
POLICY AND PROCEDURES

Office of Generic Drugs

Communicating Certain Deficiencies Identified During Filing Review of ANDAs

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PURPOSE

This MAPP outlines the policies and procedures for how the Division of Filing Review (DFR), Office of Regulatory Operations (ORO) in the Office of Generic Drugs (OGD), will communicate with applicants regarding abbreviated new drug applications (ANDAs)¹ that contain minor technical deficiencies and/or deficiencies that may be resolved with additional clarification from the applicant. This MAPP applies specifically to the DFR Reviewers and DFR Project Managers (DFR PMs).

BACKGROUND

FDA evaluates each submitted ANDA individually to determine whether the ANDA can be received. The receipt of an ANDA means that FDA made a threshold determination that the ANDA is a substantially complete application, that is, an ANDA that on its face is sufficiently complete to permit a substantive review.² Sufficiently complete means that the ANDA contains all the information required under section 505(j)(2)(A) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) and does not contain a deficiency described in 21 CFR § 314.101(d) and (e).³ FDA regulations at 21 CFR 314.101 provide the regulatory authority by which FDA may in certain cases, and will in others, refuse-to-accept (RTR) an ANDA.⁴

¹ For purposes of this MAPP, “ANDA” means ANDAs and prior approval supplements (PASs) for which the applicant is seeking approval of a new strength.

² See 21 CFR 314.101(b)(1) and 314.3(b).

³ 21 CFR 314.3(b).

⁴ See 21 CFR 314.101(d)-(e).

As part of the reauthorization of the Generic Drug User Fee Amendments (GDUFA II), FDA committed to issue a MAPP setting forth procedures for filing reviewers on the communication of minor technical deficiencies and deficiencies potentially resolved with information in the ANDA at original submission, in order to provide applicants with an opportunity for resolution within 7 calendar days. This MAPP fulfills that GDUFA II commitment.

After the GDUFA II negotiations, FDA revised the guidance for industry *ANDA Submissions – Refuse to Receive Standards* (RTR Standards Guidance) to change the classification of certain deficiencies previously identified as major to minor deficiencies. The reclassification of these deficiencies as minor satisfies the obligation to communicate minor technical deficiencies as contemplated in the GDUFA II Commitment Letter. This MAPP focuses on how to issue an Information Request (IR) for minor deficiencies as described in the RTR Standards Guidance and notify applicants of major deficiencies that may be resolved with information in the original ANDA submission.

POLICY

FDA will follow the definitions for minor and major deficiencies as discussed in the RTR Standards Guidance.⁵

If a deficiency is not specified in the RTR Standards Guidance, FDA will characterize the deficiency consistent with the principles set forth in the guidance.

If FDA determines that an ANDA contains 10 or more minor deficiencies or one or more major deficiencies, FDA will not consider the ANDA to be a substantially complete application under 21 CFR 314.101(b)(1)⁶ and will RTR the application.⁷

In its discretion, if FDA determines that an ANDA contains fewer than 10 minor⁸ deficiencies (i.e., nine minor deficiencies or fewer), FDA will notify the applicant of the deficiencies and provide the applicant with the opportunity to correct the minor deficiencies within 7 calendar days.⁹

⁵ For example, an applicant's failure to provide the signed Form FDA 356h will be classified as a major deficiency. If a deficiency is not delineated in the RTR Standards Guidance, FDA will characterize the deficiency that is consistent with the principles in the guidance.

⁶ See RTR Standards Guidance at 3-4.

⁷ In such cases, FDA notifies the applicant that FDA considers the ANDA not to have been "received" (i.e., FDA will issue an RTR for the application).

⁸ Some examples of minor deficiencies (i.e. deficiencies for which an applicant is afforded an opportunity to remedy within 7 calendar days) are provided in Appendix A of the RTR Standards guidance.

⁹ See RTR Standards Guidance. The response period will begin the day after notification is provided. If the seventh calendar day falls on a Saturday, Sunday, or Federal holiday, the deadline for amending the ANDA to correct the deficiencies will be the next day that is not a Saturday, Sunday, or Federal holiday.

When the applicant's response to an IR is received within 7 calendar days, the DFR Reviewer will review the applicant's response as soon as it is received.

If, within 7 calendar days, the requested information is not received, including an incomplete response to the minor deficiencies, FDA will RTR the ANDA.

FDA has noted that in some instances, certain deficiencies appear to be omissions of required data or information that may be remedied by identifying the location of such data or information in the original application (i.e., the data or information required for technical review is misplaced within the original submission), prior to FDA making a receipt determination. A DFR Reviewer may determine that a major deficiency as identified in the RTR Standards Guidance may be due to potentially omitted data or information. If, as contemplated in this scenario, the DFR Reviewer identifies a major deficiency that, in the DFR Reviewer's judgment, may be resolved by identifying the location of the data or information in the ANDA as originally submitted, the DFR Reviewer will notify the applicant of such potential major deficiency in the IR. If that potential major deficiency is resolved by the applicant's identification of the location of the data or information in the original submission, DFR will not consider such a misplacement a major deficiency, for the purposes of making an RTR determination.

