Dated: December 3, 2013.

Leslie Kux,

Assistant Commissioner for Policy.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2013–D–1478]

Agency Information Collection Activities; Proposed Collection; Comment Request; Providing Waiver-Related Materials in Accordance With Draft Guidance for Industry on Providing Postmarket Periodic Safety Reports in the International Conference on Harmonisation E2C(R2) Format

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 the information collection associated with the submission of periodic safety reports as described in the guidance entitled ''Periodic Benefit-Risk Evaluation Report (PBRER) (E2C(R2)).'' The guidance was prepared under the auspices of the International Conference on Harmonisation (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use, and describes the format, content, and timing of a PBRER for an approved drug or biologic. This notice also solicits comments on the information collection associated with the submission of waiver-related materials as described in the draft guidance entitled ''Providing Postmarket Periodic Safety Reports in the ICH E2C(R2) Format.'' The draft guidance is intended to inform applicants of the conditions under which FDA will exercise its waiver authority to permit applicants to submit an ICH E2C(R2) PBRER in place of the ICH E2C(R1) Periodic Safety Update Report (PSUR), U.S. periodic adverse drug experience report (PADER), or U.S. periodic adverse experience report (PAER), to satisfy the periodic safety reporting requirements in FDA regulations.

DATES: Submit either electronic or written comments on the collection of information by February 10, 2014.

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.

Reporting in Accordance With International Conference on Harmonisation—Periodic Benefit-Risk Evaluation Report (E2C(R2)) Guidance

I. Background

ICH was organized to provide an opportunity for tripartite harmonization initiatives to be developed with input from both regulatory and industry representatives. ICH is concerned with harmonization of technical requirements for the registration of pharmaceutical products among three regions: The European Union, Japan, and the United States. In January 2012, the ICH Steering Committee agreed that the ''E2C(R2) Periodic Benefit-Risk Evaluation Report'' draft guidance (the draft PBRER guidance) should be made available for public comment. The PBRER is intended to provide a common standard for periodic reporting on approved drugs or biologics among the ICH regions. The harmonized PBRER is intended to promote a consistent approach to periodic postmarket safety reporting among the ICH regions and to enhance efficiency by reducing the number of reports generated for submission to the regulatory authorities.

The draft PBRER guidance revises an earlier version of this guidance issued in 1997 with an addendum issued in 2004. In the **Federal Register** of April 11, 2012 (77 FR 21782), FDA announced the availability of the draft PBRER guidance for public comment. FDA presented the comments received as part of the considerations by the E2C(R2) Expert Working Group for revisions of the guidance. A final version of the guidance was subsequently endorsed by the ICH on November 15, 2012, and published as the ICH harmonized tripartite guideline ''Periodic Benefit-Risk Evaluation Report (PBRER) E2C(R2)'' (the PBRER guidance), available at *http://www.ich.org/products/guidelines/efficacy/article/efficacy-guidelines.html.* FDA anticipates issuing final guidance on this topic that is consistent with the final ICH document, published November 2012, and thus is seeking PRA approval for information collections consistent with that document.

The April 11, 2012, **Federal Register** notice stated that the draft PBRER guidance includes information collection provisions that are subject to review by OMB under the PRA, and that before publication of the final guidance document, FDA intends to solicit public comment and obtain OMB approval for any information collections recommended in the guidance that are

new or that would represent material modifications to previously approved collections of information found in FDA regulations. This **Federal Register** notice begins the process of requesting public comment and obtaining OMB approval for collections of information associated with reporting in accordance with the PBRER guidance.

II. Voluntary Preparation of Periodic Safety Reports in Conformance With the ICH E2C(R2) PBRER Guidance, in Lieu of PADERs/PAERs Required Under 21 CFR 314.80(c)(2) and 600.80(c)(2)

FDA currently has OMB approval for the required submission of PADERs for drugs subject to a new drug application (NDA) or an abbreviated new drug application (ANDA) (§ 314.80(c)(2) (21 CFR 314.80(c)(2)); OMB control number 0910–0230), and for the required submission of PAERs for drugs subject to a biologics license application (BLA) (§ 600.80(c)(2) (21 CFR 600.80(c)(2)); OMB control number 0910–0308). Such reports include, for the reporting interval, reports of serious, expected adverse experiences and all non-serious adverse experiences and an index of these reports, a narrative summary and analysis of adverse experiences, an analysis of the 15-day Alert reports submitted during the reporting interval, and a history of actions taken because of adverse experiences. Applicants must submit each PADER/PAER to FDA quarterly for the first 3 years after the product is approved by FDA and annually thereafter. As described in the supporting documentation under OMB control numbers 0910–0230 and 0910–0308, FDA currently has OMB approval for approximately 60 hours for the preparation and submission of each PADER under § 314.80(c)(2) and 28 hours for the preparation and submission of each PAER under § 600.80(c)(2).

