of the FD&C Act.

The device may, however, be distributed for investigational use if the manufacturer, importer, or other sponsor of the device complies with the IDE regulations. If a PMA or notice of completion of a PDP is not filed by the later of the two dates, and the device does not comply with IDE regulations, the device is deemed to be adulterated within the meaning of section 501(f)(1)(A) of the FD&C Act, and subject to seizure and condemnation under section 304 of the FD&C Act (21 U.S.C. 334) if its distribution continues. Shipment of devices in interstate commerce will be subject to injunction under section 302 of the FD&C Act (21 U.S.C. 332), and the individuals responsible for such shipment will be subject to prosecution under section 303 of the FD&C Act (21 U.S.C. 333). In the past, FDA has requested that manufacturers take action to prevent the further use of devices for which no PMA or PDP has been filed and may determine that such a request is appropriate for the cranial electrotherapy stimulator.

The FD&C Act does not permit an extension of the 90-day period after issuance of a final rule within which an application or a notice is required to be filed. The House Report on the 1976 amendments states that: ''[t]he thirty month grace period afforded after

classification of a device into class III * * * is sufficient time for manufacturers and importers to develop the data and conduct the investigations necessary to support an application for premarket approval (H. Rept. 94–853, 94th Cong., 2d sess. 42 (1976)).''

The SMDA added section 515(i) to the FD&C Act requiring FDA to review the classification of preamendments class III devices for which no final rule requiring the submission of PMAs has been issued, and to determine whether or not each device should be reclassified into class I or class II or remain in class III. For devices remaining in class III, the SMDA directed FDA to develop a schedule for issuing regulations to require premarket approval. The SMDA does not, however, prevent FDA from proceeding immediately to rulemaking under section 515(b) of the FD&C Act on specific devices, in the interest of public health, independent of the procedures of section 515(i). Proceeding directly to rulemaking under section 515(b) of the FD&C Act is consistent with Congress' objective in enacting section 515(i), i.e., that preamendments class III devices for which PMAs have not been previously required either be reclassified to class I or class II or be subject to the requirements of premarket approval. Moreover, in this proposal, interested persons are being offered the opportunity to request reclassification of the cranial electrotherapy stimulator.

## II. Dates New Requirements Apply

In accordance with section 515(b) of the FD&C Act, FDA is proposing to require that a PMA or a notice of completion of a PDP be filed with the Agency for the cranial electrotherapy stimulator within 90 days after issuance of any final rule based on this proposal. An applicant whose device was legally in commercial distribution before May 28, 1976, or whose device has been found to be substantially equivalent to such a device, will be permitted to continue marketing such class III devices during FDA's review of the PMA or notice of completion of the PDP. FDA intends to review any PMA for the device within 180 days, and any notice of completion of a PDP for the device within 90 days of the date of filing. FDA cautions that under section 515(d)(1)(B)(i) of the FD&C Act, the Agency may not enter into an agreement to extend the review period for a PMA beyond 180 days unless the Agency finds that ''the continued availability of the device is necessary for the public health.''

FDA intends that under § 812.2(d), the preamble to any final rule based on this proposal will state that, as of the date on which the filing of a PMA or a notice of completion of a PDP is required to be filed, the exemptions from the requirements of the IDE regulations for preamendments class III devices in § 812.2(c)(1) and (c)(2) will cease to apply to any device that is: (1) Not legally on the market on or before that date or (2) legally on the market on or before that date but for which a PMA or notice of completion of a PDP is not filed by that date, or for which PMA approval has been denied or withdrawn.

If a PMA or notice of completion of a PDP for the cranial electrotherapy stimulator is not filed with FDA within 90 days after the date of issuance of any final rule requiring premarket approval for the device, commercial distribution of the device must cease. The device may be distributed for investigational use only if the requirements of the IDE regulations are met. The requirements for significant risk devices include submitting an IDE application to FDA for its review and approval. An approved IDE is required to be in effect before an investigation of the device may be initiated or continued under § 812.30. FDA, therefore, cautions that IDE applications should be submitted to FDA at least 30 days before the end of the 90-day period after the issuance of the final rule to avoid interrupting investigations.

## III. Proposed Findings With Respect to Risks and Benefits

As required by section 515(b) of the FD&C Act, FDA is publishing its proposed findings regarding: (1) The degree of risk of illness or injury designed to be eliminated or reduced by requiring that the cranial electrotherapy stimulator have an approved PMA or a declared completed PDP and (2) the benefits to the public from the use of the cranial electrotherapy stimulator.

