

Premarket Approval of Medical Devices
21 CFR Part 814 and Section 515 of the FD&C Act
OMB Control Number 0910-0231

SUPPORTING STATEMENT

Terms of Clearance: None.

A. Justification

1. Circumstances Making the Collection of Information Necessary

The Food and Drug Administration (FDA) is requesting an extension of approval of the information collection requirements regarding Premarket Approval of Medical Devices.

Under section 515 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) ([21 U.S.C. 360\(e\)](#)) all devices placed into class III by FDA are subject to premarket approval requirements. Premarket approval is the process of scientific and regulatory review to ensure the safety and effectiveness of class III devices. An approved PMA is, in effect, a private license granted to the applicant for marketing a particular medical device. A class III device that fails to meet PMA requirements is considered to be adulterated under section 501(f) of the FD&C Act ([21 U.S.C. 351\(f\)](#)) and cannot be marketed. Premarket approval requirements apply differently to preamendments devices, postamendments devices, and transitional class III devices.

Manufacturers of class III preamendments devices (devices that were in commercial distribution before May 28, 1976) are not required to submit a PMA until 30 months after the issuance of a final classification regulation or until 90 days after the publication of a final regulation requiring the submission of a PMA, whichever period is later. FDA may allow more than 90 days after issuance of a final rule for submission of a PMA.

A postamendments device is one that was first distributed commercially on or after May 28, 1976. Postamendments devices determined by FDA to be substantially equivalent to preamendments class III devices are subject to the same requirements as the preamendments devices. FDA determines substantial equivalence after reviewing an applicant's premarket notification submitted in accordance with section 510(k) of the FD&C Act. Postamendments devices determined by FDA to be not substantially equivalent to either preamendments devices or postamendments devices classified into class I or II are "new" devices and fall automatically into class III. Before such devices can be marketed, they must have an approved PMA or be must reclassified into class I or class II.

The Food and Drug Modernization Act of 1997 (FDAMA) (Public Law 105-115), amended the FD&C Act by streamlining the process of bringing safe and effective drugs, medical devices, and other therapies to the U.S. market.

FDAMA added section 515(d)(6) to the FD&C Act (21 U.S.C. 360e(d)(6)), which provided that PMA supplements were required for all device changes that affect safety and effectiveness unless such changes are modifications to manufacturing procedures or method of manufacture. That type of manufacturing change will require a 30-day notice, or where FDA finds such notice inadequate, a 135-day PMA supplement.

The implementing regulations, contained in 21 CFR part 814, further specify the contents of a PMA for a medical device and the criteria FDA will employ in approving, denying, or withdrawing approval of a PMA and supplements to PMAs. The regulation's purpose is to establish an efficient and thorough procedure for FDA's review of PMAs and supplements to PMAs for class III medical devices. The regulations 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 allow for the denial 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.

Section 12a of this Supporting Statement contains a detailed description of the information collections and estimated burden.

This information collection is not related to the American Recovery and Reinvestment Act of 2009 (ARRA).

2. Purpose and Use of the Information Collection

Respondents to the information collection are private sector, for-profit businesses.

The data reported to FDA and the records that are maintained by the applicants allow FDA and industry to make decisions and take actions to protect the public health from defective medical devices.

The PMA regulation establishes procedures that FDA utilizes in approving, denying, or withdrawing approval of any PMA. It provides specific, clear, and flexible instructions to applicants so they know what information is required in a PMA. PMA supplements are also used by FDA to determine any additional action the agency must take to protect the public health.

3. Use of Improved Information Technology and Burden Reduction

The final rule, "Amending Premarket Regulations That Require Multiple Copies and Specify Paper Copies to be Allowed in Electronic Format" (84 FR 68334, December 16, 2019) amended requirements for medical device premarket submissions to remove paper and multiple copies and replace them with requirements for a single submission in electronic format. Therefore, FDA estimates that 100% of the respondents will use electronic means to fulfill the agency's requirement or request.

