
Acceptability of Draft Labeling to Support ANDA Approval Guidance for Industry

This guidance is for immediate implementation.

FDA is issuing this guidance for immediate implementation in accordance with 21 CFR 10.115(g)(2). Submit one set of either electronic or written comments on this guidance at any time. Submit electronic comments 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. You should identify all comments with the docket number listed in the notice of availability that publishes in the *Federal Register*.

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**U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)**

**October 2015
Generic Drugs**

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**U.S. Department of Health and Human Services
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This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. 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. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

I. INTRODUCTION

This guidance provides recommendations and information related to the submission of proposed labeling with abbreviated new drug applications (ANDAs) under section 505(j)(2)(A)(v) of the Federal Food, Drug, and Cosmetic Act (the Act) and FDA's implementing regulations (21 CFR 314.94(a)(8)). This guidance is intended to assist applicants submitting ANDAs under section 505(j) of the Act to the Office of Generic Drugs (OGD) in the Center for Drug Evaluation and Research (CDER). It explains FDA's interpretation of the regulatory provision related to the submission of copies of applicants' proposed labeling in ANDAs and clarifies that OGD will accept draft labeling and does not require the submission of final printed labeling (FPL) in order to approve an ANDA.

FDA is implementing this guidance without prior public comment because the Agency has determined that prior public participation is not feasible or appropriate (see 21 CFR 10.115(g)(2) and (g)(3)). FDA made this determination because this guidance presents a less burdensome policy that is consistent with the public health.

In general, FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. DISCUSSION

OGD is issuing this guidance to provide regulated industry and other interested persons with our current thinking on the requirement that ANDA applicants submit copies of proposed labeling in their applications. Specifically, OGD is clarifying whether submission of FPL as opposed to draft labeling is required in order for OGD to approve an ANDA.

¹ The Office of Generic Drugs in the Center for Drug Evaluation and Research at the Food and Drug Administration prepared this guidance.

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This guidance supersedes the “Acceptability of Draft Labeling to Support a Tentative Approval” section of OGD’s August 4, 1993, letter to industry and also supersedes the statement in the preamble of FDA’s proposed rule, “Abbreviated New Drug Applications and 505(b)(2) Applications,”² that “final printed labeling is required as a condition of approval [of ANDAs].”³ Upon further consideration of the relevant statutory and regulatory provisions, FDA has determined that an ANDA may be approved on the basis of draft labeling, provided that the only deficiencies in the draft labeling are of an editorial or similarly minor nature, and the draft labeling meets the recommendations below.⁴ This guidance also further clarifies previous guidances for industry that have described approving ANDAs based on draft labeling, including *PET Drug Applications – Content and Format for NDAs and ANDAs* and *SPL Standard for Content of Labeling Technical Qs and As*.

Section 505(j)(2)(A)(v) of the Act requires that ANDAs contain information to show that the labeling proposed for the new drug is the same as the labeling for the listed drug (with limited exceptions). FDA’s regulations (21 CFR 314.94(a)(8)(ii)) require ANDAs to contain copies of the label and all labeling for the proposed drug product, and indicate that applicants should submit copies of draft or final printed labeling. ANDA applicants are also required to submit the content of labeling, including the prescribing information and FDA-approved patient labeling, in electronic format (21 CFR 314.94(d)(ii)).

In the past, OGD generally asked that ANDA applicants submit FPL in order to receive approval, with certain exceptions (e.g., for marketing applications for positron emission tomography (PET) drugs). OGD generally requested FPL before approving ANDAs because this version of the labeling reflected an accurate presentation of the layout, print size, color, prominence, and readability, which allowed OGD to determine whether the labeling conformed to applicable content and formatting requirements.

As ANDA labeling submissions have evolved over time, particularly with respect to the submission of electronic versions of labeling, OGD has found that draft electronic versions can enable an appropriate labeling review before a final printed version is produced.⁵

In the past, when the applicant had not submitted FPL to OGD and the application was otherwise approvable, OGD would issue applicants “approvable letters” to indicate that the application substantially met the requirements for approval except for a minor labeling deficiency

² 80 FR 6802 (Feb. 6, 2015).

³ 80 FR at 6813.

⁴ FDA will not approve an ANDA with labeling deficiencies of a degree that cause the ANDA not to meet the statutory and regulatory requirements to feature the same labeling as the listed drug. *See* Section 505(j)(2)(A)(v) of the FD&C Act; 21 CFR 314.127(a)(7).

⁵ *See* FDA’s draft guidance for industry *ANDA Submissions – Content and Format of Abbreviated New Drug Applications*, available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM400630.pdf>, for information about acceptable electronic formats for submitting labeling as part of an ANDA. FDA revises and updates guidances regularly. To make sure you have the most recent version, check this web site <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>.

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(submission of FPL). FDA's regulations were amended in 2008 to discontinue the use of approvable and not approvable letters when taking action on applications. The Agency now uses complete response (CR) letters to indicate that the review cycle is complete and the application is not ready for approval (73 FR 39588).

OGD's current thinking is that issuance of a CR letter is not appropriate if the only deficiency is the submission of draft labeling as opposed to FPL, provided that OGD is able to make a determination that the draft labeling complies with applicable requirements (other than editorial or similar minor deficiencies).

With respect to the prescribing information and any FDA-approved patient labeling, the draft version should reflect the full content of the labeling as well as the planned ordering of the content of the labeling in order for OGD to make this determination.

For carton and container labeling, OGD reviews the labeling to ensure that, among other things, it is adequate from a safety perspective.⁶ This review includes an evaluation of formatting factors such as the colors used (e.g., to differentiate multiple strengths of the product), the font size and style used to present required information (e.g., the established name), and any other techniques used to ensure the required information is presented with appropriate prominence. Thus, draft versions of this labeling should reflect the content as well as an accurate representation of the layout, text size and style, color, and other formatting factors that will be used with the FPL in order for OGD to determine whether there are any significant deficiencies in the carton and container labeling.

Draft labeling that reflects the above considerations for the prescribing information, FDA-approved patient labeling, and/or carton and container labeling will allow OGD to perform the necessary review of the labeling to determine whether it complies with applicable requirements.

Thus, OGD intends to approve ANDAs on the basis of such draft labeling, consistent with the statute and regulations and the recommendations in this guidance. Applicant holders who receive approval based on draft labeling are responsible for ensuring the content of the FPL is identical to the approved labeling. Marketing the product with FPL that is not identical to the approved labeling text⁷ may render the drug product misbranded and an unapproved new drug.

⁶ See FDA's draft guidance for industry *Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors*, available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM349009.pdf>, for more information about FDA's review of various safety aspects of carton and container labeling.

⁷ If there are editorial or similar minor deficiencies in the draft labeling, the approval will be conditioned on the applicant incorporating specified labeling changes exactly as directed.