4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2022-N-1794]

Agency Information Collection Activities; Proposed Collection; Comment Request; General Drug Labeling Provisions and Over-the-Counter Monograph Drug User Fee Submissions

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing an opportunity for public comment on the proposed collection of certain information by the Agency. Under the Paperwork Reduction Act of 1995 (PRA), Federal Agencies are required to publish notice in the *Federal Register* concerning each proposed collection of information, including each proposed revision of an existing collection of information, and to allow 60 days for public comment in response to the notice. This notice solicits comments on information collections related to general drug product labeling and to over-the-counter (OTC) Monograph Drug User Fee (OMUFA) submissions.

DATES: Either electronic or written comments on the collection of information must be submitted by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*].

ADDRESSES: You may submit comments as follows. Please note that late, untimely filed comments will not be considered. The https://www.regulations.gov electronic filing system will accept comments until 11:59 p.m. Eastern Time at the end of [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]. Comments received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are received on or before that date.

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: https://www.regulations.gov. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to https://www.regulations.gov will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on https://www.regulations.gov.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2022-N-1794 for "Agency Information Collection Activities; Proposed Collection; Comment Request; General Drug Labeling Provisions and OTC Monograph Drug User Fee Submissions." Received

comments, those filed in a timely manner (see ADDRESSES), will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at https://www.regulations.gov or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, 240-402-7500.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states "THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION." The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on https://www.regulations.gov. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as "confidential." Any information marked as "confidential" will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to https://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 Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240-402-7500.

FOR FURTHER INFORMATION CONTACT: Domini Bean, Office of Operations, Food and Drug Administration, Three White Flint North, 10A-12M, 11601 Landsdown St., North Bethesda, MD 20852, 301-796-5733, PRAStaff@fda.hhs.gov.

SUPPLEMENTARY INFORMATION: Under the PRA (44 U.S.C. 3501-3521), 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, including each proposed revision of an existing 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.

General Drug Labeling Provisions and OTC Monograph Drug User Fee Submissions--21 CFR Part 201

OMB Control Number 0910-0340--Revision

I. OTC Drug Product Labeling

This information collection supports implementation of general drug labeling provisions, including certain OTC drug product labeling requirements found in FDA regulations in 21 CFR part 201 and in section 502(x) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 352(x)), as well as OTC drug product labeling recommendations discussed in FDA guidance documents enumerated below. Although we are including the information collection associated with section 502(x) in OMB control number 0910-0340, we are evaluating whether the placement of that information collection is better located in another approval.

The requirements and recommendations contained in the authority above help ensure that OTC drug product labeling includes information to assist consumers with product selection and with the safe and effective use of products that protect the public health from potential harm that could result from the dissemination of false and misleading statements regarding FDA-regulated products. As described further below, the information collection provisions of one guidance also apply to prescription drug labeling.

A. Principal Display Panel Labeling

Certain information collection provisions address the labeling (third-party disclosures) that drug companies provide on the principal display panel of every OTC drug product in package form--the part of that drug product's label that is most likely to be displayed or examined in a retail sale setting (see 21 CFR 201.60). Information on this panel supports consumers' product selection, as well as identification after purchase. OTC drug product companies must include a declaration of the net quantity of the OTC product contents on the principal display panel (see § 201.62 (21 CFR 201.62)). They also must include a statement of identity (see § 201.61 (21 CFR 201.61)).

Elsewhere in this issue of the *Federal Register*, FDA has made available a draft guidance for industry entitled "Statement of Identity and Strength--Content and Format of Labeling for Human Nonprescription Drug Products"[1] (available at https://www.fda.gov/regulatory-

[1] When final, this guidance will represent FDA's current thinking on this topic.

information/search-fda-guidance-documents/quantitative-labeling-sodium-potassium-and-phosphorus-human-over-counter-and-prescription-drug) that further addresses content and format of statement of identity information and drug product strength information to be included in the principal display panel labeling of human nonprescription drug products. The guidance provides recommendations to help manufacturers comply with statement of identity labeling requirements under § 201.61 and also provides a recommended alternative to the statement required by that regulation to provide consumers with consistent information about the active ingredients, strength, and dosage form of the product. Consistent information about the active ingredients, strength, and dosage form of the product on the principal display panel may aid consumers in comparing nonprescription drug products and assist consumers in appropriate self-selection of these products and in subsequent identification of the products after purchase.