These findings are based on the reports and recommendations of the advisory committee (panel) for the classification of this device along with information submitted in response to the 515(i) Order, (74 FR 16214, April 9, 2009), and any additional information that FDA has encountered. Additional information regarding the risks as well as classification associated with this device type can be found in the following documents published in the **Federal Register** on these dates: November 28, 1974 (43 FR 55716), September 4, 1979 (44 FR 51770), January 6, 1989 (54 FR 550), August 31, 1993 (58 FR 45865), August 24, 1995 (60 FR 43967), November 22, 1996 (61 FR 59448), January 28, 1997 (62 FR 4023), and June 4, 1997 (62 FR 30456 and 62 FR 30600).

## IV. Devices Subject to This Proposal

Cranial electrotherapy stimulator (21 CFR 882.5800)

### *A. Identification*

A cranial electrotheraphy stimulator is a device that applies electrical current to a patient's head to treat insomnia, depression, or anxiety.

### *B. Summary of Data*

The Neurological Devices Panel that discussed original classification for the cranial electrotherapy stimulator (CES) device in 1977 and 1978 ultimately recommended that the device be classified into class III because satisfactory device effectiveness had not been demonstrated. The panel considered information from the National Research Council, which reviewed 88 published studies on CES and concluded that the device has not been shown to be effective in treating any of the conditions for which it was prescribed. In addition, the panel indicated that it was not possible to establish an adequate performance standard for CES because the characteristics of the electrical current necessary for potential effectiveness were not known. The panel believed that general controls would not provide sufficient control over these characteristics, and that the device presented a potential unreasonable risk of illness or injury to the patient if the practitioner relied on the device, and it was ineffective in treating the patient's illness. Therefore, the panel recommended that premarket approval was necessary to assure the safety and effectiveness of CES devices.

In support of a subsequent proposed rule in 1993 for classification of CES into class III, FDA performed a literature review and identified additional studies that had been performed for CES. After a review of the scientific literature, FDA concluded that the effectiveness of CES had still not been established by adequate scientific evidence.

FDA has performed a literature search for studies of CES published after the 1993 proposed rule (January 1, 1993, to present). Many studies were excluded from further review because they were conducted on very specific populations (*e.g.,* alcoholics or other types of substance abuse), and therefore were not representative of the general population suffering from insomnia, anxiety, or depression. Six studies were identified for further review (Refs. 1 through 6). FDA also identified two relevant meta-analyses (Refs. 7 and 8).

The Bystritsky et al. study (Ref. 1) was conducted open-label, and on only 12

subjects. The study involved observational baseline versus post-treatment without a control and therefore provided insufficient evidence of safety and effectiveness. The Heffernan study (Ref. 2) concludes that a single CES treatment may have physiologic effects; however, no outcomes of anxiety, depression or insomnia were measured and the study was conducted on only 20 subjects. The Overcash study (Ref. 3) was a retrospective study design and used an anxiety rating scale that was not validated. The Voris study (Ref. 4) analyzed only a subgroup of ''psychiatric subjects'' which included many types of anxiety disorders as well as non-anxiety psychiatric disorders. The subgroup represents a diagnostically heterogeneous group. The subgroup analysis was not pre-specified and the number of subjects per subgroup was not specified. The Hyun study (Ref. 5) was a randomized controlled trial of 60 subjects. However, the indication under investigation was preoperative anxiety, which may not be indicative of an Axis I anxiety disorder. Moreover, the outcome measure, a 5-point Likert scale rating of anxiety, was not a standardized validated rating instrument. The Winick study (Ref. 6), which was a randomized controlled trial of 33 subjects with anxiety prior to dental procedures and utilized a 7-point Likert scale, suffers from the same limitations as the Hyun study.

The O'Conner meta-analysis (Ref. 7) examined the effect of CES on reduction of primary and secondary withdrawal symptoms among various chemically dependent populations. The results of this analysis do not relate to the question of safety and effectiveness since the labeled indications for CES currently include insomnia, depression, or anxiety, and not withdrawal symptoms of chemical dependence. The Klawansky meta-analysis (Ref. 8) was based on an examination of literature on CES versus sham treatment. Although the analysis showed CES to be more effective than sham for anxiety, the study populations showed great heterogeneity of diagnostic categories (*e.g.,* in many cases anxiety was not the primary diagnosis, but rather one of a number of symptomatic outcome measures collected during a trial). Therefore, it is unclear whether the finding can be generalized to support the effectiveness of CES in homogeneous populations of individuals suffering from anxiety, depression, or insomnia. Also, many of the studies evaluated in the Klawansky meta-analysis involved insufficient blinding.

FDA has concluded from a review of the scientific literature and the information provided in the 515(i) call for information (74 FR 16214) that the effectiveness of CES has not been established by adequate scientific evidence and the Agency continues to agree with the panel's recommendation.

