Requests for Reconsideration at the Division Level Under GDUFA

Guidance for Industry

DRAFT GUIDANCE

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

January 2024
Generic Drugs

Revision 1

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TABLE OF CONTENTS

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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic.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 on the procedures for applicants of abbreviated new drug applications (ANDAs) that wish to pursue a request for reconsideration within the review discipline at the division level or original signatory authority. As described further below in section III, requests within the scope of this guidance document should concern certain actions that relate to an ANDA and have scientific significance.[2] During the assessment of an ANDA, FDA considers important issues that are central to product evaluation. Sometimes, an applicant may disagree with FDA, and because these disagreements often involve intricate matters, it is critical to have procedures in place to ensure open and prompt consideration of an applicant's concern(s). The procedures and policies described in this guidance are intended to formalize FDA's current and historical practices and to continue to promote rapid and fair resolution of eligible requests between an applicant and FDA.

This draft guidance revises the draft guidance of the same title issued in October 2017. This revision is being issued to reflect the most recent reauthorization of the Generic Drug User Fee Amendments (GDUFA) in the Continuing Appropriations and Ukraine Supplemental Appropriations Act, 2023[3] and to clarify what matters are appropriate for requests for reconsideration.

This guidance does not describe the formal dispute resolution procedures for resolving eligible requests between FDA and sponsors or applicants that cannot be resolved through the request for

[1] This guidance has been prepared by the Office of Generic Drugs in the Center for Drug Evaluation and Research at the Food and Drug Administration.

[2] See section III. A of this guidance that discusses matters that are appropriate requests for reconsideration. See also the Generic Drug Use Fee Amendments (GDUFA) III commitment letter titled "GDUFA Reauthorization Performance Goals and Program Enhancements Fiscal Years 2023–2027" available at https://www.fda.gov/media/153631/download (describing processes and goals for dispute resolution).

[3] See Title III of Division F (the FDA User Fee Reauthorization Act of 2022) of the Continuing Appropriations and Ukraine Supplemental Appropriations Act, 2023 (Public Law 117-180).

reconsideration process at the division level.[4] This guidance also does not describe the procedures for resolving administrative matters, such as disputes regarding user fee assessments.[5]

In general, FDA's guidance documents 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. BACKGROUND

The Generic Drug User Fee Amendments of 2012 (GDUFA I)[6] amended the Federal Food, Drug, and Cosmetic Act to authorize FDA to assess and collect user fees to provide the Agency with resources to help ensure patients have access to quality, affordable, safe, and effective generic drugs. GDUFA fee resources[7] bring greater predictability and timeliness to the review of generic drug applications. GDUFA has been reauthorized every 5 years to continue FDA's ability to assess and collect GDUFA fees, and this user fee program has been reauthorized two times since GDUFA I, most recently in the Continuing Appropriations and Ukraine Supplemental Appropriations Act, 2023 (for GDUFA III).[8] As described in the GDUFA III commitment letter applicable to this latest reauthorization,[9] FDA has agreed to performance goals and program enhancements regarding aspects of the generic drug assessment program that build on previous authorizations of GDUFA. New enhancements to the program are designed to maximize the efficiency and utility of each assessment cycle, with the intent of reducing the number of assessment cycles for ANDAs and facilitating timely access to generic medicines for American patients.

As described in the GDUFA III commitment letter applicable to this latest reauthorization, an ANDA applicant "may pursue a request for reconsideration within the assessment discipline at

[4] For information on the formal dispute resolution process, see the guidance for industry and review staff *Formal Dispute Resolution: Sponsor Appeals Above the Division Level* (November 2017). We update guidances periodically. To make sure you have the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

[5] For information about user fee assessments and the procedures to dispute such assessments, see the Generic Drug User Fee Amendments web page at https://www.fda.gov/industry/fda-user-fee-programs/generic-drug-user-fee-amendments.

[6] Title III of the Food and Drug Administration Safety and Innovation Act, (Public Law 112-144) (21 U.S.C. 301).

[7] User fees are available for obligation in accordance with appropriations acts.

[8] See Title III of Division F (the FDA User Fee Reauthorization Act of 2022) of the Continuing Appropriations and Ukraine Supplemental Appropriations Act, 2023 (Public Law 117-180).

