Post-Complete Response Letter Meetings Between FDA and ANDA Applicants 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DRAFT GUIDANCE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)

October 2017
Generics

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TABLE OF CONTENTS

I. INTRODUCTION 1

II. BACKGROUND 2

III. GDUFA II PERFORMANCE GOALS 2

IV. POST-COMPLETE RESPONSE LETTER MEETING REQUESTS 3

V. ASSESSING POST-COMPLETE RESPONSE LETTER MEETING REQUESTS 4

A. Meeting Denied 4

B. Meeting Granted 5

C. Written Responses 6

VI. RESCHEDULING AND CANCELLING POST-CRL MEETINGS 6

VII. PROCEDURES FOR THE CONDUCT OF POST-CRL MEETING TELECONFERENCES 6

VIII. DOCUMENTATION OF MEETINGS 7

IX. RESOLUTION OF DISPUTES ABOUT MEETING MINUTES 7

Post-Complete Response Letter Meetings Between FDA and ANDA Applicants Under GDUFA Guidance for Industry[1]

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic.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 to industry on post-complete response letter (CRL) meetings between FDA and abbreviated new drug application (ANDA) applicants for the purpose of clarifying deficiencies identified in a CRL to an ANDA[2] submitted under section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355(j)). For purposes of this guidance, a post-CRL meeting is a meeting[3] that is requested in writing by an ANDA applicant pursuant to the procedures described in this guidance following receipt of a CRL.

It is important that there are efficient, consistent procedures for the timely and effective conduct of post-CRL meetings. This guidance will assist applicants in generating and submitting a request for a post-CRL meeting and the associated meeting package to FDA as contemplated in the Generic Drug User Fee Amendments of 2017 (GDUFA II), reauthorizing generic drug user fees for Fiscal Years 2018-2022.[4] This guidance is intended to provide procedures that will promote well-managed post-CRL meetings and help ensure that such meetings are scheduled and conducted in accordance with the time frames set forth in the GDUFA Reauthorization Performance Goals and Program Enhancements Fiscal Years 2018-2022 (GDUFA II Goals or Commitment Letter).[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

[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 purposes of this guidance, *ANDA* means the original application including all amendments and supplements to the application.
[3] For purposes of this guidance, a *meeting* is a teleconference or written response.
[4] Generic Drug User Fee Amendments of 2017, Public Law 115-52 , Title III.
[5] Available at http://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM525234.pdf.

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, in order to facilitate timely access to quality, affordable generic medicines. In accordance with the GDUFA II Commitment Letter that accompanied the legislation, FDA agreed to certain review goals and procedures for the scheduling and conduct of post-CRL meetings.

The GDUFA II Commitment Letter adds time frames within which FDA will provide a scheduled date for, and will conduct, post-CRL meetings. Under GDUFA I, FDA committed to close out a certain number of teleconference requests in fiscal year (FY) 2015 through FY 2017. In accordance with the GDUFA II Commitment Letter, FDA committed to schedule and conduct 90 percent of post-CRL meetings within prescribed time frames.

As described in the GDUFA II Commitment Letter, post-CRL meetings will be used by applicants "to seek clarification concerning deficiencies identified in a CRL."[6] Under GDUFA II, post-CRL meetings are available for both major and minor CRLs and for first and subsequent review cycles. FDA will grant any complete post-CRL meeting request that satisfies the criteria outlined in section IV of this guidance. FDA will only grant post-CRL meeting requests that pose questions to clarify identified deficiencies. Other issues, including questions requiring further Agency review, disputes about classification of complete response amendments,[7] or new information submitted by the applicant, will not be addressed in a post-CRL meeting.

III. GDUFA II PERFORMANCE GOALS

In accordance with the GDUFA II Commitment Letter, FDA agreed to certain goals and procedures for the scheduling and conduct of post-CRL meetings for all ANDAs.[8]

FDA has committed to providing a scheduled date for 90 percent of post-CRL meetings within 10 calendar days[9] of receipt[10] of a written request.[11] FDA has further committed to conducting

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[6] GDUFA II Commitment Letter at 12.