*C. Risks to Health*

- *Worsening of the condition being treated*—If the device is not effective and the patient is not treated in a conventional manner, the patient's psychological condition may worsen.
- *Skin irritation*—The electrodes or the conductive cream used with the electrodes may cause skin irritation.
- *Headaches*—Reported cases of adverse effects of CES devices include headaches following treatment with electrical stimulation.
- *Potential risk of seizure*—electrical stimulation of the brain may result in seizures, particularly in patients with a history of seizure.
- *Blurred vision*—placement of electrodes over the eyes may cause blurred vision.
- *Potential adverse effects from electrical stimulation of the brain*—The physiological effects associated with electrical stimulation of the brain by these devices have not been studied systematically; therefore, adverse effects which may be caused by these electrical stimuli remain unknown.

## V. PMA Requirements

A PMA for the cranial electrotherapy simulator must include the information required by section 515(c)(1) of the FD&C Act. Such a PMA should also include a detailed discussion of the risks identified previously, as well as a discussion of the effectiveness of the device for which premarket approval is sought. In addition, a PMA must include all data and information on: (1) Any risks known, or that should be reasonably known, to the applicant that have not been identified in this document; (2) the effectiveness of the device that is the subject of the application; and (3) full reports of all preclinical and clinical information from investigations on the safety and effectiveness of the device for which premarket approval is sought.

A PMA must include valid scientific evidence to demonstrate reasonable assurance of the safety and effectiveness of the device for its intended use (see § 860.7(c)(2)). Valid scientific evidence is ''evidence from well-controlled investigations, partially controlled studies, studies and objective trials without matched controls, well-documented case histories conducted by qualified experts, and reports of significant human experience with a marketed device, from which it can fairly and responsibly be concluded by qualified experts that there is reasonable assurance of the safety and effectiveness of a device under its conditions of use. * * * Isolated case reports, random experience, reports lacking sufficient details to permit scientific evaluation, and unsubstantiated opinions are not regarded as valid scientific evidence to show safety or effectiveness. * * *'' (21 CFR 860.7(c)(2)).

## VI. PDP Requirements

A PDP for the cranial electrotherapy stimulator may be submitted in lieu of a PMA, and must follow the procedures outlined in section 515(f) of the FD&C Act. A PDP must provide: (1) A description of the device, (2) preclinical trial information (if any), (3) clinical trial information (if any), (4) a description of the manufacturing and processing of the device, (5) the labeling of the device, and (6) all other relevant information about the device. In addition, the PDP must include progress reports and records of the trials conducted under the protocol on the safety and effectiveness of the device.

## VII. Opportunity To Request a Change in Classification

Before requiring the filing of a PMA or notice of completion of a PDP for a device, FDA is required by section 515(b)(2)(A)(i) through (b)(2)(A)(iv) of the FD&C Act and § 860.132 to provide an opportunity for interested persons to request a change in the classification of the device based on new information relevant to the classification. Any proceeding to reclassify the device will be under the authority of section 513(e) of the FD&C Act.

A request for a change in the classification of these devices is to be in the form of a reclassification petition containing the information required by § 860.123, including new information relevant to the classification of the device.

The Agency advises that to ensure timely filing of any such petition, any request should be submitted to the Division of Dockets Management (see **ADDRESSES**) and not to the address provided in § 860.123(b)(1). If a timely request for a change in the classification of these devices is submitted, the Agency will, within 60 days after receipt of the petition, and after consultation with the appropriate FDA resources, publish an order in the **Federal Register** that either denies the

request or gives notice of its intent to initiate a change in the classification of the device in accordance with section 513(e) of the FD&C Act and 21 CFR 860.130 of the regulations.

**VIII. Environmental Impact**

The Agency has determined under 21 CFR 25.30(h) 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.

**IX. Analysis of Impacts**

FDA has examined the impacts of the proposed 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 proposed rule is not a significant 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. The Agency proposes to certify that the rule would 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 one-year expenditure that would meet or exceed this amount.

*A. Benefits of the Proposed Rule*

The proposed requirement for PMAs or PDPs for CES would generate social benefits equal to the value of the information generated by the safety and effectiveness tests that CES producers would be required to conduct under the proposed call for PMAs or PDPs. Provided first to FDA, this information would eventually assist physicians, patients and insurance providers in making more informed decisions about CES.

There is reason to believe that current decisions about CES use are based on incomplete information. In their 1995 meta-analysis of CES research, Klawansky et al. (Ref. 8) find that most CES studies in the literature are beset with weaknesses, such as small sample size, incomplete statistical reporting, and potential bias from authors who have commercial interests in CES products. Klawansky and coauthors also express concern that only three of the 18 studies they examined were truly double-blinded, and patient blinding may have been insufficient in some cases due to the difficulty of mimicking in sham treatment the sensation produced by CES. More recent literature indicates that there is still much uncertainty about the safety and effectiveness of CES.

