DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2013–N–0825]

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.

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 March 9, 2020.

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: 202–395–7285, or emailed to *oira_submission@omb.eop.gov*. All comments should be identified with the OMB control number 0910–0231. Also include the FDA docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: Amber Sanford, Office of Operations, Food and Drug Administration, Three White Flint North, 10A–12M, 11601 Landsdown St., North Bethesda, MD 20852, 301–796–8867, *PRAStaff@fda.hhs.gov*.

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

OMB Control Number 0910–0231—Extension

Under section 515 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 360e) all devices placed into class III by FDA are subject to premarket approval application (PMA) requirements. PMA 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. PMA 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 must be reclassified into class I or class II.

The Food and Drug Administration Modernization Act of 1997 (FDAMA) (Pub. L. 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, 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 requires 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 regulations' 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.

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

Section 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 in 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.

Section 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 is 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 remanufacturers of single-use devices, 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).

Section 814.37(a) through (c) and (e)—PMA Amendments and Resubmitted PMAs. As part of the review process, FDA often requests the 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, on their own initiative, submit additional information to FDA during the review process. These amendments contain information ranging from additional test results and reanalysis of the original data set to revised device labeling. Almost all PMAs received by the Agency have amendments submitted during the review process.

Section 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).

Section 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.

Section 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.

Section 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. 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.

Section 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—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. 360e-3), 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-led 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.

Section 520(g)(7) of the FD&C Act (21 U.S.C. 360j(g)(7))—Agreement Meeting. Applicants planning to submit a PMA may submit a written request to reach agreement with FDA on the key parameters of the investigational plan.

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

Section 515(c)(3) of the FD&C Act—Panel of Experts. 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 that has previously been reviewed by the panel.

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

Section 814.82(a)(5) and (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.

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

In the **Federal Register** of October 24, 2019 (84 FR 57030), FDA published a 60-day notice requesting public comment on the proposed collection of information. No comments were received.

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

TABLE 1—ESTIMATED ANNUAL REPORTING BURDEN [1]

Activity/21 CFR or FD&C Act section	Number of respondents	Number 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

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.

TABLE 2—ESTIMATED ANNUAL RECORDKEEPING BURDEN [1]

Activity/21 CFR section	Number of recordkeepers	Number of records per recordkeeper	Total annual records	Average burden per recordkeeping	Total hours
Maintenance of records (814.82(a)(5) and (6))	446	1	446	17	7,582

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.

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.

Dated: January 31, 2020.

Lowell J. Schiller,

Principal Associate Commissioner for Policy.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2019–D–5270]

Biosimilars and Interchangeable Biosimilars: Licensure for Fewer Than All Conditions of Use for Which the Reference Product Has Been Licensed; Draft Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled ''Biosimilars and Interchangeable Biosimilars: Licensure for Fewer Than All Conditions of Use for Which the Reference Product Has Been Licensed.'' When finalized, this draft guidance will provide recommendations to applicants seeking licensure under the Public Health Service Act (the PHS Act) of a proposed biosimilar or proposed interchangeable biosimilar for fewer than all of the reference product's licensed conditions of use. Additionally, when finalized, this draft guidance will also provide recommendations on the submission of a supplement to a licensed biologics license application (BLA) seeking to add a condition of use that previously has been licensed for the reference product to the labeling of a licensed biosimilar or interchangeable product, including considerations related to the timing of such submissions.

DATES: Submit either electronic or written comments on the draft guidance by April 7, 2020 to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance.

ADDRESSES: You may submit comments on any guidance at any time as follows: