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**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**Food and Drug Administration**

[Docket No. 2007N-0231]

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Certifier A. Corbin

**Agency Information Collection Activities; Submission for Office of Management and Budget Review; Comment Request; Premarket Approval of Medical Devices**

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

**ACTION:** Notice.

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**SUMMARY:** The Food and Drug Administration (FDA) is announcing that a proposed collection of information has been submitted to the Office of Management and Budget (OMB) for review and clearance under the Paperwork Reduction Act of 1995.

**DATES:** Fax written comments on the collection of information by *[insert date 30 days after date of publication in the Federal Register]*.

**ADDRESSES:** To ensure that comments on the information collection are received, OMB recommends that written comments be faxed to the Office of Information and Regulatory Affairs, OMB, Attn: FDA Desk Officer, FAX: 202-395-6974, or e-mailed to *baguilar@omb.eop.gov*. All comments should be identified with the OMB control number 0910-0073. Also include the FDA docket number found in brackets in the heading of this document.

**FOR FURTHER INFORMATION CONTACT:** Denver Presley Jr., Office of the Chief Information Officer (HFA-250), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-1472.

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**SUPPLEMENTARY INFORMATION:** In compliance with 44 U.S.C. 3507, FDA has submitted the following proposed collection of information to OMB for review and clearance:

**Premarket Approval of Medical Devices—21 CFR Part 814 and Food and Drug Administration Modernization Act Sections 201, 202, 205, 208, and 209 (OMB Control Number 0910–0231)—Extension**

Section 515 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 360e) sets forth the requirements for premarket approval of certain class III medical devices. Class III devices are either preamendments devices that have been classified into class III, or postamendments devices which are not substantially equivalent to a preamendments device, or transitional devices. Class III devices are devices such as implants, life sustaining or life supporting devices, devices that are of substantial importance in preventing impairment of human health, and devices that otherwise present a potentially unreasonable risk of illness or injury. Most premarket approval application (PMAs) are for postamendments class III devices.

Under section 515 of the act, an application must contain certain specific information, including full reports of all information concerning investigations showing whether the device is reasonably safe and effective. The application should also include a statement of components, ingredients, and properties of the principles of operation for such a device. In addition, the application should also include a full description of the methods used in, and the facilities and controls used for, the manufacture and processing of the device and labeling specimens. The implementing regulations, contained in part 814 (21 CFR part 814), further specify the contents of a PMA for a class III medical device and the criteria FDA sets forth in approving, denying, or withdrawing approval of a PMA as well as supplements to PMAs. The purpose of these

regulations is to establish an efficient and thorough procedure for FDA's review of PMAs and supplements to PMAs for certain class III (premarket approval), medical devices. The regulations under part 814 facilitate the approval of PMAs and supplements to PMAs for devices that have been shown to be reasonably safe and effective and otherwise meet the statutory criteria for approval. The regulations also ensure the disapproval of PMAs and supplements to PMAs for devices that have not been shown to be reasonably safe and effective and that do not otherwise meet the statutory criteria for approval.

The Food and Drug Administration Modernization Act of 1997 (FDAMA) (Public Law 105-115) was enacted on November 21, 1997, to implement revisions to the act by streamlining the process of bringing safe and effective drugs, medical devices, and other therapies to the U.S. market. Several FDAMA provisions affect the PMA process, such as section 515(d)(6) of the act. This section provided that PMA supplements were required for all device changes that affect safety and effectiveness of a device unless such changes are modifications to manufacturing procedures or method of manufacture. This type of manufacturing change now requires a 30-day notice, or where FDA finds such notice inadequate, a 135-day PMA supplement.

To make the PMA process more efficient, in the past several years FDA has done the following: (1) Made changes to the PMA program based on comments received, (2) complied with changes to the program mandated by FDAMA and Medical Device User Fee Modernization Act (Public Law 107-250), and (3) worked toward completion of its PMA reinvention efforts.

Respondents to this information collection are persons filing a PMA application or a PMA supplement with FDA for approval of certain class III

medical devices. Part 814 defines a person as any individual, partnership, corporation, association, scientific or academic establishment, Government agency or organizational unit, or other legal entity. These respondents include entities meeting the definition of manufacturers, such as manufacturers of commercial medical devices in distribution prior to May 28, 1976 (the enactment date of the Medical Device Amendments). In addition, hospitals that reuse single use devices (SUDs) are also included in the definition of manufacturers. It is expected that FDA will receive four PMA applications from hospitals that remanufacture SUDs annually. This figure has been included in table 1 of this document, as part of the reporting burden in § 814.15.

In the **Federal Register** of June 28, 2007 (72 FR 35494), FDA published a 60-day notice requesting public comment on the information collection provisions. No comments were received.

FDA estimates the burden of this collection of information as follows:

TABLE 1.—ESTIMATED ANNUAL REPORTING BURDEN<sup>1</sup>

Section	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
<b>21 CFR</b>					
814.15(b)	10	1	10	2	20
814.20(a) through (c) and (e)	48	1	48	668	32,064
814.37	48	1	48	167	8,016
814.39(a)	460	1	460	60	27,600
814.39(d)	70	1	70	6	420
814.39(f)	254	1	254	16	4,064
814.82(a)(9)	34	1	34	135	4,590
814.84(b)	34	1	34	10	340
<b>FDAMA</b>					
201—Agreement Meeting	3	1	3	50	150
202—Expedited Reviews	7	1	7	10	70
205—Determination Meeting	5	1	5	50	250
208—Classification Panel Meetings	19	1	19	30	570
209—100-day Meeting	36	1	36	10	360
<b>Total</b>	<b>1,028</b>	<b>13</b>	<b>1,028</b>	<b>1,214</b>	<b>78,514</b>

<sup>1</sup>There are no capital costs or operating and maintenance costs associated with this collection of information.

TABLE 2.—ESTIMATED ANNUAL RECORDKEEPING BURDEN<sup>1</sup>

21 CFR Section	No. of Recordkeepers	Annual Frequency per Recordkeeping	Total Annual Records	Hours per Record	Total Hours
814(a)(5) and (a)(6)	1,128	1	1,128	17	19,176

<sup>1</sup>There are no capital costs or operating and maintenance costs associated with this collection of information.

The industry-wide burden estimate for PMAs is based on an FDA actual average fiscal year (FY) annual rate of receipt of 48 PMA original applications, 530 PMA supplements, and 254 30-day notices using FY 2002 through FY 2006 data. The burden data for PMAs is based on data provided by manufacturers by device type and cost element in an earlier study. The specific burden elements for which FDA has data are as follows:

- Clinical investigations: 67 percent of total burden estimate;
- Submission of additional data or information to FDA during a PMA review: 12 percent;
- Additional device development cost (e.g., testing): 10 percent; and
- PMA and PMA supplement preparation and submissions, and development of manufacturing and controls data: 11 percent.

#### Reporting Burden

The reporting burden can be broken out by certain sections of the PMA regulation as follows:

##### **§ 814.15—Research Conducted Outside the United States**

Approximately 20 percent of the clinical studies submitted in support of a PMA application are conducted outside the United States. Each study should be performed in accordance with the “Declaration of Helsinki” or the laws and regulations of the country in which the study was conducted. If the study was conducted in accordance with the laws of the country, the PMA applicant is required to explain to FDA in detail the differences between the laws of the country and the “Declaration of Helsinki.” Based on the number of PMAs

received that contained studies from overseas, FDA estimates that the burden estimate necessary to meet this requirement is 20 hours.

#### **§ 814.20(a) through (c) and (e)—Application**

The majority of the 32,064 hourly burden estimate is due in part to this requirement. Included in this requirement are the conduct of laboratory and clinical trials as well as the analysis, review, and physical preparation of the PMA application. FDA estimates that 48 manufacturers, including hospital re-manufacturers of single use devices (SUDs), will be affected by these requirements which are based on the actual average of FDA receipt of new PMA applications in FY 2002 through 2006. FDA's estimate of the hours per response (668), was derived through FDA's experience and consultation with industry and trade associations. In addition, FDA also based its estimate on the results of an earlier study which accounts for the bulk of the hourly burden for this requirement, identified by manufacturers.

#### **§ 814.37—PMA Amendments and Resubmitted PMAs**

As part of the review process, FDA often requests PMA applicant to submit additional information regarding the device necessary for FDA to file the PMA or to complete its review and make a final decision. The PMA applicant may, also on their own initiative, submit additional information to FDA during the review process. These amendments contain information ranging from additional test results, re-analysis of the original data set to revised device labeling. Almost all PMAs received by the Agency have amendments submitted during the review process. FDA estimates that 8016 burden hours are necessary to satisfy this requirement.