If consumers, up until now, have been overestimating the safety and effectiveness of CES devices, then demand for these products would decrease as a result of the call for PMAs or PDPs, and consumers would purchase fewer CES devices and services than under the previous process whereby CES devices were cleared under the 510(k) process. For all the units purchased under the 510(k) clearance process that would not be purchased under the PMA or PDP approval process, society is currently incurring a cost equal to the difference between the producer's cost of producing that unit and the dollar value of the health benefit experienced by the consumer. The avoidance of this cost represents the per-unit benefit to society of the proposed requirement for PMAs or PDPs; summing over all currently-marketed units yields society's total benefit. This sum is bounded above by current consumer expenditure on CES devices (further discussion of this point appears in the Technical Appendix in section IX.D of this document).

Consumer expenditure on CES can be approximated by finding total producer revenue (this is only an approximation because any applicable taxes drive a wedge between expenditure and revenue). FDA estimates that there are approximately 11 producers currently marketing CES devices. Six of these producers appear in FDA's Data universal numbering system database, with sales revenue for the six ranging from $100,000 to $1.2 million per year. Manta.com (Ref. 9) reports sales revenue of less than $0.5 million for one of the producers not appearing in Data universal numbering system. (It appears that few CES producers market non-CES goods or services, so most of the firms' revenue can be attributed to CES sales.) The average annual sales revenue of the 7 producers for whom we have data is $515,000. Assuming that this average equals the CES industry's overall average yields an estimate of annual CES producer revenue of $11 \times \$515{,}000 = \$5.67$ million. As mentioned previously, in the case where additional safety and effectiveness information decreases demand, this revenue total provides an upper bound on the estimated benefit to society of requiring PMAs or PDPs for CES devices.

If the additional testing associated with class III PMA or PDP were to reveal that CES devices are safer and more effective than consumers currently believe, then demand for these products would increase. In this case, consumers currently purchase too few rather than too many CES devices as a result of incomplete information, and the benefit of the requirement for PMAs or PDPs would come from the increased use and associated health benefits of the devices. As discussed in the Technical Appendix in section IX.D of this document, FDA cannot in this case estimate a bound on the total social benefit of requiring PMAs or PDPs. FDA requests comment on this issue and on all methods and results of our benefits estimation.

*B. Costs of the Proposed Rule*

Under the proposed rule, FDA would require producers in this industry to obtain PMA or establish a PDP before marketing new products. Currently, a CES producer receives clearance to market by submitting a 510(k). Therefore, the rule-induced cost per new product would be the difference between the cost of preparing and submitting a PMA application (which we assume to be approximately the same with PDP as with traditional PMA) and the cost of preparing and submitting a 510(k) application. Blozan and Tucker (Ref. 10) estimate the cost of an average 510(k) at $500; since the mean number of pages for the 510(k) submissions in their sample is 24, the estimated cost per page is $21, or $36 after adjusting for inflation (Ref. 11). FDA records indicate that, recently, the one or two cranial electrotherapy stimulator 510(k) submissions received per year have consisted of several hundred pages each. Assuming an average of 300 pages per submission and a cost per page of $36 yields an average cost of preparing and submitting a 510(k) of $11,000. FDA

has estimated an upper bound on the cost of PMA at approximately $1,000,000 (see, for example, 73 FR 7498 at 7501, February 8, 2008); this yields a difference of $989,000 between the costs of PMA and 510(k) preparation. Multiplying this cost difference by the recent average of 1.5 new CES submissions per year yields an annual rule-induced cost equal to $1.48 million. Additionally, producers of CES products that are already on the market would need to submit PMA applications, costing approximately $1 million each. FDA believes that there are approximately 13 such products, so there would be a rule-induced upfront cost of $13 million.

These cost estimates are only correct if no producers would be dissuaded from introducing new products or seeking approval for currently-marketed products by the cost of submitting a PMA application or by changes in the possibility that FDA grants approval. In cases where producers are dissuaded from entering or attempting to stay in the market, the cost to industry of the proposed rule would be the foregone expected profit on the withdrawn or withheld CES devices, which is necessarily less than the cost of PMA submission (otherwise, the producers in question would not be dissuaded from seeking PMA); the $13 million upfront and $1.48 million annual estimates mentioned previously thus provide upper bounds on the submission-related cost that would be borne by industry. Excluded from these totals is the welfare loss that would be borne by consumers who would, in the absence of the proposed rule, use the CES devices that would be withdrawn or withheld from the market as a result of the call for PMAs or PDPs. Due to the lack of sufficient market data, we cannot quantify these consumers' welfare loss. FDA requests comment on this issue and on all methods and results of our cost estimation.