RESPONSIBILITIES AND PROCEDURES

1. The DFR Reviewer conducts a filing review of the submitted ANDA and identifies any and all minor and major deficiencies.
2. If the DFR Reviewer determines that the ANDA contains a major deficiency that, in the DFR Reviewer's judgment, may be remedied by identifying the location of such data or information within the original ANDA:
 - a. The DFR Reviewer will prepare an IR clearly identifying the major deficiency as a potential misplacement and any identified minor deficiencies (as long as the DFR Reviewer has identified 9 or fewer minor deficiencies) and prepare an IR stating that the applicant has 7 calendar days from the date of the IR in which to provide a complete response.
 - b. The DFR PM will contact the applicant's designated point of contact¹⁰ by phone and advise that an IR will be issued.

If unable to reach the point of contact, the DFR PM will leave a voicemail¹¹ with the DFR PM's contact information.

¹⁰ The designated point of contact is the applicant's responsible official for applicants located in the U.S. or the U.S. Agent, if applicable, as identified on the Form FDA 365h.

¹¹ A voicemail will only be left if the outgoing message clearly identifies the designated point of contact (i.e., is a direct line). No voicemail will be left to a general mailbox.

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- c. The DFR PM will send the IR to the email address identified on the Form FDA 356h.
 - i. The DFR PM will not send an IR to an individual not identified as the point of contact on the Form FDA 356h.
 - ii. The DFR PM will send an IR to a general electronic mailbox for the applicant, if one is identified on the Form FDA 356h.
 - d. If the applicant's response to the IR is received within the 7 calendar days, the DFR Reviewer will review the applicant's response as soon as it is received, even if the response is received before the seventh calendar day, to help ensure that the performance review goal associated with the ANDA is met.
 - i. If the applicant adequately addresses the potential major deficiency by identifying the location of the misplaced data or information in the original ANDA submission, the DFR Reviewer will continue to review the entire IR response (if minor deficiencies are identified as well).
 - ii. If the applicant does not adequately address the potential major deficiency (i.e., the applicant fails to identify the missing data or information in the original submission), such that the original submission is not substantially complete, the DFR Reviewer will prepare an RTR determination for issuance by the DFR PM to the applicant's designated point of contact.
 3. If the DFR Reviewer has not identified any major deficiencies that may, in the DFR Reviewer's judgment, be remedied by identifying the location of data or information within the original ANDA, but has identified 9 or fewer minor deficiencies:
 - a. The DFR Reviewer will prepare an IR identifying the 9 or fewer minor deficiencies and stating the applicant has 7 calendar days from the date of the IR in which to provide a complete response.
 - b. The DFR PM will contact the applicant's designated point of contact by phone and advise that an IR will be issued.

If unable to reach the point of contact, the DFR PM will leave a voicemail with the DFR PM's contact information.
 - c. The DFR PM will send the IR to the email address identified on the Form FDA 356h.
 - i. The DFR PM will not send an IR to an individual not identified as the point of contact on the Form FDA 356h.

- ii. The DFR PM will send an IR to a general electronic mailbox for the applicant, if one is identified on the Form FDA 356h.
- d. If the applicant's response to the IR is received within the 7 calendar days, the DFR Reviewer will review the applicant's response as soon as it is received, even if the response is received before the seventh calendar day, to help ensure that the performance review goal associated with the ANDA is met.
- i. If the applicant adequately addresses all deficiencies, such that the submission is substantially complete, the DFR Reviewer will prepare and the DFR PM will issue an acknowledgment letter or paragraph IV acknowledgment letter, as appropriate, indicating that the submission has been received for review.
 - ii. If the applicant has not adequately addressed all deficiencies within 7 calendar days, such that the submission is not substantially complete, the DFR Reviewer will prepare an RTR determination.

When the RTR determination is complete, the DFR PM will contact the applicant's designated point of contact by phone and advise that a communication from DFR will be issued to the applicant's designated point of contact.

- iii. The DFR PM will send the RTR determination to the email address identified on the Form FDA 356h.
 - 1. The DFR PM will not send an RTR determination to an individual not identified as the point of contact on the Form FDA 356h.
 - 2. The DFR PM will send an RTR determination to a general electronic mailbox for the applicant, if one is identified on the Form FDA 356h.
4. The DFR Reviewer will prepare an RTR determination if any of the following are true:
- a. The applicant fails to respond to an IR within 7 calendar days, as provided in the RTR Standards Guidance.
 - b. An ANDA contains one or more major deficiencies that, in the DFR's Reviewer's judgment may not be resolved by identifying the location of data or information in the original ANDA.
 - c. An ANDA contains 10 or more minor deficiencies.

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5. When the RTR determination is complete, the DFR PM will contact the applicant's designated point of contact and advise that a communication from DFR will be issued to the applicant's designated point of contact.
 - a. The DFR PM will send the RTR determination to the email address identified on the Form FDA 356h.
 - b. The DFR PM will not send an RTR determination to an individual not identified as the point of contact on the Form FDA 356h.
 - c. The DFR PM will send an RTR determination to a general electronic mailbox for the applicant, if one is identified on the Form FDA 356h.
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REFERENCES

1. GDUFA Reauthorization Performance Goals and Program Enhancements Fiscal Years 2018-2022
 2. Guidance for industry *ANDA Submissions – Refuse to Receive Standards* (Rev. 2, December 2016)
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EFFECTIVE DATE

This MAPP is effective upon date of publication.

CHANGE CONTROL TABLE

| Effective Date | Revision Number | Revisions |
|----------------|-----------------|-----------|
| 9/28/2017 | Initial | N/A |