[9] See the GDUFA III commitment letter.

the Division level or original signatory authority, as needed."[10] The GDUFA III commitment letter also states that the "Office of Generic Drugs, Office of Regulatory Operations Associate Director will track each request for Division-level reconsideration through resolution."[11] At the conclusion of a request for reconsideration, an applicant may pursue formal dispute resolution above the division level.[12]

This guidance provides information for applicants to consider before pursuing a request for reconsideration, procedures for submitting a request for reconsideration, and the Agency's process for responding to such a request.

III. CONSIDERATIONS FOR APPLICANTS BEFORE SUBMITTING A REQUEST FOR RECONSIDERATION

A. What Is an Appropriate Matter for a Request for Reconsideration?

An FDA regulatory action that relates to an ANDA and has scientific significance is a matter that could be handled appropriately through a request for reconsideration. Appropriate regulatory actions[13] for a request for reconsideration include, but are not limited to the following:

- Refuse-to-receive decision
- Tentative approval letter
- Complete response letter (CRL)[14]

[10] Id. at section II.E.1. For purposes of identifying the *original signatory authority*, any decision made on behalf of the division is deemed to be made by the Division Director of that division. For example, if an acknowledgement letter is signed by a project manager in the Division of Project Management, then the original signatory authority is the Division Director of the Division of Project Management.

[11] Id. at section II.E.2.

[12] Id. at section II.E.3.

[13] FDA has determined that an applicant may pursue a request for reconsideration of an acknowledgement letter even though the Agency does not consider this to be a regulatory action.

[14] If FDA issues a CRL, the CRL will set forth the deficiencies that an applicant must satisfactorily address before the ANDA can be tentatively approved or approved (see 21 CFR 314.110; 21 CFR 314.3(b)). See also 21 CFR 314.102. A CRL may contain additional or fewer deficiencies than were provided in previously issued discipline review letters (DRLs), depending on the final assessment of the ANDA. If the Agency has communicated deficiencies to an applicant in a CRL, FDA will not rescind the CRL and instead communicate the deficiencies in an information request (IR) or DRL. FDA does not consider IRs or DRLs to be CRLs because they do not represent a complete assessment of the entire application and therefore do not stop the assessment clock. See the guidance for industry *Information Requests and Discipline Review Letters Under GDUFA* (October 2022) at 3.

- FDA determination that a supplement-changes being effected or a supplement-changes being effected in 30 days is a prior approval supplement (PAS)

- Classification of a major amendment to an ANDA or PAS[15]

- Classification of the standard assessment status of an ANDA, ANDA amendment, PAS, or PAS amendment

- Denial of a reclassification of a facility-based major CRL amendment[16]

- Denial of a pre-ANDA meeting

B. When Is a Matter Not Appropriate for a Request for Reconsideration?

Advice communicated during meetings or teleconferences, in meeting minutes, and in other correspondence (e.g., information requests, discipline review letters) is not a regulatory action taken by FDA; therefore, such advice would not be an appropriate subject for a request for reconsideration by an applicant.[17] Matters not appropriate for a request for reconsideration by an applicant include, but are not limited to, general advice letters and advice communicated during meetings or in meeting minutes to discuss generic drug development before ANDA submission (pre-ANDA meetings),[18] including meetings for complex generic drug products as noted in the GDUFA III commitment letter.[19]

Under GDUFA III, an applicant may request a post-CRL clarification teleconference concerning deficiencies identified in a CRL.[20] Additionally, applicants can request post-CRL scientific meetings for FDA's scientific advice on possible approaches to identified deficiencies in a CRL

[15] FDA agreed to certain assessment goals and procedures for requests for reclassification of a major amendment to an ANDA or a PAS as described in the GDUFA III commitment letter at section II.C.1–6. These goals and procedures do not apply to a request for reclassification of a major amendment in response to a CRL that was deemed major only because of a facility deficiency, which is subject to the goals and procedures described in the GDUFA III commitment letter at section II.C.7.

[16] GDUFA III commitment letter at section II.C.7.

[17] See the guidance for industry and review staff *Formal Dispute Resolution: Sponsor Appeals Above the Division Level* at 5.

[18] Ibid.

[19] See the guidance for industry *Formal Meetings Between FDA and ANDA Applicants of Complex Products Under GDUFA* (October 2022).

