



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2017-D-0114]

Referencing Approved Drug Products in Abbreviated New Drug Application Submissions; Draft Guidance for Industry; Availability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SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled “Referencing Approved Drug Products in ANDA Submissions.” Any person is permitted to submit an abbreviated new drug application (ANDA) in order to seek approval to market a generic version of a previously approved drug product. The purpose of this guidance is to provide information to potential applicants on how to identify a reference listed drug (RLD), reference standard, and the basis of submission in an ANDA submission.

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on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance, submit either electronic or written comments on the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

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-2017-D-0114 for “Referencing Approved Drug Products in ANDA Submissions.” 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 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: Gail Schmerfeld, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Silver Spring, MD 20993-0002, 301-796-9291, gail.schmerfeld@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled “Referencing Approved Drug Products in ANDA Submissions.” To obtain approval of an ANDA submitted under section 505(j) of the FD&C Act (21 U.S.C 355(j)), an ANDA applicant generally must show, among other things, that the proposed generic drug has the same active ingredient(s), conditions of use, route of administration, dosage form, strength, and, with certain permissible differences, labeling as the specific listed drug referred to in the ANDA, i.e., the RLD. Under section 505(j)(2)(A)(iv) of the FD&C Act, the ANDA applicant also must demonstrate that the

proposed generic drug is bioequivalent to the RLD and, if in vivo bioequivalence studies are required for approval of the ANDA, the applicant must use the reference standard selected by FDA in such testing (21 CFR 314.3(b)). Further, under section 505(j)(2)(A)(vi) of the FD&C Act, a generic drug must meet the same high standards of quality and manufacturing as drug products approved under section 505(c) of the FD&C Act.

This guidance provides information to potential applicants on how to identify a “reference listed drug,” “reference standard,” and the “basis of submission” in ANDA submissions. A variety of factors has led to confusion among stakeholders on what these terms mean and how an ANDA applicant should use them. These factors include the discontinued marketing of many approved drug products and FDA’s identification of reference standards with the RLD symbol (“+”) in the printed version, and under the “RLD” column in the electronic version, of FDA’s “Approved Drug Products with Therapeutic Equivalence Evaluations” (the “Orange Book”). This guidance is intended to address this confusion by explaining what these terms mean and clarifying the differences among them. This guidance provides recommendations on how to accurately use these terms in an ANDA, how persons can request FDA designation of an RLD, and how persons can request FDA selection of a reference standard.

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 Referencing Approved Drug Products in ANDA Submissions. 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 draft guidance at either <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm> or <https://www.regulations.gov>.

Dated: January 11, 2017.

Leslie Kux,

Associate Commissioner for Policy.

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