In addition to the cost to industry of preparing and submitting PMAs or PDPs, the proposed rule would impose review costs on FDA. Geiger (Ref. 12) estimated that, for devices reviewed by FDA's Center for Devices and Radiological Health in 2003 and 2004, review costs were $563,000 per PMA and $13,400 per 510(k). Updated for inflation (with Ref. 11) to 2010 dollars, these review costs become $653,000 per PMA and $15,500 per 510(k). Thus, the proposed rule's review-related costs are expected to equal $8.49 million (= 13 × $653,000) upfront and $956,000 (= 1.5 × [$653,000 − $15,500]) per subsequent year. A portion of this total will be paid by industry in the form of user fees, with the remainder coming from general revenues. The CES manufacturers currently registered with FDA have annual revenues well under $100 million, so they would likely be eligible for small business user fees, which are currently set at $59,705 for a premarket application (PMA or PDP) and $2,174 for a 510(k) submission (75 FR 45641 at 45643). Thus, user fees would likely cover $776,000 (= 13 × $59,705) of upfront and $86,000 (= 1.5 × [$59,705 − $2,174]) of subsequent annual rule-induced review costs. Because annual revenues for CES manufacturers are also below $30 million, CES manufacturers submitting first premarket applications may qualify for user fee waivers; such cases would increase the portion of FDA review costs coming from general revenues above the current estimates of $7.71 million upfront and $870,000 per subsequent year and decrease the anticipated rule-induced change in user fee collections.

Table 1 of this document displays all quantified benefits and costs of the proposed rule. We reiterate that most of our estimates represent extreme upper bounds. For both benefits and costs, the likely effects of the rule would be much smaller than the estimates appearing in table 1.

TABLE 1—ESTIMATED UPPER BOUNDS OF BENEFITS AND COSTS

[$ thousands]

| | 3% Discount rate | | 7% Discount rate | |
|---|---|---|---|---|
| | Annual | Present value | Annual | Present value |
| Ongoing Benefit: | | | | |
| Better-Informed Consumer Decisions | 5,665 | 48,324 | 5,665 | 39,789 |
| Benefits: Ten-Year Total | ..... | 48,324 | ..... | 39,789 |
| Upfront Costs: | | | | |
| Industry PMA or PDP Preparation | 13,000 | 13,000 | 13,000 | 13,000 |
| User Fees | 776 | 776 | 776 | 776 |
| FDA Review, Net of User Fees | 7,710 | 7,710 | 7,710 | 7,710 |
| Ongoing Costs: | | | | |
| Industry PMA or PDP Preparation | 1,484 | 12,656 | 1,484 | 10,421 |
| User Fees | 86 | 736 | 86 | 606 |
| FDA Review, Net of User Fees | 870 | 4,945 | 870 | 4,072 |
| Costs: Ten-Year Total [1] | ..... | 39,823 | ..... | 36,584 |

[1] Costs borne by consumers (in the form of welfare loss) are not estimated.

*C. Impact on Small Entities*

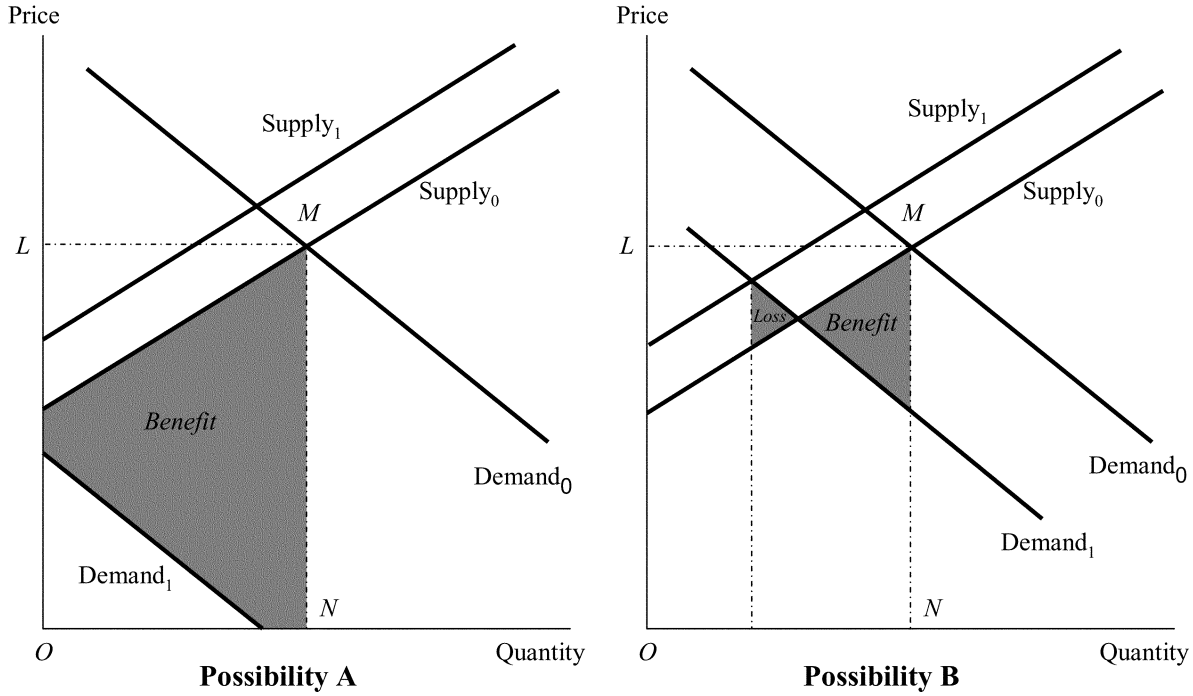
The Regulatory Flexibility Act requires Agencies to prepare an initial regulatory flexibility analysis if a proposed rule would have a significant effect on a substantial number of small businesses, non-profit organizations, local jurisdictions or other entities. Even though the producers of CES devices do tend to be small, only a very few entities participate in this market. FDA estimates that there are approximately 11 producers currently marketing CES devices; there may also be a handful of affiliated businesses that would be affected by the requirement for PMAs or PDPs. Therefore, FDA tentatively concludes that this proposed rule would not have a significant economic impact on a substantial number of small entities. We request comment on this issue.