In estimating burden for statement of identity labeling, we have excluded the burden for disclosing any statement of identity specified in a final OTC monograph order under section 505G of the FD&C Act (21 U.S.C. 355h), because FDA regulations state that for purposes of § 201.61, the statement of identity shall be the term or phrase used in an applicable OTC monograph (see 21 CFR 330.1(c)(1)). By operation of law, OTC monographs are now established by order under section 505G of the FD&C Act, and information collections made under section 505G are exempt from the PRA under section 505G(o).

B. OTC Drug and Prescription Drug Facts Labeling

In addition to labeling that drug companies provide on the principal display panel, companies must also comply with Agency regulations in § 201.66 (21 CFR 201.66), which requires standard content elements and formatting for the "Drug Facts" labeling (DFL) of all OTC drug products. This standardized labeling helps consumers understand the information that appears on OTC drug products to help ensure that consumers can use those products safely and effectively. The use of consistent language in labeling headings and subheadings helps

consumers comprehend information, and consistent formatting helps consumers more efficiently locate information.

The DFL is where OTC drug product labeling presents certain specific, standardized content required or recommended under other regulations or guidance documents. For this reason, our burden estimates address these information collections together. One such provision authorizes the optional use of a symbol to convey warnings regarding use of an OTC drug product while pregnant or breast-feeding (see § 201.63(a) (21 CFR 201.63(a)). In addition, the DFL is where OTC drug product labeling presents information (if applicable) on the quantity per dosage unit of certain specific substances. Some consumers need to restrict their total daily intake of these substances because of their impact on the consumers' underlying health conditions. Specific quantitative information must be presented in OTC drug product labeling for phenylalanine/aspartame (§ 201.21(b) (21 CFR 201.21(b))), sodium (§ 201.64(b) (21 CFR 201.64(b))), calcium (§ 201.70(b) (21 CFR 201.70(b))), magnesium (§ 201.71(b) (21 CFR 201.71(b))), and potassium (§ 201.72(b) (21 CFR 201.72(b))).

The quantitative labeling requirements in those regulations cited above are complemented by the draft guidance for industry entitled "Quantitative Labeling of Sodium, Potassium, and Phosphorus for Human Over-the-Counter and Prescription Drug Products", which FDA has made available elsewhere in this edition of the *Federal Register*[2] (available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/quantitative-labeling-sodium-potassium-and-phosphorus-human-over-counter-and-prescription-drug) (Quantitative Sodium, Potassium, and Phosphorus Labeling Guidance). This guidance document provides content and formatting recommendations for presenting quantitative information about sodium, potassium, and phosphorus that can help firms comply with the requirements under §§ 201.64 and 201.72 for conveying information about these substances in OTC drug product labeling. The guidance also provides parallel recommendations for drug companies to provide

[2] When final, this guidance will represent FDA's current thinking on this topic.

quantitative information about phosphorus in OTC drug product labeling. This quantitative information about sodium, potassium, and phosphorus helps patients who need to limit their overall consumption of any of these substances because of its impact on underlying health conditions, such as heart failure, hypertension, or chronic kidney disease. Quantifying these substances in drug labeling can also help healthcare providers and patients select drug products with lower amounts of these substances when such alternatives are available. The guidance recommends approaches to improve consistency in the presentation of this information, including clarifying quantities per dosage unit and rounding consistency. The information collections addressed in the guidance with regard to OTC drug products are included with our estimates for preparing the DFL panel of labeling, where this information appears.

The Quantitative Sodium, Potassium, and Phosphorus Labeling Guidance also recommends how drug firms can provide quantitative information on sodium, potassium, and phosphorus in prescription drug labeling to help patients who need to limit their overall consumption of these substances. Prescription drugs are not subject to the OTC labeling regulations, but the content and format of prescription drug labeling is set forth in 21 CFR 201.56 and 201.57 and approved under OMB control number 0910-0572. In the guidance, FDA recommends that when the recommended quantitative information about sodium, potassium, and phosphorus is included in prescription drug labeling, it should be presented within the DESCRIPTION section of that labeling, following the list of inactive ingredients. We estimate that the recommendations of the guidance regarding disclosing quantitative information about sodium, potassium, and phosphorus in prescription drug labeling will have no effect on the overall burden estimate for prescription drug labeling as a whole, which is addressed under OMB control number 0910-0572.

