TABLE 1—ESTIMATED ANNUAL REPORTING BURDEN [1]—Continued

GFI: Formal meetings between FDA and biosimilar biological product sponsors or applicants	Number of respondents	Number of responses per respondent	Total annual responses	Average burden per response	Total hours
CBER Information Packages	2	2	4	30	120
Total					3,405

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

Since last OMB approval, there has been an increase in meeting requests with CDER and a corresponding increase in the number of information packages. Accordingly, we have adjusted our estimate upward by six respondents to CDER meeting requests. We attribute this change to an increase in biosimilar product development.

Dated: September 4, 2018.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2018–19674 Filed 9–10–18; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2018–D–3151]

Postapproval Changes to Drug Substances; Draft Guidance for Industry; Availability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SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled ''Postapproval Changes to Drug Substances.'' This draft guidance provides recommendations to holders of approved new drug applications, abbreviated new drug applications, new animal drug applications, abbreviated new animal drug applications, and holders of drug master files and veterinary master files who may want to make a change to the drug substance manufacturing process during the drug product application postapproval period. The draft guidance applies to synthetic drug substances and the synthetic steps involved in the preparation of semisynthetic drug substances. The draft guidance covers facility, scale, and equipment changes associated with all steps of drug substance manufacturing; specification changes to starting materials, raw materials, intermediates, and the unfinished and final drug substance; synthetic manufacturing process changes; changes in the source of drug substance; and change to container closure system of the drug substance.

DATES: Submit either electronic or written comments on the draft guidance by November 13, 2018 to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance.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–2018–D–3151 for ''Postapproval Changes to Drug Substances.'' 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.

- 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.gpo.gov/fdsys/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.

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. 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.

FOR FURTHER INFORMATION CONTACT: Carolyn Cohran, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm 4151, Silver Spring, MD 20993–0002, 240–402–8612; Stephen Ripley, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg.71, Rm. 7301, Silver Spring, MD 20993–0002, 240–402–7911; or Dennis Bensley, Center for Veterinary Medicine, Food and Drug Administration, 7500 Standish Place, Rm. E334, Rockville, MD 20855, 240–402–0696.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled ''Postapproval Changes to Drug Substances.'' As part of the reauthorization of the Generic Drug User Fee Amendments (GDUFA II), FDA committed to issuing a guidance on postapproval changes to Type II Active Pharmaceutical Ingredients Drug Master Files (DMFs) and submission mechanisms for abbreviated new drug application holders who reference such DMFs (see GDUFA Reauthorization Performance Goals and Program Enhancements Fiscal Years 2018–2022, known as the GDUFA II Commitment Letter, at *https://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM525234.pdf*). This draft guidance is intended to fulfill that commitment by describing the documentation for master file holders or drug substance manufacturers, as appropriate. The documentation to be submitted by the approved application holder is also outlined, and references to the appropriate pathways for such submissions are provided.

A letter of authorization must be provided for an applicant to reference a DMF for the proposed drug substance § 314.420(b) (21 CFR 314.420(b)). Any addition, change, or deletion of information in the master file must be submitted to the master file in the form of an amendment (see § 314.420(c)). Further, the master file holder must notify each person authorized to reference the DMF of the nature of the changes, and should provide as much detail as is consistent with the confidentiality agreement between the master file holder and the authorized person, so that the authorized person can determine how to report the changes in the approved application (see § 314.420(c)). In turn, application holders must notify FDA of each change in each condition established in an approved application, excluding the variations already provided for in the application (§§ 314.70, 314.97, 514.8).

When drug substance information is contained in an application, rather than in a referenced DMF, such changes must be submitted to FDA in the form of a supplement to the approved application or in an annual report (§§ 314.70, 314.97, 514.8).

This draft guidance addresses how the risk of one or more change(s) to the drug substance should be assessed and provides recommendations regarding the documentation needed to support such changes for the drug substance, and where applicable, for the drug product made with modified drug substance. The draft guidance covers the following changes: (1) facility, scale, and equipment changes associated with all steps of drug substance manufacturing; (2) specification changes to starting materials, raw materials, intermediates, and the unfinished and final drug substance; (3) synthetic manufacturing process changes; (4) changes in the source of drug substance; and (5) change to container closure system of the drug substance.

This draft guidance does not address postapproval changes to peptides, oligonucleotides, radiopharmaceuticals; or drug substances isolated from natural sources or produced by procedures involving biotechnology; or nonsynthetic steps (such as fermentation) for semisynthetic drug substances. This draft guidance also does not address complex active ingredients as defined in the GDUFA II Commitment Letter.

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 Postapproval Changes to Drug Substances. 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. This guidance is not subject to Executive Order 12866.

II. Paperwork Reduction Act of 1995

This draft guidance refers to previously approved collections of information found in FDA regulations. These collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520). The collections of information in § 314.70 have been approved under OMB control number 0910–0001; the collections of information in 21 CFR part 211 have been approved under OMB control number 0910–0139; and the collections of information in 21 CFR 514.8 have been approved under OMB control number 0910–0032. 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 draft guidance that are new or that would represent material modifications to those previously approved collections of information found in FDA regulations or guidances.

III. Electronic Access

Persons with access to the internet may obtain the draft guidance at either *https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm, https://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/default.htm,* or *https://www.regulations.gov.*

Dated: September 4, 2018.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2018–19666 Filed 9–10–18; 8:45 am]

BILLING CODE 4164–01–P