4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2011-D-0164]

Safety Labeling Changes--Implementation of Section 505(o)(4) of the Federal Food, Drug, and Cosmetic Act; Draft Guidance for Industry; Availability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SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled "Safety Labeling Changes--Implementation of Section 505(o)(4) of the Federal Food, Drug, and Cosmetic Act." This draft guidance provides information on the implementation of the statutory provision that authorizes FDA to require application holders for certain drug and biological products to make labeling changes based on new safety information that becomes available after approval of the drug that FDA determines should be included in the labeling of the drug. This guidance is being updated and reissued in draft to, among other things, include the addition of information related to Congress' 2018 changes to the definition of *adverse drug experience* regarding reduced effectiveness and make other changes to reflect current Agency processes and procedures regarding safety labeling changes. This draft guidance revises and, when finalized, will replace the guidance for industry entitled "Safety Labeling Changes--Implementation of Section 505(o)(4) of the FD&C Act" issued in July 2013.

DATES: Submit either electronic or written comments on the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*] to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance.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:

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-2011-D-0164 for "Safety Labeling Changes--Implementation of Section 505(o)(4) of the Federal Food, Drug, and Cosmetic Act." 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 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.

You may submit comments on any guidance at any time (see 21 CFR 10.115(g)(5)).

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, 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, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 3103 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.

FOR FURTHER INFORMATION CONTACT: Kimberly Lehrfeld, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave, Bldg. 51, Rm. 6250, Silver Spring, MD 20993-0002, 301-796-3137, Kimberly.Lehrfeld@fda.hhs.gov or Phillip Kurs, Center for Biologics Evaluation and Research, Food and Drug Administration, 240-402-7911.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled "Safety Labeling Changes--Implementation of Section 505(o)(4) of the Federal Food, Drug, and Cosmetic Act." Section 505(o)(4) of the FD&C Act (21 U.S.C. 355(o)(4)) authorizes FDA to require application holders for certain drugs[1] to make labeling changes based on new safety information, including information related to reduced effectiveness, that becomes available after approval of the drug that FDA determines should be included in the labeling of the drug.

In the *Federal Register* of July 30, 2013 (78 FR 45930), FDA announced the availability of a guidance for industry entitled "Safety Labeling Changes--Implementation of Section 505(o)(4) of the Federal Food, Drug, and Cosmetic Act" (available at

[1] For the purposes of the *Safety Labeling Changes--Implementation of Section 505(o)(4) of the Federal Food, Drug, and Cosmetic Act Guidance for Industry*, references to *drug* include drug products approved under section 505 of the FD&C Act (21 U.S.C. 355) and biological products licensed under section 351 of the Public Health Service Act (42 U.S.C. 262), other than biological products that also meet the definition of a device in section 201(h) of the FD&C Act (21 U.S.C. 321(h)).

https://www.fda.gov/media/116594/download) (the 2013 guidance). The 2013 guidance provided information on the implementation of section 505(o)(4) of the FD&C Act, including a description of the types of safety labeling changes (SLCs) that generally may be required under this section; how FDA determines what constitutes new safety information; the procedures involved in requiring SLCs; and enforcement of the requirements for SLCs.

In 2018, Congress enacted the Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment for Patients and Communities Act (Pub. L. 115-271) (SUPPORT Act) which, among other things, changed the statutory definition of *adverse drug experience* in section 505-1(b)(1) of the FD&C Act. The SUPPORT Act also revised section 505(o)(4) of FD&C Act to define new information to include "information related to reduced effectiveness."

This draft guidance revises and, when finalized, will replace the guidance for industry of the same name issued on July 30, 2013 (78 FR 45930). Updates in this draft guidance include the addition of information related to Congress' 2018 changes to the definition of *adverse drug experience* regarding reduced effectiveness such as the clarification that the Agency can require changes to labeling to include information about a serious risk that results from reduced effectiveness. Additional changes were made reflecting current SLC processes and procedures adding a description of how FDA reviews and acts on SLCs when new safety information applies to multiple application holders, and clarifying when FDA may disclose SLC notification and order letters.

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 current thinking of FDA on "Safety Labeling Changes--Implementation of Section 505(o)(4) of the FD&C Act." 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.

As we develop final guidance on this topic, FDA will consider comments on costs or cost savings the guidance may generate, relevant for Executive Order 14192.

II. The Paperwork Reduction Act of 1995

While this guidance contains no collection of information, it does refer to previously approved FDA collections of information. The previously approved collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501-3521). The collections of information in 21 CFR part 314 pertaining to the submission of new drug applications (NDAs), abbreviated new drug applications (ANDAs), and supplements to NDAs and ANDAs have been approved under OMB control number 0910-0001. The collections of information in 21 CFR part 601 pertaining to biologics license applications (BLAs) and supplements to BLAs have been approved under OMB control number 0910-0338. The collections of information pertaining to medication guides for prescription drug products have been approved under OMB control number 0910-0393. The collections of information pertaining to the labeling of human prescription drug and biological products have been approved under OMB control number 0910-0572.

III. Electronic Access

Persons with access to the internet may obtain the draft guidance at https://www.fda.gov/regulatory-information/search-fda-guidance-documents, https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs, https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/biologics-guidances, or https://www.regulations.gov.

Grace R. Graham,

Deputy Commissioner for Policy, Legislation, and International Affairs.

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