4160-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2014-N-0539]

Agency Information Collection Activities; Proposed Collection; Comment Request; Prescription Drug Labeling Improvement and Enhancement Initiative

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing an opportunity for public comment on the proposed collection of certain information by the Agency. Under the Paperwork Reduction Act of 1995 (the PRA), Federal Agencies are required to publish notice in the Federal Register concerning each proposed collection of information and to allow 60 days for public comment in response to the notice. This notice solicits comments on information collection for the Prescription Drug Labeling Improvement and Enhancement Initiative (the initiative); specifically, information collection associated with the use of Government contractor-assisted labeling conversion resources and services for certain older drug and biological products (approved before June 30, 2001). The intent of the initiative is to enhance the safe and effective use of prescription drugs by facilitating optimal communication through labeling.

DATES: Submit either electronic or written comments on the collection of information by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: Submit electronic comments on the collection of information to http://www.regulations.gov. Submit written comments on the collection of information to the

Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: FDA PRA Staff, Office of Operations, Food and Drug Administration, 1350 Piccard Dr., PI50-400B, Rockville, MD 20850, PRAStaff@fda.hhs.gov.

SUPPLEMENTARY INFORMATION: Under the PRA (44 U.S.C. 3501-3520), Federal Agencies must obtain approval from the Office of Management and Budget (OMB) for each collection of information they conduct or sponsor. "Collection of information" is defined in 44 U.S.C. 3502(3) and 5 CFR 1320.3(c) and includes Agency requests or requirements that members of the public submit reports, keep records, or provide information to a third party. Section 3506(c)(2)(A) of the PRA (44 U.S.C. 3506(c)(2)(A)) requires Federal Agencies to provide a 60-day notice in the Federal Register concerning each proposed collection of information before submitting the collection to OMB for approval. To comply with this requirement, FDA is publishing notice of the proposed collection of information set forth in this document.

With respect to the following collection of information, FDA invites comments on these topics: (1) Whether the proposed collection of information is necessary for the proper performance of FDA's functions, including whether the information will have practical utility; (2) the accuracy of FDA's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) ways to minimize the burden of the

collection of information on respondents, including through the use of automated collection techniques, when appropriate, and other forms of information technology.

Prescription Drug Labeling Improvement and Enhancement Initiative--(OMB Control Number 0910-NEW)

In the Federal Register of January 24, 2006 (71 FR 3922), FDA published the final rule "Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products," which revised the content and format requirements to make labeling easier to access, read, and use. This final rule is commonly referred to as the physician labeling rule (PLR) because it addresses prescription drug labeling used by prescribers, including physicians and other health care practitioners.[1]

The PLR applies to products for which a new drug application (NDA), biologics license application (BLA), or efficacy supplement (ES) to an NDA or BLA was approved between June 30, 2001, and June 30, 2006; was pending on June 30, 2006; or was submitted after June 30, 2006. Older drug and biological products (approved before June 30, 2001) are not subject to the mandatory PLR conversion requirements, but the NDA or BLA holder may voluntarily convert the labeling to PLR format. If application holders have not voluntarily converted labeling to PLR format, labeling for older drug and biological products must be in compliance with the requirements under 21 CFR 201.56(e) and 201.80.

The PLR established a staggered implementation schedule under which cohorts of drugs, from newest to oldest, would be converted to the PLR labeling format over time.[2] The staggered

[1] In this Federal Register document, the term "PLR format" refers to labeling that meets the content and format requirements in §§ 201.56(d) and 201.57 (21 CFR 201.56(d) and 201.57).

[2] See § 201.56(c). The Agency adopted this approach because research conducted during the PLR's development indicated that this was the "most reasonable approach to maximizing the public health benefit and best utilizing available resources." See 71 FR 3922 at 3962, January 24, 2006.

implementation for conversion to PLR format expired on June 30, 2013.[3] As of November 2013, approximately 15 percent of all prescription drugs and biological products have labeling in the PLR format.[4] If no further action is taken, the only additional drug products with labeling in the PLR format will be new NDAs, BLAs, and ESs, which are required to be submitted in PLR format, and labeling for older drug products for which the NDA or BLA holder voluntarily converts to PLR format.