4. Efforts to Identify Duplication and Use of Similar Information

FDA is the only Agency authorized to regulate the manufacture and distribution of medical devices. The information collected cannot be obtained from any other source other than the applicant, therefore this effort is not duplicated anywhere else. No similar data are available to or collected by FDA because each PMA is product and manufacturer specific. Most information in a PMA is unique and is presented to support claims of safety and effectiveness for that particular purpose.

5. Impact on Small Businesses or Other Small Entities

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. Based on User Fee payments, approximately 24 percent of PMA original application user fees were from small businesses. Approximately 7 percent of PMA supplement application user fees were from small businesses.

The efforts described below help to assure that the burden on all manufacturers, including small manufacturers, are minimized.

The Office of Regulatory Programs (ORP) within the Office of Product Evaluation and Quality, FDA, routinely participates in conferences and device submission workshops designed to educate the medical device industry on how to prepare a PMA submission such that it can be filed and reviewed in an expeditious manner. ~~PO~~ ORP also annually meets with organizations such as Advanced Medical Technology Association (AdvaMed), Medical Device Manufacturers Association (MDMA), or Regulatory Affairs Professional Society (RAPS) to discuss issues regarding the PMA review process. FDA answers any questions that these organizations may have and provides them with information to improve their submissions. In addition, OPEQ also issues many device specific guidance documents and general guidance documents to assist the industry in improving the quality of their submissions.

FDA also maintains a fax on demand system (FACTS) which provides firms with information pertaining to medical devices and radiological health. FDA's Center for Devices and Radiological Health (CDRH), Division of International and Consumer Education (DICE) provides technical and non-technical assistance to small firms (and firms of any size) expressly to aid them in complying with requirements of the FD&C Act.

FDA also aids small business in dealing with the requirements of the regulations by providing guidance and information through the DICE, and through the scientific and administrative staff, and through the CDRH website at <http://www.fda.gov/MedicalDevices/default.htm>.

DICE participates in and presents conferences, workshops, and seminars on the application and interpretation of relevant regulations, consults with individual applicants,

and develops and disseminates educational materials. Staff is available to respond to questions and a toll-free telephone number was established to facilitate this communication.

6. Consequences of Collecting the Information Less Frequently

Respondents will respond to the data collection annually and occasionally. Applicants determine when a product will be submitted for premarket approval. Notices and supplements are required only when an affected person or entity determines that a change that affects safety or effectiveness in their device is necessary. PMA applicants with approved PMAs are required to submit an annual report concerning their PMA. FDA determines subsequent reporting requirements and their frequency based on the necessity for applicants to provide reasonable assurance of their device's continued safety and effectiveness.

There are legal obstacles to reduce the burden as this collection is required by the FD&C Act and implementing regulations (21 CFR part 814). If this information were collected less frequently or, not collected, FDA could not ensure that the devices are reasonably safe and effective for their intended use.

7. Special Circumstances Relating to the Guidelines of 5 CFR 1320.5

There are no special circumstances relating to the guidelines of 5 CFR 1320.5.

8. Comments in Response to the Federal Register Notice and Efforts to Consult Outside the Agency

In accordance with 5 CFR 1320.8(d), FDA published a 60 day notice for public comment in the FEDERAL REGISTER of October 24, 2019 (84 FR 57030). No comments were received.

The Office of Regulatory Programs (ORP) within the Office of Product Evaluation and Quality, FDA, annually meets with organizations such as Advanced Medical Technology Association (AdvaMed), Medical Device Manufacturers Association (MDMA), or Regulatory Affairs Professional Society (RAPS) to discuss issues regarding the PMA review process.

9. Explanation of Any Payment or Gift to Respondents

There is no payment or gift provided to respondents of this information collection.