There is considerable overlap in the information required under §§ 314.80(c)(2) and 600.80(c)(2) and the information requested in a periodic safety report using the ICH E2C(R2) PBRER format. As a result, and as discussed further in this document, FDA, in the **Federal Register** of April 8, 2013 (78 FR 20926), announced the availability of a draft guidance to indicate its willingness to accept postmarket periodic safety reports using the ICH PBRER format in lieu of the specific reports described in FDA regulations. (As described further in this document, the April 2013 draft guidance also addresses waiver-related information that should be submitted to FDA by companies who wish to exercise this alternative reporting.)

Companies who submit periodic reports on the same drug to multiple regulators, including not only the United States, but, also the European Union, Japan, and regulators in other countries who have elected to adopt the ICH standards, may find it in their interest to prepare a single PBRER, rather than preparing multiple types of reports for multiple regulators. Companies who choose to submit a PBRER to FDA would include some information beyond that required by FDA regulations, including worldwide marketing approval status; estimated exposure and use patterns; information from clinical trials, non-interventional studies, non-clinical data, and literature; benefit evaluation, and benefit-risk analysis for approved indications, and should use a particular format described in that guidance.

FDA is not proposing to require submission of the PBRER; applicants subject to periodic safety reporting requirements under FDA regulations could choose to continue to submit the reports as specified in those regulations, and would be permitted to alternate between submission of reports in the PBRER format and submission of reports as specified in FDA regulations with an approved waiver. Based on FDA's experience with submission of periodic safety reports under previous ICH periodic reporting guidance, FDA believes that applicants would elect to submit the PBRER to FDA only in cases where they are also submitting that report to other regulatory authorities, some of which have underlying legal requirements that closely parallel the elements of the PBRER. For this reason, FDA believes that the additional burden associated with preparation of a PBRER in lieu of existing PADERs/PAERs is not attributable to the proposed collection of information by FDA, but rather is a ''usual and customary'' expenditure of time, effort, and financial resources that would be ''incurred by persons in the normal course of their activities,'' and thus is excluded from the calculation of burden under the PRA (5 CFR 1320.5(b)(2).) Cf. 5 CFR 1320.5(b)(3) (permitting exclusion from Federal burden of burden incurred in complying with an information collection that is also conducted by a State or local government if the State or local requirement would be imposed even in the absence of a Federal requirement).

We therefore believe that the existing estimate of burden for submission of periodic safety reports, approved under OMB control numbers 0910–0230 and 0910–0308, would be unchanged by this proposed collection, which would permit, but not require, the substitution of a PBRER for the periodic safety report otherwise required. We request comment on the assumption that all PBRERs submitted to FDA would be prepared in any event to submit to other jurisdictions, or alternatively, on the number of PBRERs that applicants will choose to prepare solely for submission to FDA, and the estimated burden for submitting such a report.

III. Materials Related to Waivers Permitting Submission of a PBRER To Satisfy the Periodic Safety Reporting Requirements in §§ 314.80(c)(2) and 600.80(c)(2)

Because FDA regulations in §§ 314.80(c)(2) and 600.80(c)(2) include specific requirements for periodic safety reports, in order for an applicant to submit an alternative report, such as the PBRER, for a given product, FDA must grant a waiver. Existing regulations permit applicants to request waivers of any postmarketing safety reporting requirement, and the information collections associated with such waiver requests generally are approved under existing control numbers. (See § 314.90(a), waivers for drugs subject to NDAs and ANDAs (approved under OMB control number 0910–0001); and § 600.90(a), waivers for products subject to BLAs (approved under OMB control number 0910–0308).)