To address this issue, FDA proposed the Prescription Drug Labeling Improvement and Enhancement Initiative in the Federal Register of February 6, 2013 (78 FR 8446), and solicited public comments. Specifically, FDA sought feedback on various issues related to the feasibility and implementation of the initiative, including the following:

- Approaches for identifying and prioritizing drugs and/or drug classes for voluntary PLR conversions;
- approaches that application holders would find helpful in facilitating voluntary PLR conversions for the specified drugs or drug classes;
- approaches for harmonizing labeling for generic drugs for which approval of the NDA for the reference listed drug (RLD) has been withdrawn;
- use of a Government contractor to provide PLR conversion resources and services; and
- overall interest in participating in the initiative.

In general, public comments posted to the docket (Docket No. FDA-2013-N-0059) supported the initiative, including the use of a Government contractor to ease the resource burden on application holders and to facilitate conversion to the PLR format. Some comments

[3] For the last cohort of drugs approved from June 30, 2001, to June 29, 2002, applicants were required to submit PLR conversion supplements to FDA by June 30, 2013.
[4] Data obtained from http://labels.fda.gov.

stated that having FDA (through a Government contractor) facilitate conversion of labeling to PLR format for the application holder may: (1) Allow for greater clarity and a better understanding of FDA's expectations, (2) result in a more efficient review process, and (3) expedite the availability of labeling in the PLR format. Thus, as part of the initiative, FDA intends to provide PLR conversion resources and services, including preparation of draft PLR format labeling, through the use of a Government contractor. For this part of the initiative, in a phased approach over 5 years, FDA proposes to identify and prioritize for PLR conversion approximately 750 prescription drug products not subject to the mandatory requirements under §§ 201.56(d) and 201.57 based on criteria that would maximize the benefit to the public health, including volume of prescriptions, clinical relevance, and risk-based considerations. This part of the initiative includes the following two collections of information: (1) The application holder's submission of its proposed PLR format labeling to FDA in a supplement to its application for products identified by FDA for the initiative and (2) the abbreviated new drug application (ANDA) holder's submission of a labeling supplement to FDA with conforming revisions for generic drug products affected by FDA's approval of a labeling change for the corresponding RLD.

Submitting a Supplement to FDA for the Proposed PLR Format Labeling

FDA will identify labeling to be converted to PLR based on the criteria established and, as recommended in comments submitted to the public docket, FDA will send an inquiry letter to the respective application holders to request their voluntary participation in this part of the initiative. The request will include information about the initiative, the labeling identified for PLR conversion, and a request for participation. FDA intends to provide Government contractor-assisted PLR conversion resources and services to application holders who

participate. FDA will review the draft PLR format labeling prepared by the contractor for content and format, and send a draft version to the application holder for review. FDA will request that the application holder review the draft labeling and submit a supplement to its application to FDA with its proposed PLR format labeling, which may include proposed revisions to the draft labeling. It should be emphasized that the application holder always bears responsibility for the content of its product labeling, and FDA's provision of contract resources is intended to facilitate conversion to the PLR format.

Submitting a Labeling Supplement to FDA for Generic Drug Products Affected by the RLD Labeling Change

After FDA approves a supplement to an NDA as a result of this part of the initiative, ANDA holders that relied on the NDA as their RLD will be required to revise the generic drug product labeling so that it conforms to the approved PLR-converted labeling of the RLD (see 21 CFR 314.94(a)(8)(iv) and 314.150(b)(10)). The guidance for industry entitled "Revising ANDA Labeling Following Revision of the RLD Labeling" provides information to ANDA holders on how to submit conforming labeling changes as a Special Supplement--Changes Being Effected.[5]

Description of Respondents: The respondents to this collection of information are persons and businesses, including small businesses and manufacturers.

Burden Estimates: FDA currently has OMB approval for the submission of labeling supplements under 21 CFR 314.70 and 314.97 (OMB control number 0910-0001) and approval for the design, testing, and production of prescription drug labeling under §§ 201.56 and 201.57

[5] This guidance is available on the Internet at http://www.fda.gov//Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm under Guidances (Drugs).

(OMB control number 0910-0572). This notice provides burden estimates associated with submitting additional labeling supplements as a result of this initiative.

Table 1 of this document provides an estimate of the reporting burden for: (1) Submitting a supplement to FDA for the proposed PLR format labeling and (2) submitting a labeling supplement to FDA for generic drug products affected by an FDA-approved change to the RLD labeling. In table 1, the estimated averages for the number of respondents and the hours per response were obtained using the collections of information described in the PLR (71 FR 3922, January 24, 2006).

