4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2013-D-0349]

Providing Postmarketing Periodic Safety Reports in the International Council for Harmonisation E2C(R2) Format (Periodic Benefit-Risk Evaluation Report); 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 guidance for industry entitled "Providing Postmarketing Periodic Safety Reports in the ICH E2C(R2) Format (Periodic Benefit-Risk Evaluation Report)." This guidance is intended to inform applicants of the conditions under which FDA will exercise its waiver authority to permit applicants to submit an International Council for Harmonisation (ICH) (formerly International Conference on Harmonisation) E2C(R2) Periodic Benefit-Risk Evaluation Report (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. The guidance describes the steps applicants can take to submit the PBRER, and discusses the format, content, submission deadline, and frequency of reporting for the PBRER.

DATES: Submit either electronic or written comments on the guidance at any time.

ADDRESSES: You may submit comments as follows:

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): Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Division of Dockets Management, 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-2013-D-0349 for "Providing Postmarketing Periodic Safety Reports in the ICH E2C(R2) Format (Periodic

Benefit-Risk Evaluation Report)." Received comments will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at https://www.regulations.gov/ or at the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

- 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 Division of Dockets Management. 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: http://www.fda.gov/regulatoryinformation/dockets/default.htm.

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 Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

Submit written requests for single copies of this guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993-0002; or the Office of Communication, Outreach and Development, Center for Biologics Evaluation and Research (CBER), Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, rm. 3128, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your requests. The guidance may also be obtained by mail by calling CBER at 1-800-835-4709 or 240-402-8010. See the SUPPLEMENTARY INFORMATION section for electronic access to the guidance document.

FOR FURTHER INFORMATION CONTACT: Jean Chung, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, rm. 4466, Silver Spring, MD 20993-0002, 301-796-2380; or Stephen Ripley, Center for Biologics Evaluation and Research, Food and Drug Administration,10903 New Hampshire Ave., Bldg. 71, rm. 3128, Silver Spring, MD 20993-0002, 240-402-7911.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a guidance for industry entitled "Providing Postmarketing Periodic Safety Reports in the ICH E2C(R2) Format (Periodic Benefit-Risk Evaluation Report)." We are issuing the guidance to describe the conditions under which FDA will exercise its waiver authority to permit the holders of approved new drug applications,

abbreviated new drug applications, and biologics license applications (applicants) to use the reporting format of the PBRER to submit periodic safety reports for their marketed products. The harmonized PBRER is intended to promote a consistent approach to periodic postmarketing safety reporting among the ICH regions and to enhance efficiency by reducing the number of reports generated for submissions to the regulatory authorities.

FDA's postmarketing safety reporting regulations require applicants to submit periodic safety reports in the form of a Periodic adverse drug experience report (PADER) (for drugs) or a Periodic adverse experience report (PAER) (for biologics) (21 CFR 314.80(c)(2) and 600.80(c)(2), respectively). FDA has routinely granted waivers under 21 CFR 314.90(b) and 600.90(b) permitting applicants to submit an internationally harmonized Periodic Safety Update Report (PSUR) prepared in accordance with ICH E2C (see 62 FR 27470, May 19, 1997) and 69 FR 5551, February 5, 2004)) instead of a PADER/PAER under conditions stated in the waiver. On November 15, 2012, the ICH Steering Committee signed off on the ICH harmonized guideline "Periodic Benefit-Risk Evaluation Report (PBRER) E2C(R2) " and recommended that the PBRER format be adopted by the ICH regulatory bodies of the three regions. Therefore, the new and more comprehensive report format, the PBRER, has superseded the PSUR report format.

This guidance provides information on the steps applicants can take to submit a PBRER to the FDA in place of a PSUR, PADER, or PAER. The guidance discusses: (1) Applicants who have a waiver for their approved product to submit a PSUR instead of a PADER/PAER and (2) applicants who have not obtained a waiver and are currently submitting PADERs/PAERs as required under FDA regulations. Because the PBRER has replaced the PSUR as the ICH E2C harmonized postmarketing safety report format, FDA is permitting applicants with an existing

PSUR waiver to substitute the PBRER for the PSUR without submitting a new waiver request. This guidance describes the steps an applicant should take to submit the PBRER instead of the PSUR. For applicants who do not have a PSUR waiver for their approved application but would like to submit the PBRER instead of the PADER/PAER, this guidance provides information on how to submit a waiver request if they wish to do so.

This guidance describes the content, format, and submission deadlines applicants should follow when submitting the PBRER, as well as U.S.-specific appendices that should be submitted with the PBRER. It also explains how applicants can fulfill FDA's annual reporting requirement while submitting a harmonized PBRER that covers a longer reporting interval. In addition, FDA will consider requests to waive the quarterly reporting requirement.

This guidance finalizes the draft guidance for industry entitled "Providing Postmarket Periodic Safety Reports in the ICH E2C(R2) Format (Periodic Benefit-Risk Evaluation Report)," which was announced in the Federal Register of April 8, 2013 (78 FR 20926). We reviewed the comments received on the draft guidance and revised several sections of the guidance in response to comments and questions on topics such as the submission of the nonexpedited individual case safety reports, waivers of the quarterly reporting requirement, the supplemental information to be provided with the PSUR/PBRER, handling gaps in reporting with changes to the date of the data lock point for the reporting interval, and accepted formats for the periodic safety report. In response to comments, we also clarified the text in the examples that were given in the draft guidance.

This guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The guidance represents the current thinking of FDA on providing postmarketing periodic safety reports in the ICH E2C(R2) PBRER format. It does not establish

any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

II. Electronic Access

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

III. The Paperwork Reduction Act of 1995

This guidance refers to previously approved collections of information that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501-3520). The collections of information related to submission of waiver requests under §§ 314.90(a) and 600.90 have been approved under OMB control numbers 0910-0001 and 0910-0308. The guidance also refers to collections of information that have been approved under OMB control number 0910-0771 related to providing waiver-related materials in accordance with the guidance.

Dated: November 22, 2016.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2016-28606 Filed: 11/28/2016 8:45 am; Publication Date: 11/29/2016]