[20] GDUFA III commitment letter at section II.B.8.a. See also the guidance for industry *Post-Complete Response Letter Clarification Teleconferences Between FDA and ANDA Applicants Under GDUFA* (October 2022).

related to establishing equivalence.[21] FDA encourages applicants to request meetings under GDUFA III before submitting a request for reconsideration.

Agency communications, such as meeting minutes or other correspondence, typically include recommendations or advice that generally convey FDA's current thinking on a particular topic raised by the applicant. However, applicants are not bound by such recommendations or advice. Applicants can follow the advice from meeting minutes or other correspondence, or they can use an alternative approach, if the approach satisfies the requirements of the applicable statutes and regulations.

In addition, to further ensure efficient use of Agency resources, the applicant submitting a request for reconsideration should not actively engage with other entities within FDA or pursue other regulatory or legal pathways on the same matter at the same time because this will at best lead to inefficiencies in Agency review and could impede FDA's consideration of a request for reconsideration. Such engagement with other entities may also result in a determination that the applicant failed to exhaust administrative remedies.

C. Can the Applicant Submit New Information With a Request for Reconsideration?

The applicant should not submit new information as part of a request for reconsideration because FDA's decision must be based on the same information that was used to make the original decision (i.e., information already in the ANDA file).[22] If the applicant wants FDA to consider new information, the applicant should submit it as an amendment to the ANDA or PAS for review by the division and the original signatory authority.[23] FDA considers new analyses of previously reviewed data submitted by the applicant to be new information, because the original signatory authority might have made a different decision if given the opportunity to review the new analyses.

IV. TIMELINES AND PROCEDURES FOR SUBMITTING AND RESPONDING TO A REQUEST FOR RECONSIDERATION

A. Timelines for Responding to Requests for Reconsideration

As a general matter, FDA will review and respond to requests for reconsideration as expeditiously as possible. However, as stated in the GDUFA III commitment letter, for requests to "reclassify a Major Amendment or standard assessment status, FDA will schedule and conduct the teleconference and decide 90 percent of such reclassification requests within 30 days of the

[21] GDUFA III commitment letter at section II.B.8.c. See also the guidance for industry *Formal Meetings Between FDA and ANDA Applicants of Complex Products Under GDUFA*.

[22] 21 CFR 10.75(d).

[23] For a refuse-to-receive decision, the applicant should submit new information as part of the formal refuse-to-receive response (ANDA resubmission) and remit any applicable user fees.

date of FDA's receipt of the request for a teleconference."[24] This 30-day goal only applies to a request for reconsideration when the applicant accepts the first scheduled teleconference date the FDA offers,[25] and the applicant submits the request for reconsideration within 7 calendar days from the date of the regulatory action taken by FDA, as described below in section IV.B.

B. How to Submit a Request for Reconsideration

The applicant should submit a request for reconsideration in the following manner:

- For all requests for reconsideration, applicants should clearly identify on the cover letter or checklist that a request for reconsideration is included within the amendment submission; and a copy should be emailed to ANDAReconsideration@fda.hhs.gov.

- For requests for reconsideration of the denial of a pre-ANDA meeting, the applicant should submit the request to the project manager identified in the communication for which the reconsideration is being requested, and a copy should be emailed to ANDAReconsideration@fda.hhs.gov.

- For requests for reconsideration of a filing decision (e.g., refuse-to-receive decisions), the applicant should submit the request as a separate amendment to the ANDA;[26] a copy should be emailed to ANDAReconsideration@fda.hhs.gov and the Division of Filing Review at DFRSupervisor@fda.hhs.gov.

- For all other requests for reconsideration, the applicant should submit the request as a separate amendment to the ANDA; a copy should be emailed to ANDAReconsideration@fda.hhs.gov and to the project manager identified in the communication for which the reconsideration is being requested.

The applicant should submit the request for reconsideration within 7 calendar days from the date of the regulatory action taken by FDA.[27] For example:

- If an applicant would like to submit a request for reconsideration of a CRL, the applicant should submit the request within 7 calendar days from FDA's issuance of the CRL.

[24] GDUFA III commitment letter at section II.C.5.

[25] Ibid.

[26] For purposes of GDUFA III, a request for reconsideration will be received by the Agency when it is submitted to the ANDA (or to the project manager for denials of pre-ANDA meetings), Monday through Friday from 12:00 a.m. to 11:59 p.m. Eastern Standard Time/Eastern Daylight Savings Time, excluding Federal holidays and days when the FDA office reviewing the request is closed. See the guidance for industry *Providing Regulatory Submissions in Electronic Format — Receipt Dates* (February 2014).

