Requests for Reconsideration at the Division Level Under GDUFA

Guidance for Industry

DRAFT GUIDANCE

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For questions regarding this draft document, contact (CDER) Lisa Bercu at 240-402-6902.

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

October 2017
Generics

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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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic.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 for industry on the procedures for resolving scientific and/or regulatory issues or matters between FDA and 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. This guidance does not describe the formal dispute resolution procedures for resolving scientific and/or regulatory disputes between FDA and sponsors or applicants that cannot be resolved through the request for reconsideration process at the division level.[2] This guidance also does not describe the procedures for resolving administrative matters, such as disputes regarding user fee assessments.[3]

During the course of review of an ANDA, important scientific and/or regulatory issues are considered that are central to product evaluation. Sometimes, an applicant may disagree with FDA, and because these disagreements often involve complex scientific and/or regulatory matters, it is critical to have procedures in place to ensure open and prompt consideration of an applicant's concern. 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 scientific and/or regulatory disputes between an applicant and FDA.

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

[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] For information on the formal dispute resolution process, see FDA draft guidance for industry and review staff, *Formal Dispute Resolution: Appeals Above the Division Level* (September 2015, Revision 2). When final, this guidance will represent FDA's current thinking on this topic. For the most recent version of a guidance, check the FDA Drugs guidance web page at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

[3] For information about user fee assessments and the procedures to dispute such assessments, please visit https://www.fda.gov/forindustry/userfees/genericdruguserfees/default.htm.

the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

GDUFA II was signed into law on August 18, 2017 to facilitate timely access to quality, affordable generic medicines. As agreed to by FDA and industry in the GDUFA Reauthorization Performance Goals and Program Enhancements Fiscal Years 2018-2022 (GDUFA II Commitment Letter or GDUFA II Goals Letter)[4] that accompanied the legislation, an ANDA applicant "may pursue a request for reconsideration within the review discipline at the Division level or original signatory authority, as needed."[5] The GDUFA II 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."[6] At the conclusion of a request for reconsideration, an applicant may pursue formal dispute resolution above the division level.[7]

In addition, FDA agreed to certain review goals and procedures for requests for reconsideration of the classification of a major amendment to an ANDA or a prior approval supplement (PAS). FDA also agreed to certain review goals and procedures for requests for reconsideration of the classification of the standard review status of an ANDA, ANDA amendment, PAS, or PAS amendment (i.e., an FDA determination that the regulatory submission is subject to standard review and not priority review).[8] Specifically, the Agency agreed that if an applicant requests a teleconference as part of its request to reclassify: (1) a major amendment to an ANDA or a PAS, or (2) the standard review status of an ANDA, ANDA amendment, PAS, or PAS amendment, "FDA will schedule and conduct the teleconference and decide 90% of such reclassification requests within 30 days of the date of FDA's receipt of the request for a teleconference. This [30-day] goal only applies when [the] applicant accepts the first scheduled teleconference date offered by FDA."[9]

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 a request.

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[4] Available at http://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM525234.pdf.

[5] Id. at 13. 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.

[6] Id at 13.

[7] Id.

[8] As defined in the GDUFA II Commitment Letter, *priority* "means submissions affirmatively identified as eligible for expedited review pursuant to CDER's Manual of Policy and Procedures (MAPP) 5240.3, *Prioritization of the Review of Original ANDAs, Amendments, and Supplements*, as revised (the CDER Prioritization MAPP)." In contrast, *standard* "means submissions not affirmatively identified as eligible for expedited review pursuant to the CDER Prioritization MAPP." GDUFA II Commitment Letter at 27.

[9] GDUFA II Commitment Letter at 12-13.

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 appropriately handled through a request for reconsideration. Regulatory actions[10] that would be appropriate for a request for reconsideration include, but are not limited to, the following:

- Refuse to receive decision
- Tentative approval letter
- Complete response letter
- FDA determination that a *Supplement-Changes Being Effected* or a *Supplement-Changes Being Effected in 30 days* is a PAS
- Classification of a major amendment to an ANDA or PAS
- Classification of the standard review status of an ANDA, ANDA amendment, PAS, or PAS amendment
- 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 and 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.[11] Agency communications such as meeting minutes or other correspondences typically include recommendations or advice to an applicant 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 may follow the advice in meeting minutes or other correspondences, or they may 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 may waste Agency resources and/or 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.

[10] 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.

[11] See FDA draft guidance for industry and review staff, *Formal Dispute Resolution: Appeals Above the Division Level*, at 5 (September 2015, Revision 2). 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 prior to ANDA submission (pre-ANDA meetings), including meetings provided for complex generic drug products in the GDUFA II Commitment Letter.