10. Assurance of Confidentiality Provided to Respondents

This information collection request (ICR) is collecting personally identifiable information (PII) or other data of a personal nature. Information is collected via FDA Form 3514 (CDRH Premarket Review Submission Cover Sheet) and FDA Form 3601 (MDUFMA

Cover Sheet/User Fee Account Creation). PII collected via FDA Form 3514 name, title, address, and email address. PII collected via FDA Form 3601 is name, title, address, phone number, fax number, username, and password. PII is collected in the context of the individual's professional capacity. This ICR creates PMA records with contact information to relay the status of the review. An approved PMA is granted a private license to market a particular device in the US. 21CFR 814.20 specified the information required in a PMA which includes both PII and non-PII.

FDA further determined that although PII is collected the collection is not subject to the Privacy Act of 1974 and the particular notice and other requirements of the Act do not apply. Specifically, FDA does not use name or any other personal identifier to routinely retrieve records from the information collected.

In preparing this Supporting Statement, FDA staff consulted with the FDA Privacy Office to ensure appropriate handling of information collected. FDA minimized the PII to be collected to protect the privacy of the individuals.

Confidentiality of data and disclosure regarding the existence of a PMA are governed by 21 CFR 814.9, the Freedom of Information Act (FOIA) (5 U.S.C. 552), and sections 301(j) and 520(c) and (h) of the FD&C Act (21 U.S.C. 331(j), 360(c) and (h)). Under FOIA, the public has broad access to government documents.

However, FOIA provides certain exemptions from mandatory public disclosure of government records (5 U.S.C. 552(b)(1)-(b)(9)). One such provision, 5 U.S.C. 552(b)(4), exempts "trade secrets and commercial or financial information that is privileged or confidential" from the requirement of public disclosure.

Section 520(c) of the FD&C Act prohibits FDA from disclosing any information exempted from public disclosure under 5 U.S.C. 552(b)(4). Part 20 of FDA's regulations (21 CFR part 20) sets forth FDA's general policy concerning public availability of FDA records. Under section 520(h) of the FD&C Act, FDA is required to make publicly available a detailed summary of the safety and effectiveness information contained in a PMA that is the basis for an order approving, denying approval of, or withdrawing approval of a PMA.

11. Justification for Sensitive Questions

The information required in a premarket approval or premarket supplement application does not include questions of a sensitive nature, such as, sexual behavior and attitudes, religious beliefs, and other matters that are commonly considered private.

12. Estimates of Annualized Burden Hours and Costs

12 a. Annualized Hour Burden Estimate

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

Table 1.--Estimated Annual Reporting Burden

Activity/21 CFR or FD&C Act Section	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
Research conducted outside the United States (814.15(b))	25	1	25	2	50
PMA application (814.20)	46	1	46	668	30,728
Information on clinical investigations conducted outside the United States (814.20(b)(6)(ii)(C))	10	1	10	0.5 (30 minutes)	5
PMA amendments and resubmitted PMAs (814.37(a)-(c) and (e))	1,528	1	1,528	167	255,176
PMA supplements (814.39(a))	777	1	777	60	46,620
Special PMA supplement —changes being affected (814.39(d))	75	1	75	6	450
30-day notice (814.39(f))	1,722	1	1,722	16	27,552
Postapproval requirements (814.82(a)(9))	121	1	121	135	16,335
Periodic reports (814.84(b))	764	1	764	10	7,640
Agreement meeting (520(g)(7))	1	1	1	50	50
Breakthrough Devices Program (515(B) of the FD&C Act)	11	1	11	10	110
Determination Meeting (513(1)(3)(D) of the FD&C Act)	1	1	1	50	50
Panel meeting (515(c)(3) of the FD&C Act)	1	1	1	30	30
Day 100 meeting (515(d)(3) of the FD&C Act)	14	1	14	10	140
Total					384,936

Table 2.--Estimated Annual Recordkeeping Burden

Activity/21 CFR Section	No. of Recordkeepers	No. of Records per Recordkeeper	Total Annual Records	Average Burden per Recordkeeping	Total Hours
Maintenance of records (814.82(a)(5) and (a)(6))	446	1	446	17	7,582

The burden estimate is based on the annual rate of receipt of PMA submissions for fiscal years (FYs) 2016 through 2018 and our expectation of submissions to come in the next few years. The burden data for PMAs is based on data provided by applicants by device type and cost element in an earlier study.