[27] The Agency believes that 7 calendar days provides an applicant sufficient time to review FDA's regulatory action and determine whether the applicant would like to pursue a request for reconsideration.

- If an applicant would like to submit a request for reconsideration of the assessment classification of a major amendment, the applicant should submit the request within 7 calendar days from FDA's CRL to receive a GDUFA III goal date for the request for reconsideration.

- If an applicant would like to submit a request for reconsideration of the assessment classification of a standard review status, the applicant should submit the request within 7 calendar days from FDA's acknowledgement letter to receive a GDUFA III goal date for the request for reconsideration.

If the applicant does not submit the request for reconsideration of the CRL, assessment classification of a major amendment or standard review status within 7 calendar days, FDA will respond as expeditiously as possible, but the request for reconsideration will not receive a GDUFA III goal date.

C. Content and Format of a Request for Reconsideration

To facilitate efficient review, any request for reconsideration should include adequate information to explain the nature of the eligible request and to allow the signatory authority to determine the appropriate steps to resolve the matter quickly and efficiently. If FDA determines that the request does not contain the information specified in the bulleted list in this section, the request will not be considered to be received for purposes of GDUFA III. The applicant should submit each request as a separate amendment to the ANDA and include the following:

- Identification of the applicant's submission as a request for reconsideration on the Form FDA 356h (Application to Market a New or Abbreviated New Drug or Biologic for Human Use) and cover letter

- Application number for the ANDA and, if applicable, the supplement number

- Established name of the drug product(s)

- Brief, but comprehensive, statement of each matter to be resolved, including the following:

  – Description of the eligible request to be resolved

  – Summary of the relevant regulatory history

  – Statement of the applicant's proposed possible solutions or outcomes

- Statement identifying the Office of Generic Drugs or Office of Pharmaceutical Quality suboffice that issued the decision on the matter that is the subject of the request for reconsideration.

- Statement that the applicant is requesting discussion of the reclassification of a major amendment or standard assessment status via a teleconference with FDA, if applicable.[28]

  – If the applicant is requesting discussion via a teleconference, the request should also include a list of all individuals, with their titles and affiliations, who will participate in the requested teleconference from the applicant's organization, including consults and interpreters, if applicable.

- List of documents previously submitted to the ANDA that are deemed appropriate for resolution of the matter, with reference to submission dates so the documents may be readily located.

- Statement that no new information has been submitted in support of the request for reconsideration.

D. FDA's Procedures for Reviewing and Responding to a Request for Reconsideration

Depending on the eligible request that is the subject of the request for reconsideration, the Division of Filing Review or the project manager will conduct a preliminary review of the applicant's request for reconsideration to evaluate whether the request satisfies the procedural factors (as described in section IV.C) and can be accepted. If FDA accepts the applicant's request for reconsideration, the Division of Filing Review or the project manager will forward the request to the signatory authority and send the applicant an acknowledgment letter identifying the signatory authority, the GDUFA III goal date for a response to the request for reconsideration (if applicable, as described in section IV.A.), and the date of any teleconference (if applicable, as described in section IV.C.). If FDA does not accept a request for reconsideration, the Division of Filing Review or the project manager will inform the applicant on behalf of the signatory authority and state the reason(s) the request was not accepted.

The signatory authority or the signatory authority's designee will send a written decision to an applicant that submits a request for reconsideration that is accepted for review. The written decision will grant or deny the request for reconsideration. If the signatory authority does not agree with the applicant's proposal for the reconsideration request, the signatory authority should provide the reasons for not agreeing with the applicant's proposal.

[28] If the applicant is requesting reconsideration of a matter other than the classification of a major amendment or standard review status and would like to request a teleconference, the applicant should include a statement requesting a teleconference. FDA, at its discretion, will determine whether to grant the request for the teleconference. Although the teleconference for a request for reconsideration is an opportunity for the applicant to explain their reasoning for the request, it is not an opportunity to seek a decision from FDA.

V. FORMAL DISPUTE RESOLUTION

If the eligible request cannot be resolved through the request for reconsideration process at the division level or original signatory authority, the applicant may pursue formal dispute resolution above the division level (see the guidance for industry and review staff *Formal Dispute Resolution: Sponsor Appeals Above the Division Level*).