*D. Technical Appendix*

The supply-demand diagrams of figure 1 of this document illustrate the changes in the market for CES devices and services that would occur if the additional testing associated with class III pre-market approval were to reveal that CES devices are less safe and effective than consumers currently believe. In Panel A, the benefit of proposed requirement for PMAs or PDPs is represented by the shaded area below

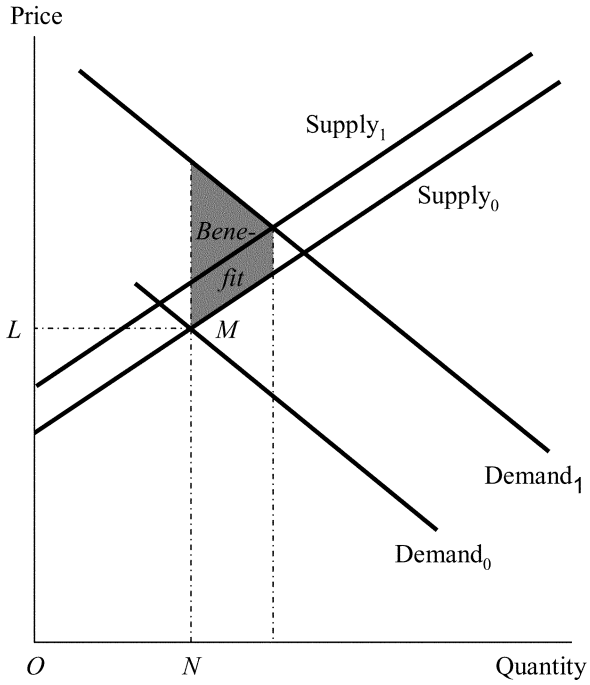
the current market supply curve, above the better-informed, post-call for PMA demand curve (*Demand$_1$*) and between the old and new quantities purchased (determined by the intersections of the pre- and post-call for PMAs or PDPs demand curves with the current supply curve or the vertical axis). A similar shaded benefit area appears in Panel B, but in that case, there is an offsetting loss (shown as the shaded triangle between the pre- and post-call for PMAs or PDPs supply curves) caused by CES producers passing on some costs related to PMAs and PDPs to consumers and consumers therefore purchasing even fewer CES devices or services than new information indicates they should. The overall benefit of the rule in Panel B is the difference between the areas of the Benefit and Loss triangles. In both panels of Figure 1, total CES spending by consumers, equal to the revenue collected by CES producers and shown as the rectangle *LMNO,* provides an upper bound on the amount of the shaded rule-induced social benefit. While total spending/revenue always provides an overestimate of the social benefit, the amount of the over-estimation may range from moderate, as in Panel A (the case in which CES products disappear from the market), to extreme, as in Panel B (the case in which there is continued use of at least some CES products).

**Figure 1. The Benefit of Information in the Market for CES Devices and Services**




If the additional testing associated with class III marketing approval increases consumers' confidence in the safety and effectiveness of CES devices, then demand for these products would increase, as depicted in figure 2 of this document. In this case, consumers currently purchase too few rather than too many CES devices and services as a result of incomplete information. The benefit to society of providing information can, as in Panel A of figure 1, be depicted graphically as the area between the pre-call for PMA or PDP supply curve and the post-call for PMA or PDP demand curve, and between the old and new quantities consumed (determined by the intersections of the pre- and post-call for PMA or PDP demand curves with the pre- and post-call for PMA or PDP supply curves), but because the revenue rectangle *LMNO* does not contain the shaded benefit area, FDA cannot in this case estimate a bound on the total social benefit.