Reporting Burden:

§ 814.15(b)--Research Conducted Outside the United States

FDA will accept information on a clinical investigation conducted outside the United States (OUS) to support a PMA if the investigation is well-designed and well-conducted and certain other conditions are met, including that the investigation was conducted in accordance with good clinical practice (GCP) as specified 21 CFR 812.28. If the OUS clinical investigation did not conform to GCP, then the PMA submission should include a waiver request or a statement explaining the reason for not conducting the investigation in accordance with GCP and a description of steps taken to ensure that the data and results are credible and accurate and that the rights, safety, and well-being of subjects have been adequately protected. Based on the number of PMAs received that contained studies from overseas, FDA estimates that the burden estimate necessary to meet this requirement is 50 hours.

§ 814.20 --Application

Specifies the information required in a PMA and update reports such as the applicant's name and address, a description of the device, its labeling, its indications for use, and summary of clinical and non-clinical studies. 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 38 applicants, 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 FYs 2016 through 2018.

Additionally, the “Human Subject Protection; Acceptance of Data from Clinical Investigations for Medical Devices” final rule (83 FR 7366; February 21, 2018) amended this section to address requirements for a PMA supported by data from clinical investigations conducted outside the United States. The applicant will be required to submit the information as described in § 814.20(b)(6)(ii)(C). We estimate this will take 30 minutes per respondent. We estimate that 10 respondents annually will submit such information.

The collections in OMB control number 0910-0741, “Human Subject Protection; Acceptance of Data from Clinical Studies for Medical Devices,” were submitted to OMB as a new information collection request with the expectation that the currently approved requirements will be amended. As noted in the Supporting Statement for OMB control number 0910-0741, we are amending OMB control number 0910-0231 to reflect the information collections associated with the rulemaking under § 814.20(b)(6)(ii)(C).

§ 814.37(a) through (c) and (e)--PMA Amendments and Resubmitted PMAs

As part of the review process, FDA often requests PMA applicants 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, on their own initiative, submit additional information to FDA during the review process. These amendments contain information ranging from additional test results, reanalysis of the original data set

to revised device labeling. Almost all PMAs received by the Agency have amendments submitted during the review process.

§ 814.39(a)--PMA Supplements

This information collection includes the requirements for the range of PMA supplements (panel track, 180-day fee-based, 180-day non-fee based, and real-time supplements).

§ 814.39(d)--Special PMA Supplements--Changes Being Affected

This type of supplement 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 75 per year based on the numbers received from FYs 2016 through 2018.

§ 814.39(f)--30-Day Notice

Under section 515(d) of the FD&C 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 paragraph (a) of that section 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 applicant 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.

§ 814.82(a)(9)--Postapproval Requirements

Postapproval requirements concerns approved PMAs that were not reclassified and require a periodic report. After approval, all PMAs require a submission of an annual report. A majority of the submitted PMAs 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.

§ 814.84(b)--Periodic 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.

The Breakthrough Devices Program--Section 515(b) of the FD&C Act (21 U.S.C. 360e-3)

The Breakthrough Devices Program supersedes the Expedited Access Pathway and Priority Review for medical devices. The guidance document “Breakthrough Devices Program” implements section 515B of the FD&C Act (21 U.S.C. 360, as created by section 3051 of the 21st Century Cures Act (Pub. L. 114-255) and amended by section 901 of the FDA Reauthorization Act of 2017 (Pub. L. 115-52). The Breakthrough Devices Program is a voluntary program for certain medical devices and device-let combination products that provide for more effective treatment or diagnosis of life-

threatening or irreversibly debilitating diseases or conditions. The program is intended to help patients have more timely access to these medical devices by expediting their development, assessment, and review, while preserving the statutory standards for premarket approval, 510(k) clearance, and De Novo marketing authorization, consistent with the Agency's mission to protect and promote public health.