Our estimate of burden for OTC drug labeling that appears within the DFL reflects several considerations. For those OTC drug products that are marketed pursuant to an application approved under section 505 of the FD&C Act (21 U.S.C. 355), we assume a

substantial part of the burden of developing labeling is addressed in the submission of the new drug application, which includes submission of the proposed labeling. The information collections associated with new drug applications are approved under OMB control number 0910-0001. For OTC drugs that are legally marketed under section 505G of the FD&C Act that do not have an approved application under section 505 of the FD&C Act, a substantial part of the DFL's content, including applicable Uses (Indications), Warnings, and Directions, is established under section 505G, either by final administrative orders or by section 505G(a)(3). Collections of information made under section 505G of the FD&C Act are exempt from the PRA. Therefore, labeling required by administrative orders under section 505G of the FD&C Act or required by section 505G(a)(3) of the FD&C Act, even if it would ordinarily be a collection of information,[3] is exempt from the PRA and is not considered in our burden estimate for the DFL (see section 505G(o) of the FD&C Act). Finally, we note that the DFL of many individual products already being marketed will remain unchanged within a given year. Thus, our annualized burden estimate encompasses only new products or those otherwise undergoing changes, such as reformulation, or changes in package quantity that necessitate revisions to the DFL, whether those products are marketed under approved applications (e.g., new drug application/abbreviated new drug application) or pursuant to section 505G of the FD&C Act.

Our annualized estimate of burden addresses new products and products for which the DFL and/or net quantity of contents otherwise change in a 12-month period.

C. Labeling Related to Adverse Event Reporting

Section 502(x) of the FD&C Act requires the label of a nonprescription drug product marketed in the United States without an application approved under section 505 of the FD&C Act to include a domestic address or domestic telephone number through which a manufacturer, packer, and distributor may receive a report of a serious adverse event associated with its

[3] Some labeling required by these administrative orders or section 505G(a)(3) of the FD&C Act is not a collection of information at all, but rather, is the public disclosure of information originally supplied by the Federal government to the recipient for the purpose of disclosure to the public (see 5 CFR 1320.3(c)(2))).

product(s). To help implement this provision, we developed the guidance for industry entitled "Labeling of Nonprescription Human Drug Products Marketed Without an Approved Application as Required by the Dietary Supplement and Nonprescription Drug Consumer Protection Act: Questions and Answers" (September 2009) (available at https://www.fda.gov/media/77411/download). This guidance document is intended to assist respondents in complying with this statutory labeling requirement and provides recommendations for manufacturers to include an additional labeling statement identifying the purpose of the domestic address or telephone number to improve the usefulness of the labeling for consumers.

D. Submissions To Request Exemptions or Deferrals From OTC Drug Labeling Requirements

FDA regulations in § 201.66(e) authorize FDA to exempt or defer specific requirements in § 201.66 if FDA finds that the requirement is inapplicable, impracticable, or contrary to public health or safety. A manufacturer, packer, or distributor can seek such an exemption or deferral by submitting a written request in accordance with the requirements of § 201.66(e), which address the content of such a written request submission and how and where to submit it. A request for an exemption or deferral must be submitted in triplicate for each OTC drug product and contain certain information allowing the Agency to make an informed decision on the request. FDA uses the submitted information to assess whether the grounds for an exemption or deferral are met. Based on historical experience and from feedback received from respondents who have submitted similar requests, FDA estimates that it will take 24 hours to prepare and submit each submission and that on average annually, the Agency will receive one request for a waiver or exemption from the drug labeling requirement.

In addition, § 201.63(d) states that FDA may grant exemptions from the specific OTC drug product warning for patients who are pregnant or breast feeding that is ordinarily required to appear in labeling by § 201.63(a). To request such an exemption, the regulations call for submission of a citizen petition in accordance with § 10.30 (21 CFR 10.30). The submission of

citizen petitions under § 10.30, including those petitions that request this labeling exemption, is approved under OMB control number 0910-0191, and we do not address its burden further in this document.

