4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2013-D-1165]

Draft Guidance for Industry on Reference Product Exclusivity for Biological Products Filed Under Section 351(a) of the Public Health Service Act; Availability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SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry entitled "Reference Product Exclusivity for Biological Products Filed Under Section 351(a) of the PHS Act." This draft guidance is intended to assist sponsors developing biological products, sponsors holding biologics license applications (BLAs), and other interested parties in providing information and data that will help the Agency determine the date of first licensure for a reference product under 351(k)(7)(C) of the Public Health Service Act (PHS Act), as added by the Biologics Price Competition and Innovation Act of 2009 (BPCI Act). The BPCI Act amends the PHS Act and other statutes to create an abbreviated licensure pathway for biological products shown to be biosimilar to, or interchangeable with, an FDA-licensed biological reference product.

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comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance, submit either electronic or written comments on the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER]. Submit either electronic or written comments concerning the proposed

collection of information by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 2201,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, or Office of Communication, Outreach and Development (HFM-40), Center for Biologics Evaluation and Research, 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. See the SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance document.

Submit electronic comments on the draft guidance to http://www.regulations.gov.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: Sandra Benton, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 6340, Silver Spring, MD 20993-0002, 301-796-1042; or Stephen Ripley, Center for Biologics Evaluation and Research (HFM-17), Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, rm. 7301, Silver Spring, MD 20993-0002, 240-402-7911.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled "Reference Product Exclusivity for Biological Products Filed Under Section 351(a) of the PHS Act." This draft guidance is intended to assist sponsors who are developing biological products, sponsors of

BLAs, and other interested parties in providing information that will help the Agency determine the date of first licensure for a reference product under 351(k)(7)(C) of the Public Health Service Act (PHS Act) as added by the Biologics Price Competition and Innovation Act of 2009 (BPCI Act).

The BPCI Act amends the PHS Act and other statutes to create an abbreviated licensure pathway for biological products shown to be biosimilar to, or interchangeable with, an FDA-licensed biological reference product (see sections 7001 through 7003 of the Patient Protection and Affordable Care Act (Pub. L. 111-148)). Section 351(k)(7) of the PHS Act, entitled "Exclusivity for Reference Product," describes reference product exclusivity, the period of time in which a 351(k) sponsor is not permitted to submit and FDA is not permitted to license a 351(k) application that references a reference product, the single biological product licensed under section 351(a) of the PHS Act against which a biological product is evaluated in a 351(k) application. Under this section, exclusivity for the reference product is described in terms of a prohibition on acceptance or approval of an application for a biosimilar or interchangeable product for a period of time starting from the date of first licensure. Specifically, approval of a 351(k) application may not be made effective until 12 years after the date of first licensure of the reference product which under the statute excludes the date of licensure of supplements and certain other applications. A 351(k) application for a biosimilar or interchangeable biological product cannot be submitted for review until 4 years after the date on which the reference product was first licensed under section 351(a) of the PHS Act.

Determining the date of first licensure for a reference product, in turn, determines whether a particular biological product qualifies for a period of exclusivity under 351(k)(7) of the PHS Act and the date on which such exclusivity, if any, will expire. Making this

determination can present unique challenges given the requirements of section 351(k)(7) of the PHS Act. These are made more acute because of the scientific and technical complexities that may be associated with the larger and typically more complex structures of biological products as compared with small molecule drugs, as well as the processes by which such biological products are made. Therefore, the 351(a) applicant may provide information to FDA, such as that described in this guidance or other relevant information, to assist FDA with its analysis of the date of first licensure for a biological product under section 351(k)(7) of the PHS Act.

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 determining the date of first licensure for biological products filed under section 351(a) of the PHS Act. 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. 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.

III. Paperwork Reduction Act of 1995

Under the Paperwork Reduction Act of 1995 (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.

This draft guidance also refers to previously approved collections of information found in FDA regulations. The collections of information in 21 CFR 314.50 and 21 CFR part 601 (BLA) have been approved under OMB control numbers 0910-0001 and 0910-0338, respectively. The general licensing provisions under section 351(k) (biosimilar applications) of the BPCI Act have been approved under OMB control number 0910-0719.

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.

Title: Draft Guidance for Industry on Reference Product Exclusivity for Biological Products Filed Under Section 351(a) of the PHS Act

Description of Respondents: Respondents to the proposed collection of information include sponsors developing biological products and sponsors holding BLAs.

Burden Estimate: The draft guidance proposes a new collection of information by requesting information and data from sponsors to assist FDA in determining the date of first licensure for a reference product filed under section 351(a) of the PHS Act described under section 351(k)(7) of the PHS Act as added by the BPCI Act. The proposed collection of information includes information that would describe and explain how a proposed product is structurally the same as or different from any previously licensed biological product, along with supporting information that describes how such modification results in a change in safety, purity, or potency of the product. FDA recommends that the sponsor include information as described in the draft guidance at the time the 351(a) application is submitted or, in the case of a previously approved 351(a) application, as a supplement to the application. Alternatively, this information may be submitted as an amendment to the 351(a) application. A summary of the recommended information includes the following: (1) A list of all licensed biological products that are structurally related to the biological product that is the subject of the 351(a) application being considered; (2) of those licensed biological products identified in item 1, the identification of the products for which the sponsor or one of the sponsor's affiliates, including any licensors, predecessors in interest, successors in interest, or related entities, are the current or previous license holder; (3) description of the structural differences between the proposed product and any products identified in item 2; and (4) description of the change in safety, purity, and/or potency between the proposed product and any products identified in item 2. The proposed collection of information also includes any other information and data that would assist FDA in making a determination of the date of first licensure for biological products and BLAs as described under

section 351(k)(7) of the PHS Act. FDA estimates the burden of this collection of information as follows:

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

Reporting Activity	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
Information for Determination of the Date of First Licensure	10	1	10	150	1,500

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

As indicated in table 1 of this document, FDA estimates that it will receive a total of approximately 10 requests annually for determination of the date of first licensure of a 351(a) product under 351(k)(7) of the PHS Act. The average burden per response (hours) is based on FDA experience with similar information collection requirements.

IV. Electronic Access

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

Dated: July 29, 2014.

Leslie Kux,

Assistant Commissioner for Policy.

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