Submitting a Supplement to FDA for the Proposed PLR Format

Based on the labeling conversion of approximately 750 prescription drug products not subject to the mandatory requirements under §§ 201.56 and 201.57, we estimate that 375 application holders will be contacted for voluntary participation in this part of the initiative, which is intended to occur in a phased approach over 5 years. Some application holders may receive more than one request to participate based on the process to identify and prioritize labeling.

The hours per response is the estimated number of hours an application holder would spend reviewing and responding to the request to participate, reviewing the draft PLR format labeling, modifying the labeling as appropriate, and submitting a supplement to FDA. We estimate that approximately 196 hours on average would be needed per submission, totaling 147,000 hours (see row 1 of table 1).

Submitting a Labeling Supplement to FDA for Generic Drug Products Affected by the RLD Labeling Change

FDA estimates that 1,864 generic drug products[6] will require labeling supplements from approximately 233 application holders, based on approved PLR-converted RLD labeling from this part of the initiative. The hours per response is the estimated number of hours a generic drug application holder would spend revising the ANDA labeling so that it conforms to the PLR-converted RLD labeling and submitting a labeling supplement to FDA. We estimate that approximately 27 hours on average would be needed per submission, totaling 50,328 hours (see row 2 of table 1).

Capital Costs

In 2006, the PLR described that a small number of carton-enclosed products may require new packaging to accommodate longer inserts for labeling in PLR format (71 FR 3922 at 3966). The PLR indicates that up to 5 percent of existing products affected by the rule may require equipment changes at an estimated cost of $200,000 for each product. Because the PLR has been in effect since 2006, we estimate that equipment changes may only be required for up to 1 percent of existing products that may be involved with this initiative. Therefore, we estimate that approximately 26 existing products could incur capital costs as a result of participating in the initiative, at a current cost of $245,400 per product. The estimated cost of changes to equipment totals $6.4 million.

In 2006, the PLR also estimated $8,700 as the average cost to a firm to: (1) Redesign the labeling of an existing drug (e.g., drug-specific decisions regarding exactly which adverse reactions should be listed in the highlights section), (2) test the redesigned labeling (e.g., to ensure that the larger labeling will still fit in carton-enclosed products), and (3) prepare and submit the labeling to FDA for approval. The PLR estimated $6,190 as the average cost to design labeling for new applications and efficacy supplements (71 FR 3922 at 3978). Thus, the

[6] Estimate based on the ratio of ANDA to NDA labeling in http://labels.fda.gov.

2006 estimated average cost to test the redesigned labeling and to prepare and submit the labeling to FDA for approval is calculated as $2,510 ($8,700 minus $6,190). For this part of the initiative, the Government contractor will provide a draft redesign of the labeling for application holders. Therefore, we estimate that approximately 608 application holders could incur capital costs as a result of participating in the initiative, at a current cost of $2,952 per product. The estimated cost of testing, preparing, and submitting the labeling to FDA for approval totals $7.7 million.

Operating and Maintenance Costs

In 2006, the PLR described that manufacturers may incur incremental printing costs because the content and format requirements of the final rule will lengthen labeling (71 FR 3922 at 3979). The PLR estimated that the annual per-product cost for innovator and generic products was $1,165 and $700, respectively. For this initiative, we estimate the current annual per-product cost for innovator and generic products as $1,429 and $859, respectively. Therefore, we estimate that the total incremental printing costs for innovator and generic products are approximately $1.1 million and $1.6 million, respectively, over the 5-year period of the program.

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

Table 1.--Estimated Reporting Burden Over a 5-Year Period[1]

Prescription Drug Labeling Improvement and Enhancement Initiative	No. of Respondents	No. of Responses per Respondent	Total Responses	Average Burden per Response (Hours)	Total Hours	Total Capital Costs ($ Million)	Total Operating and Maintenance Costs ($ Million)
Submitting a supplement to FDA for the proposed PLR format labeling	375	2	750	196	147,000	$4.0	$1.1

Table 1.--Estimated Reporting Burden Over a 5-Year Period[1]

Prescription Drug Labeling Improvement and Enhancement Initiative	No. of Respondents	No. of Responses per Respondent	Total Responses	Average Burden per Response (Hours)	Total Hours	Total Capital Costs ($ Million)	Total Operating and Maintenance Costs ($ Million)
Submitting a labeling supplement to FDA for generic drug products affected by the RLD labeling change	233	8	1,864	27	50,328	$10.1	$1.6
Total					197,328	$14.1	$2.7

[1] Numbers may not sum due to rounding.

Dated: May 1, 2014.

Leslie Kux,

Assistant Commissioner for Policy.

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