#### **§ 814.39(a)—PMA Supplements**

FDA believes that the amendments mandated by FDAMA for § 814.39(f), permitting the submission of the 30-day notices in lieu of regular PMA supplements, will result in an approximate 20 percent reduction in the total number of hours as compared to regular PMA supplements. As a result, FDA estimates that 27,600 hours of burden are needed to complete the requirements for regular PMA supplements.

#### **§ 814.39(d)—Special PMA Supplements—Changes Being Effected**

This type of supplements is intended to enhance the safety of the device or the safe use of the device. The number of PMA supplements received that fit this category averaged 70 per year based on the numbers received from FY 2002 through FY 2006. Because of the minimal data required to be included in this type of supplement, FDA estimates that the burden hours necessary to satisfy this requirement are 420 hours.

#### **§ 814.39(f)—30-day Notice**

Under section 515(d) of the act, modifications to manufacturing procedures or methods of manufacture that affect the safety and effectiveness of a device subject to an approved PMA do not require submission of a PMA supplement under § 814.39(a) and are eligible to be the subject of a 30-day notice. A 30-day notice shall describe in detail the change, summarize the data or information supporting the change, and state that the change has been made in accordance with the requirements of part 820 (21 CFR part 820). The manufacturer may distribute the device 30 days after the date on which FDA receives the 30-day notice, unless FDA notifies the applicant within 30 days from receipt of the notice that it is not adequate. FDA estimates the burden to satisfy this requirement is 4,064 hours.

#### **§ 814.82(a)(9)—Postapproval Requirements**

Postapproval requirements concern approved PMAs that were not reclassified and require a periodic report. After approval, all PMAs require a submission of an annual report. On average, approximately half of the submitted PMAs (34), require associated postapproval studies, i.e., followup of patients used in clinical trials to support the PMA or additional preclinical information, that is labor-intensive to compile and complete; the remaining PMAs require minimal information. Based on experience and consultation with industry, FDA has estimated that preparation of reports and information required by this section requires 4,590 hours.

#### **§ 814.84(b)—Reports**

Postapproval requirements described in § 814.82(a)(7) require submission of an annual report for each approved PMA. FDA estimates that respondents will average about 10 hours in preparing their reports to meet this requirement. This estimate is based on FDA's experience and consultation with industry. Thus, FDA estimates that the periodic reporting burden required by this section will take 340 hours.

#### **Statutory Reporting Burden Estimate (FDAMA)**

The total statutory reporting burden under the requirements of FDAMA sections 201, 202, 205, 208, and 209 is estimated to be 1,400 hours. This burden estimate was based on actual real FDA data tracked from January 1, 1998, to the present, and an estimate was also derived to forecast future expectations with regard to this statutory data.

#### **§ 814.82(a)(5) and (a)(6)—Recordkeeping**

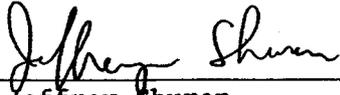
The recordkeeping burden under this section requires the maintenance of records, used to trace patients, and the organization and indexing of records into identifiable files to ensure the device's continued safety and effectiveness.

These records are required only of those manufacturers who have an approved PMA and who had original clinical research in support of that PMA. For a typical year's submissions, 70 percent of the PMAs are eventually approved with 75 percent of these having original clinical trial data. Therefore, approximately 34 PMAs a year (48 annual submissions x 70 percent), would be subject to these requirements. Also, because the requirements apply to all active PMAs, all holders of an active PMA applications must maintain these records.

PMAs have been required since 1976, and there are 1,128 active PMAs that could be subject to these requirements, based on actual FDA data. Each study has approximately 200 subjects, and at an average of 5 minutes per subject, there is a total burden per study of 1,000 minutes, or 17 hours. The aggregate burden for all 1,128 holders of approved original PMAs, therefore, is 19,176 hours (1,127 approved PMAs with clinical data x 17 hours per PMA).

The applicant determines which records should be maintained during product development to document and/or substantiate the device's safety and effectiveness. Records required by the current good manufacturing practices for medical devices regulation (part 820) may be relevant to a PMA review and may be submitted as part of an application. In individual instances, records may be required as conditions of approval to ensure the device's continuing safety and effectiveness.

Dated: 9.11.07  
September 11, 2007.



Jeffrey Shuren,  
Assistant Commissioner for Policy.

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