**Figure 2. The Benefit of Information in the Market for CES Devices and Services**




## X. Federalism

FDA has analyzed this proposed rule in accordance with the principles set forth in Executive Order 13132. FDA has determined that the proposed rule, if finalized, would not contain policies that would 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 tentatively concludes that the proposed 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.

## XI. Paperwork Reduction Act of 1995

This proposed rule refers to currently approved collections of information found in FDA regulations. These collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520). The collections of information in 21 CFR part 812 have been approved under OMB control number 0910–0078; the collections of information in 21 CFR part 814, subpart B, have been approved under OMB control number 0910–0231; and the collections of information under 21 CFR part 801 have been approved under OMB control number 0910–0485.

## XII. Proposed Effective Date

FDA is proposing that any final rule based on this proposal become effective on the date of its publication in the **Federal Register** or at a later date if stated in the final rule.

## XIII. Comments

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**), either electronic or written comments regarding this document. It is only necessary to send one set of comments. It is no longer necessary to send two copies of mailed comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

## XIV. References

The following references have been placed on display in the Division of Dockets Management (see **ADDRESSES**), and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday. (FDA has verified the Web site addresses, but we are not responsible for any subsequent changes to the Web sites after this document publishes in the **Federal Register.**)

1. Bystritsky A, L. Kerwin, J. Feusner, ''A Pilot Study of Cranial Electrotherapy Stimulation for Generalized Anxiety Disorder,'' *Journal of Clinical Psychiatry,* 69(3): 412–417, 2008.
2. Heffernan, Michael, ''The Effect of a Single Cranial Electrotherapy Stimulation on Multiple Stress Measures,'' The Townsend Letter for Doctors and Patients, 147: 60–64, 1995.
3. Overcash, Stephen J., ''Cranial Electrotherapy Stimulation in Patients Suffering From Acute Anxiety Disorders,'' *American Journal of Electromedicine,* 16(1): 49–51, 1999.
4. Voris, Marshall D, ''An Investigation of the Effectiveness of Cranial Electrotherapy Stimulation in the Treatment of Anxiety Disorders Among Outpatient Psychiatric Patients, Impulse Control Parolees and Pedophiles,'' Manuscript submitted for publication. Delos Mind/Body Institute, Dallas and Corpus Christi, TX: 1–19, 1995.
5. Hyun J.K., Y.K. Woon, S.L. Yoon, *et al.,* ''The Effect of Cranial Electrotherapy Stimulation on Preoperative Anxiety and Hemodynamic Responses.'' *Korean Journal of Anesthesiology,* 55: 657–61, 2008.
6. Winick, R.L., ''Cranial Electrotherapy Stimulation (CES): A Safe and Effective Low Cost Means of Anxiety Control in a Dental Practice,'' *General Dentistry,* 47(1): 50–55, 1999.
7. O'Connor M.E., F. Bianco, R. Nicholson, ''Meta-analysis of Cranial Electrostimulation (CES) in Relation to the Primary and Secondary Symptoms of Substance Withdrawal,'' Presented at the 12th annual meeting of the Bioelectromagnetics Society, June 14, 1991.
8. Klawansky S., A. Yeung, C. Berkey, *et al.,* ''Meta-analysis of Randomized Controlled Trials of Cranial Electrostimulation,'' The Journal of Nervous and Mental Disease, 183(7): 478–485, 1995.

9. Manta: Vital Info on Small Businesses, *http://www.manta.com,* accessed June 11, 2010.
10. Blozan, Carl F. and Steven A. Tucker, ''Premarket Notifications: The First 24,000,'' Medical Device & Diagnostic Industry: 59–69, January 1986.
11. U.S. Department of Commerce, Bureau of Economic Analysis, 2010, National Income and Product Accounts Table 1.1.9., *http://www.bea.gov/national/nipaweb/SelectTable.asp*, accessed March 25, 2011.
12. Geiger, Dale R. FY 2003 and 2004 Unit Costs for the Process of Medical Device Review, *http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/Overview/MedicalDeviceUserFeeandModernizationActMDUFMA/ucm109216.pdf,* accessed September 2005.