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

New information should not be submitted as part of a request for reconsideration because FDA reconsideration of a decision that has been requested by an applicant must be based on the same information that was relied upon to make the original decision (i.e., information already in the ANDA file).[12] If the applicant wants to have FDA 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.[13] 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 had he or she had the opportunity to review the new analyses.

D. How will GDUFA II Request for Reconsideration Goals be Applied to ANDAs, ANDA Amendments, PASs, and PAS Amendments Submitted During GDUFA I?

As stated in the GDUFA II Commitment Letter, FDA will "[c]ontinue to review and act on ANDAs and ANDA amendments, PASs and PAS amendments. . . submitted prior to October 1, 2017 that have been assigned GDUFA I goal dates pursuant to the GDUFA I review metrics applicable to those submissions."[14] For any ANDAs, ANDA amendments, PASs, or PAS amendments submitted during GDUFA I for which FDA issued a response after October 1, 2017, and for which an applicant pursues a request for reconsideration, FDA will aspire to respond to such a request for reconsideration within the performance goal identified in the GDUFA II Commitment Letter (see section IV.A. below).

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 agreed to in the GDUFA II Commitment Letter, for requests to "reclassify a major amendment or standard review status, FDA will schedule and conduct the teleconference and decide 90% of such reclassification requests within 30 days of the date of FDA's receipt of the request for a teleconference."[15] This 30-day goal only applies to a request for reconsideration when the applicant accepts the first scheduled teleconference date offered by FDA[16] and the request for reconsideration is submitted within 7 calendar days from the date of the regulatory action taken by FDA, as described in section IV.B. below.

[12] 21 CFR 10.75(d).

[13] 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.

[14] GDUFA II Commitment Letter at 9-10. To "act on an application" means that FDA will either issue a complete response letter, an approval letter, a tentative approval letter, or a refuse-to-receive letter.

[15] GDUFA II Commitment Letter at 12-13.

[16] GDUFA II Commitment Letter at 13.

B. How to Submit a Request for Reconsideration

Requests for reconsideration should be submitted in the following manner:

- 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.

- For requests for reconsideration of a filing decision, the applicant should submit the request as a separate amendment to the ANDA[17] and 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 and 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 request for reconsideration should be submitted within 7 calendar days from the date of the regulatory action taken by FDA.[18] For example:

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

- If an applicant would like to submit a request for reconsideration of the review classification of a major amendment, the applicant should submit the request within 7 calendar days from FDA's complete response letter in order to receive a GDUFA II goal date for the request for reconsideration.

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

If the applicant does not submit the request for reconsideration of the review 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 II goal date.

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[17] For purposes of GDUFA II, a request for reconsideration will be received by the Agency when it is submitted to the ANDA, 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 that will review the request is closed. See FDA guidance for industry, *Providing Regulatory Submissions in Electronic Format — Receipt Dates*.

[18] 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. It also ensures that an applicant submits a request for reconsideration regarding a recent Agency regulatory action.

C. Content and Format of a Request for Reconsideration

To make the most efficient use of FDA and industry resources, any request for reconsideration should include information adequate to explain the nature of the scientific and/or regulatory issue or matter and to allow the signatory authority to determine the necessary 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 II. Each request should be submitted as a separate amendment to the ANDA and include the following:

- Identification of the applicant's submission as a "Request for Reconsideration."
- Application number for the ANDA and the supplement number, if applicable.
- Established name of the drug products.
- Brief, but comprehensive, statement of each matter to be resolved, including:
  - Description of the scientific and/or regulatory matter 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 review status via a teleconference with FDA, if applicable.[19]
- List of documents previously submitted to the ANDA that are deemed necessary 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.

[19] 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 discuss the issue(s), it is not an opportunity to seek a decision from FDA.

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

Depending on the scientific and/or regulatory issue 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 criteria (as described in section IV.) and can be accepted. If the applicant's request for reconsideration is accepted, the Division of Filing Review or the project manager will forward the request to the signatory authority and will send an acknowledgment letter to the applicant identifying the signatory authority, the GDUFA II 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 a request for reconsideration is not accepted, the Division of Filing Review or the project manager will inform the applicant on behalf of the signatory authority and identify the reason(s) why the request was not accepted.

The signatory authority or his or her 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, he or she should provide the reasons for not agreeing with the applicant's proposal.

V. FORMAL DISPUTE RESOLUTION

If the scientific and/or regulatory issue 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, pursuant to the procedures set forth in the draft guidance for industry and review staff, *Formal Dispute Resolution: Appeals Above the Division Level*.