Agreement Meeting--Section 520(g)(7) of the FD&C Act (21 U.S.C. 360j(g)(7))

Applicants planning to submit a PMA may submit a written request to reach agreement with FDA on the key parameters of the investigational plan.

Determination Meeting--Section 513(a)(3)(D) of the FD&C Act (21 U.S.C. 360c(a)(3)(D))

Applicants planning to submit a PMA may submit a written request to FDA for a meeting to determine the type of information (valid scientific evidence) necessary to support the effectiveness of their device.

Panel of Experts--Section 515(c)(3) of the FD&C Act

An original PMA or panel track PMA supplement is taken to an advisory panel of experts unless FDA determines that the information in the application substantially duplicates information which has previously been reviewed by the panel.

Day 100 Meeting--Section 515(d)(3) of the FD&C Act

FDA must, upon the written request of the applicant, meet with that party within 100 days of receipt of the filed PMA application to discuss the review status of the application. With the concurrence of the applicant, a different schedule may be established. Prior to this meeting, FDA must inform the applicant in writing of any identified deficiencies and what information is required to correct those deficiencies. FDA must also promptly notify the applicant if FDA identifies additional deficiencies or of any additional information required to complete Agency review.

Recordkeeping:

§ 814.82(a)(5) and (a)(6)--Maintenance of Records

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 of all applicants who have an approved PMA.

PMA's have been required since 1976, and there are 801 active PMA's that could be subject to these requirements, based on actual FDA data, and approximately 39 new PMA's are approved every year. The aggregate burden for the estimated 446 PMA holders of approved original PMA's for the next few years is estimated to be 7,582 hours.

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.

12b. Annualized Cost Burden Estimate

FDA estimates that the total estimated burden cost to industry relating to this information collection will be \$28,261,296, which is the total estimated number of burden hours, 392,518, multiplied by an average wage rate of \$72 per hour.*

Type of Respondent	Total Burden Hours	Hourly Wage Rate	Total Respondent Costs
Regulatory Affairs Professional*	392,518	\$72	\$28,261,296

* The estimated wage rate for a Regulatory Affairs Professional is based on The Regulatory Affairs Professional Society (RAPS) average total annual compensation of \$150,422 for a U.S. regulatory affairs professional (<https://www.raps.org/getattachment/Careers/Scope-of-Practice-Survey/2016-Scope-of-Practice-Compensation-Report-for-the-Regulatory-Profession.pdf.aspx?lang=en-US>, p. 11, accessed 08-23-19). The hourly wage rate of \$72 assumes a 40-hour work week and is rounded to the nearest dollar.

13. Estimates of Other Total Annual Costs to Respondents and/or Recordkeepers/Capital Costs

There are no capital, start-up, operating or maintenance costs associated with this information collection.

14. Annualized Cost to the Federal Government

FDA estimates that a total of 118 full time equivalent (FTE) positions are used for PMA review and processing. Based on a cost of \$270,305 per position (which is the agency's projected average cost of an FTE including benefits*), the estimated annual Federal cost is \$31,895,990.

*Based on the Food and Drug Administration fully loaded FTE cost model (domestic) for FY 2018, as provided by agency economists.

15. Explanation for Program Changes or Adjustments

We made the following changes to the information collection:

- Added the burden estimate for “Information on clinical investigations conducted outside the United States (§ 814.20(b)(6)(ii)(C)),” which is associated with the “Human Subject Protection; Acceptance of Data from Clinical Investigations for Medical Devices” final rule as described previously in this document.
- Revised the burden description and table to reflect that the Expedited Access Pathway and Priority Review have been superseded by the Breakthrough Devices Program.

- Updated our burden estimate with Fys 2016 through 2018 data.

These adjustments resulted in an overall increase of 34,782 hours to the estimated burden.

16. Plans for Tabulation and Publication and Project Time Schedule

There are no plans to publish the collection of information under these regulations for statistical use unless requested by Congress in accordance with section 533 of the FD&C Act.

17. Reason(s) Display of OMB Expiration Date is Inappropriate

FDA will display the OMB expiration date as required by 5 CFR 1320.5.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.