In the **Federal Register** of April 8, 2013, FDA announced the availability of a draft guidance entitled ''Providing Postmarket Periodic Safety Reports in the ICH E2C(R2) Format,'' which indicates that FDA will be prepared to grant waivers to enable submission of the PBRER in the United States in place of a PADER required under § 314.80(c)(2) or in place of a PAER required under § 600.80(c)(2). The draft guidance both explains conditions under which applicants that have previously received waivers to submit reporting information in the format of the previous ICH guidance would be permitted to apply those existing waivers to the submission of PBRERs, and also advises how applicants that have not previously obtained a waiver may submit waiver requests that would be granted for the submission of PBRERs. This **Federal Register** notice solicits comment on certain information collections proposed in the April 8, 2013, draft guidance that are related to waivers specifically to enable the submission of PBRERs, and that are not already addressed under approved control numbers covering waiver submissions and periodic safety reports generally.

FDA has previously granted waiver requests, submitted under §§ 314.90(a)

and 600.90(a), that allow applicants to prepare and submit reports using the PSUR format described in the 1997 and 2004 ICH E2C guidance. In accordance with the recommendations of the April 8, 2013, draft guidance, if an applicant already has a PSUR waiver in place for a given approved application, FDA will consider the existing PSUR waiver to allow the applicant to submit a PBRER instead of a PSUR because the PBRER replaces the PSUR for postmarketing periodic safety reporting for that application. The applicant would not need to submit a new waiver request unless the applicant wishes to use a different data lock point or change the frequency of reporting.

If an applicant submits a PBRER in place of the PSUR and uses a different data lock point, the applicant should submit overlapping reports or submit a one-time PADER/PAER in order to cover the gap in reporting intervals. The applicant should request a waiver to change the data lock point and this waiver request should include a description of the measures taken to ensure that there are no resulting gaps in reporting with the change.

If an applicant submits a PBRER in place of the PSUR and uses a different reporting frequency for the PBRER than was used for the PSUR, the applicant must request a waiver. This waiver request should describe the measures taken to ensure that the periodicity requirements under §§ 314.80(c)(2)(i) and 600.80(c)(2)(i) are being met. If an applicant requests to submit a PBRER less frequently than is permitted under the applicant's PSUR waiver, the continued validity of the waiver will be conditioned on the submission of a PADER/PAER as needed to fulfill the reporting frequency requirement under FDA regulations. The draft guidance also states that if an applicant is on a quarterly reporting schedule but wishes to submit a PBRER every 6 months without submitting a quarterly PADER/PAER in the intervening quarters, the applicant may request a waiver of the quarterly reporting requirement.

FDA expects approximately 189 waiver requests to include the additional information and notifications described previously in this document for using a different data lock point and/or for using a different reporting frequency when submitting a PBRER. FDA expects approximately 55 applicants to make these submissions, and we estimate that the time for submitting the additional information and notifications described previously would be on average approximately 1 hour for each waiver request.

If an applicant does not have a PSUR waiver in place for an approved application, the applicant may submit a waiver request under § 314.90(a) or § 600.90(a) to submit a PBRER instead of the PADER/PAER. The applicant should submit a request to FDA for each approved application for which a waiver is requested, and a single waiver request letter can include multiple applications. Waiver requests should be submitted to each of the application(s) in the request, and may be submitted electronically or by mail as described in the April 8, 2013, draft guidance. Each PBRER waiver request should include the following information:

(1) The product name(s) and application number(s);

(2) A brief description of the justification for the request;

(3) The U.S. approval date for the product(s) and current reporting interval used;

(4) The reporting interval of the last PADER/PAER submitted for the product(s);

(5) The data lock point that will be used for each PBRER. If a data lock point other than one aligned to the U.S. approval date is proposed, the applicant should describe how he/she will ensure that there are no gaps in reporting intervals (e.g., by submitting overlapping reports; submitting a one-time PADER/PAER to cover the gap period; or, if the gap is less than 2 months, extending the reporting interval of the final PADER/PAER to close the gap).

(6) The frequency for submitting the PBRER, as described in section IV.C of the April 8, 2013, draft guidance.

(7) The email address and telephone number for the individual who can provide additional information regarding the waiver request.