**List of Subjects in 21 CFR Part 882**

Medical devices, Neurological devices.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 CFR part 882 be amended as follows:

## PART 882—NEUROLOGICAL DEVICES

1. The authority citation for 21 CFR part 882 continues to read as follows:

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

2. Section 882.5800 is amended by revising paragraph (c) to read as follows:

**§ 882.5800 Cranial electrotherapy stimulator.**

* * * * *

(c) *Date PMA or notice of completion of PDP is required.* A PMA or notice of completion of a PDP is required to be filed with the Food and Drug Administration on or before [A DATE WILL BE ADDED 90 DAYS AFTER DATE OF PUBLICATION OF A FUTURE FINAL RULE IN THE **FEDERAL REGISTER**], for any cranial electrotherapy stimulator device that was in commercial distribution before May 28, 1976, or that has, on or before [A DATE WILL BE ADDED 90 DAYS AFTER DATE OF PUBLICATION OF A FUTURE FINAL RULE IN THE **FEDERAL REGISTER**], been found to be substantially equivalent to any cranial electrotherapy stimulator device that was in commercial distribution before May 28, 1976. Any other cranial electrotherapy stimulator device shall have an approved PMA or declared completed PDP in effect before being placed in commercial distribution.

Dated: August 2, 2011.

**Nancy K. Stade,**

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

[FR Doc. 2011–19957 Filed 8–5–11; 8:45 am]

**BILLING CODE 4160–01–P**

## DEPARTMENT OF HOMELAND SECURITY

### Coast Guard

### 33 CFR Part 165

**[Docket No. USCG–2011–0254]**

**RIN 1625–AA11**

## Regulated Navigation Area, Zidell Waterfront Property, Willamette River, OR

**AGENCY:** Coast Guard, DHS.

**ACTION:** Notice of proposed rulemaking.

**SUMMARY:** The Coast Guard proposes the establishment of a Regulated Navigation Area (RNA) at the Zidell Waterfront Property located on the Willamette River in Portland, Oregon. This RNA is necessary to preserve the integrity of an engineered sediment cap as part of an Oregon Department of Environmental Quality (DEQ) required remedial action. This proposed RNA will do so by prohibiting activities that could disturb or damage the engineered sediment cap.

**DATES:** Comments and related material must be received by the Coast Guard on or before November 7, 2011.

**ADDRESSES:** You may submit comments identified by docket number USCG–2011–0254 using any one of the following methods:

(1) *Federal eRulemaking Portal: http://www.regulations.gov.*

(2) *Fax:* 202–493–2251.

(3) *Mail:* Docket Management Facility (M–30), U.S. Department of Transportation, West Building Ground Floor, Room W12–140, 1200 New Jersey Avenue, SE., Washington, DC 20590–0001.

(4) *Hand delivery:* Same as mail address above, between 9 a.m. and 5 p.m., Monday through Friday, except Federal holidays. The telephone number is 202–366–9329.

To avoid duplication, please use only one of these four methods. See the ''Public Participation and Request for Comments'' portion of the **SUPPLEMENTARY INFORMATION** section below for instructions on submitting comments.

**FOR FURTHER INFORMATION CONTACT:** If you have questions on this proposed rule, call or e-mail MST1 Jaime Sayers, Waterways Management Division, Marine Safety Unit Portland, Coast Guard; telephone 503–240–9319, e-mail *Jaime.a.Sayers@uscg.mil.* If you have questions on viewing or submitting material to the docket, call Renee V. Wright, Program Manager, Docket Operations, telephone 202–366–9826.

**SUPPLEMENTARY INFORMATION:**

**Public Participation and Request for Comments**

We encourage you to participate in this rulemaking by submitting comments and related materials. All comments received will be posted without change to *http://www.regulations.gov* and will include any personal information you have provided.

*Submitting Comments*

If you submit a comment, please include the docket number for this rulemaking (USCG–2011–0254), indicate the specific section of this document to which each comment applies, and provide a reason for each suggestion or recommendation. You may submit your comments and material online (via *http://www.regulations.gov*) or by fax, mail, or hand delivery, but please use only one of these means. If you submit a comment online via *http://www.regulations.gov*, it will be considered received by the Coast Guard when you successfully transmit the comment. If you fax, hand deliver, or mail your comment, it will be considered as having been received by the Coast Guard when it is received at the Docket Management Facility. We recommend that you include your name and a mailing address, an e-mail address, or a telephone number in the body of your document so that we can contact you if we have questions regarding your submission.

To submit your comment online, go to *http://www.regulations.gov*, click on the ''submit a comment'' box, which will then become highlighted in blue. In the ''Document Type'' drop down menu select ''Proposed Rule'' and insert ''USCG–2011–0254'' in the ''Keyword'' box. Click ''Search'' then click on the balloon shape in the ''Actions'' column. If you submit your comments by mail or hand delivery, submit them in an unbound format, no larger than 8½; by 11 inches, suitable for copying and electronic filing. If you submit comments by mail and would like to know that they reached the Facility, please enclose a stamped, self-addressed postcard or envelope. We will consider all comments and material received during the comment period and may