4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2017-D-6554]

Refuse to File: New Drug Application and Biologics License Application Submissions to the Center for Drug Evaluation and Research; Draft Guidance for Industry; Availability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SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled "Refuse to File: NDA and BLA Submissions to CDER." The purpose of this guidance is to clarify certain circumstances under which FDA's Center for Drug Evaluation and Research (CDER) may refuse to file a new drug application (NDA) or supplemental NDA, or a biologics license application (BLA) or supplemental BLA submitted to CDER, and to underscore the importance of submitting a complete application to minimize the chance of a refuse-to-file (RTF) action by FDA.

DATES: Submit either electronic or written comments on the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*] to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance.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-2017-D-6554 for "Refuse to File: New Drug Application and Biologics License Application Submissions to the Center for Drug Evaluation and Research; Draft Guidance for Industry." 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. 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: Amalia Himaya, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Rm. 6439, Silver Spring, MD 20993-0002, 301-796-0700.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled "Refuse to File: NDA and BLA Submissions to CDER." The purpose of this guidance is to clarify certain circumstances under which CDER may refuse to file an NDA or supplemental NDA, or a BLA or supplemental BLA submitted to CDER, and to underscore the importance of submitting a complete application to minimize the chance of an RTF action by FDA. Since the early 1990s, in conjunction with the Prescription Drug User Fee Act, FDA's processes and timelines for reviewing newly submitted applications have substantially evolved. The administrative complexity of applications, with corresponding determinations of *completeness*, has become more challenging. The overall goal is to efficiently and effectively review applications, and thus it is critical to avoid use of resources to review an application when necessary components are so deficient as to render the application incomplete. FDA exercises its RTF authority for incomplete applications to optimize the use of both the applicant's and FDA's resources.

Incomplete applications, including applications for which minor components not received within 30 calendar days after receipt of the original application, as may have been agreed upon at a presubmission meeting, may be refused for filing.

This guidance focuses on FDA's policy for refusing to file an NDA under 21 CFR 314.101(d)(3) because the NDA is incomplete because it does not on its face contain information required under section 505(b) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(b)) and 21 CFR 314.50. FDA considers incompleteness to be a basis for refusal to file for BLAs as well (21 CFR 601.2(a)).

On May 19, 2017, FDA withdrew its previously published guidance for industry entitled "Refusal to File" (issued July 12, 1993). FDA is issuing this guidance to update and clarify

CDER's procedures for determining whether an application should be refused for filing because it is incomplete. This guidance includes procedures for certain BLAs and supplemental BLAs, given that CDER has regulatory responsibility for certain therapeutic biological products subject to licensing under the Public Health Service 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 current thinking of FDA on refusal to file NDA and BLA submissions to CDER. 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. 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 (44 U.S.C. 3501-3520). The collections of information in 21 CFR part 314 have been approved under OMB control number 0910-0001. The collections of information in 21 CFR part 601 have been approved under OMB control number 0910-0338.

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 or https://www.regulations.gov.

Dated: December 7, 2017.

Leslie Kux,

Associate Commissioner for Policy.

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