As explained earlier, existing regulations at §§ 314.90(a) or 600.90(a) permit applicants to request waivers of any postmarketing safety reporting requirement, and the information collections associated with such waiver requests generally are approved under OMB control numbers 0910–0001and 0910–0308. FDA believes that the information submitted under numbers 1–4 and number 7 in the list in the previous paragraph is information that is typical of any waiver request regarding postmarketing safety reporting and is accounted for in the existing approved collections of information for waiver requests and reports. Concerning numbers 5 and 6, FDA expects approximately 67 waiver requests to include the additional information for using a different data lock point and/or for using a different reporting frequency when submitting a PBRER. FDA expects approximately 29 applicants to make these submissions, and we estimate that the time for submitting the additional information described in the previous paragraph would be on average approximately 2 hours for each waiver request.

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

TABLE 1—ESTIMATED REPORTING BURDEN [1]

Additional information and/or notifications for using a different data lock point and/or a different reporting frequency	Number of respondents	Number of responses per respondent	Total annual responses	Average burden per response	Total hours
Applicants that have a PSUR waiver for an approved application	55	3.4	187	1	187
Applicants that do not have a PSUR waiver for an approved application	29	2.3	67	2	134
Total					321

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

Dated: December 3, 2013.

Leslie Kux,

Assistant Commissioner for Policy.

[FR Doc. 2013–29393 Filed 12–9–13; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2013–N–1434]

Draft Guidance for Industry on Size, Shape, and Other Physical Attributes of Generic Tablets and Capsules; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry entitled ''Size, Shape, and Other Physical Attributes of Generic Tablets and Capsules.'' This guidance discusses FDA recommendations for the size, shape, and other physical attributes of generic tablets intended to be swallowed intact. FDA is concerned that these characteristics of generic drugs are too varied compared to the originator drug and could affect patient outcomes.

DATES: Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance, submit either electronic or written comments on the draft guidance by March 10, 2014.

ADDRESSES: Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 2201, Silver Spring, MD 20993–0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the draft guidance document.

Submit electronic comments on the draft guidance to *http://www.regulations.gov.* Submit written comments to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Debra Catterson, Center for Drug Evaluation and Research (HFD–600), Food and Drug Administration, 11919 Rockville Pike, Rockville, MD 20852, 240–402–3861; or Vilayat Sayeed, Center for Drug Evaluation and Research (HFD–630), Food and Drug Administration, 7520 Standish Pl., Rockville, MD 20855, 240–276–8486.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled ''Size, Shape, and Other Physical Attributes of Generic Tablets and Capsules.'' FDA is concerned that the differences in size, shape, and other physical characteristics between the generic and the originator could adversely affect patient outcomes. For example, studies show that tablet size can affect ease of swallowing, and generic tablets that are significantly larger than their corresponding reference drug product may be more difficult to swallow, leading to potential adverse events as well as noncompliance with treatment regimens. FDA is recommending generic manufacturers consider the size, shape, and other physical characteristics of the originator drug when developing a generic version.

This draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the Agency's current thinking on tablet size, shape, and other physical attributes of generic solid oral dosage forms. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

II. Paperwork Reduction Act of 1995

This draft guidance contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (the PRA) (44 U.S.C. 3501–3520). The collection of information requested in the draft guidance is covered under FDA regulations at 21 CFR 314 and approved under OMB control number 0910–0001. In accordance with the PRA, prior to publication of any final guidance document, FDA intends to solicit public comment and obtain OMB approval for any information collections recommended in this guidance that are new or that would represent material modifications to those previously approved collections of information found in FDA regulations or guidances.

III. Comments

Interested persons may submit either electronic comments regarding this document to *http://www.regulations.gov* or written comments to the Division of Dockets Management (see **ADDRESSES**). It is only necessary to send one set of comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at *http://www.regulations.gov.*

IV. Electronic Access

Persons with access to the Internet may obtain the document at either *http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm* or *http://www.regulations.gov.*

Dated: December 2, 2013.

Leslie Kux,

Assistant Commissioner for Policy.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2013–D–0928]

Draft Guidance for Industry on Recommendations for Preparation and Submission of Animal Food Additive Petitions; Reopening of the Comment Period

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice; reopening of the comment period.

SUMMARY: The Food and Drug Administration (FDA) is reopening the comment period for the notice published in the **Federal Register** of Wednesday, September 11, 2013 (78 FR 55727), announcing the availability of the draft guidance for industry (GFI #221) entitled ''Recommendations for Preparation and Submission of Animal Food Additive Petitions.''

DATES: Submit either electronic or written comments by January 9, 2014.

ADDRESSES: Submit electronic comments to *http://www.regulations.gov.* Submit written comments to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Sharon Benz, Center for Veterinary