We estimate the burden of this collection of information as follows:

Table 1.--Estimated Annual Third-Party Disclosure Burden for New OTC Drug Products[1]

Information Collection Activity--Labeling	No. of Respondents	No. of Disclosures per Respondent	Total Annual Disclosures	Average Burden per Disclosure	Total Hours
Declaration of Net Quantity of Contents Labeling for Nonprescription Drug Products--§ 201.62	875	9	7,918	0.5 (30 minutes)	3,959
Statement of Identity Labeling for Nonprescription Drug Products that are not covered by a final OTC Drug Monograph under section 505G of the FD&C Act--§ 201.61	292	11.5	3,383	2.5	8,457.5
Additional Statement of Identity and Strength information in labeling of nonprescription drug products that are not covered by a final OTC Drug Monograph under section 505G of the FD&C Act (Guidance For Industry (GFI): Statement of Identity and Strength--Content and Format of Labeling for Human Nonprescription Drug Products, section III)	292	11.5	3,383	2.5	8,457.5
Additional Statement of Identity and Dosage Form information in labeling of nonprescription drug products that are covered by a final OTC Drug Monograph under FD&C Act section 505G (GFI: Statement of Identity and Strength--Content and Format of Labeling for Human Nonprescription Drug Products, section III)	292	19	5,614	2.5	14,035
DFL for Nonprescription Drug Products--§ 201.66(c) and (d) (including content within DFL described in §§ 201.21(b), 201.63(a), 201.64(b), 201.70(b), 201.71(b), 201.72(b), or in guidance).	875	9	7,918	12	95,016
Address and phone number of responsible person added to labeling for nonprescription drug products marketed without an application approved under section 502(x) of the	300	3	900	4	3,600

Table 1.--Estimated Annual Third-Party Disclosure Burden for New OTC Drug Products[1]

Information Collection Activity--Labeling	No. of Respondents	No. of Disclosures per Respondent	Total Annual Disclosures	Average Burden per Disclosure	Total Hours
FD&C Act and GFI: Labeling of Nonprescription Human Drug Products Marketed Without an Approved Application as Required by the Dietary Supplement and Nonprescription Drug Consumer Protection Act: Q&A--section III)					
Total					133,525

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

Table 2.--Estimated Annual Third-Party Reporting Burden for OTC Drug Products[1]

Information Collection Activity--Labeling	No. of Respondents	No. of Disclosures per Respondent	Total Annual Disclosures	Average Burden per Disclosure	Total Hours
Requests for exemptions/deferrals of OTC drug product Drug Facts labeling requirements--§ 201.66(e)	1	1	1	24	24

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

II. OTC Monograph Drug User Fee Program Submissions

This information collection also includes submissions associated with the OTC Monograph Drug User Fee Program. Section 744M of the FD&C Act (21 U.S.C. 379j-72) establishes an OTC monograph drug user fee program (commonly called OMUFA) and authorizes FDA to assess and collect: (1) facility fees from qualifying OTC monograph drug facilities and (2) fees from submitters of qualifying OTC Monograph Order Requests (OMORs). The OMUFA program supports FDA activities related to the regulation of OTC monograph drug products, including provisions of section 505G of the FD&C Act that facilitate innovation and make it easier for FDA to better respond to safety issues when they emerge. We provide information regarding the OMUFA program on our website at https://www.fda.gov/industry/fda-user-fee-programs/over-counter-monograph-user-fee-program-omufa.

We developed Form FDA 5009, *Over-The-Counter Monograph User Fee Cover Sheet*, (available at www.fda.gov/about-fda/reports-manuals-forms/forms, Search for Form FDA 5009)

to facilitate the submission of OMUFA fees and to more efficiently administer the OMUFA program. Form FDA 5009 provides FDA with necessary information to determine the total user fee payment amount required and to help the Agency track payments. Respondents to this collection are qualifying finished dosage form manufacturers of OTC monograph drugs and submitters of qualifying OMORs submitted under section 505G(b)(5) of the FD&C Act.

We estimate the burden of collection of information as follows:

Table 3.--Estimated Annual OMUFA Reporting Burden[1]

Form FDA 5009--OMUFA Cover Sheet	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
Submission associated with facility fees	1,184	1	1,184	0.5 (30 minutes)	592
Submission associated with fees for qualifying OMORs	5	1	5	0.5 (30 minutes)	2.5
Total					594.5

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

Based on data from our electronic Drug Registration and Listing System, we estimate that there will be 1,184 respondents who will provide information in conjunction with facility fee payments annually. In addition, consistent with the Over-the-Counter Monograph User Program Performance Goals and Procedures commitment letter (available at https://www.fda.gov/media/106407/download), we estimate submitters will provide the user fee information using Form FDA 5009 in conjunction with an average of five qualifying OMORs annually. We assume the user fee-related submissions will require an average of 30 minutes to prepare, for a total of 594.5 hours annually.

Dated: September 2, 2022.

Lauren K. Roth,

Associate Commissioner for Policy.

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