[7] Please see the draft guidances for industry *Requests for Reconsideration at the Division Level Under GDUFA* and *ANDA Submissions – Amendments to Abbreviated New Drug Applications Under GDUFA* for further information on disputing the classification of a complete response amendment. When final, these guidances will represent FDA's current thinking on these topics. For the most recent version of a guidance, check the FDA Drugs guidance web page at https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

[8] GDUFA II Commitment Letter at 11-12.

[9] See the GDUFA II Commitment Letter at 12. Also see the GDUFA II Commitment Letter at 25, stating that, as used in the Letter, "days – unless otherwise specified, means calendar days."

[10] For purposes of meeting the commitments outlined in this guidance, post-CRL meeting requests will be received by the Agency, via the Electronics Submissions Gateway (ESG), Monday through Friday from 12:00 a.m. to 11:59

90 percent of post-CRL meetings held on an FDA-proposed date within 30 days of receipt of a written request.[12] In the event FDA proposes a post-CRL meeting date within 30 days of receipt of a written request, but the meeting is ultimately scheduled outside of the 30-day window at the applicant's request, FDA will consider its goal of conducting the meeting within 30 days of receipt of a written request met.

IV. POST-CRL MEETING REQUESTS

To make the most efficient use of FDA and industry resources, any post-CRL meeting request should include the information specified in this section. If FDA determines that the post-CRL meeting request does not contain the information specified in this section, the request is subject to denial (see section V.A.).

The written request should be submitted to the ANDA via the Electronic Submissions Gateway (ESG) within 10 calendar days of issuance of the CRL to help facilitate planning and coordination of post-CRL meetings. The cover page should identify the submission as a **"Post-Complete Response Letter Meeting Request."** A complete post-CRL meeting request package should include the following information:

- A list of proposed questions seeking clarification of the deficiencies identified in the CRL, grouped by discipline.

- A list of all individuals, with their titles and affiliations, who will attend the requested meeting from the applicant's organization and consultants.

- The requested format of the meeting—teleconference or written response. If requested format of the meeting is a teleconference, the meeting request package should also include the following information:

    - A proposed agenda outlining how the 30-minute[13] time allotted for the post-CRL meeting should be apportioned to each proposed question.

    - A list of specific review disciplines asked to participate in the requested teleconference.

p.m. Eastern Standard Time/Eastern Daylight Time, excluding Federal holidays and days when the FDA office that will review the post-CRL meeting request is closed.

[11] GDUFA II Commitment Letter at 12.

[12] For purposes of meeting our GDUFA goals, written responses count toward meeting these goals.

[13] Consistent with GDUFA I, post-CRL meeting teleconferences are limited to 30 minutes. This 30-minute meeting period will not be extended.

V. ASSESSING POST-CRL MEETING REQUESTS

The Project Manager (PM) assigned to the ANDA, in collaboration with the review disciplines, as necessary, will determine whether to grant or deny the post-CRL meeting request and will respond to the applicant as described below.

A. Meeting Denied

If a post-CRL meeting request is missing any of the elements outlined in section IV, FDA will deem the request incomplete and subject to denial.

Also, a post-CRL meeting request may be denied if:

- The proposed questions are not clarifying.
  - The Agency interprets nonclarifying questions to include those that fall under the following categories:[14]
    - Facility-related issues, such as plans for the remediation of current good manufacturing practice (CGMP) deficiencies or a facility's current CGMP status.
    - Requests for Agency input on study or formulation design.
    - Requests for amendment reclassification (major to minor).
    - Disputes regarding the relevance of a deficiency.
    - Disputes regarding the determined scale-up and postapproval changes (SUPAC) level.
    - Disputes regarding guidance documents.
  - Examples of nonclarifying questions include:
    - Does the Agency agree that this alternative statistical method would be acceptable?
    - Can the Agency review our proposed protocol for a new study we plan to conduct?
  - FDA will not answer such questions and will deny post-CRL meeting requests associated with questions of this nature. Applicants should submit an amendment to address deficiencies in their CRL response, and FDA will review them in its normal course.
- The proposed questions are outside the scope of the deficiencies identified in the CRL (i.e., questions do not reference a specific deficiency from the CRL).
- The proposed questions require review from the Agency.
- The post-CRL meeting request is not submitted post-CRL, (i.e., it is submitted during the review cycle, post-Information Request/Discipline Review letter, or after the applicant has already submitted a CRL response).
- The post-CRL meeting request is subsequent to an original post-CRL meeting request submitted in response to the same CRL.

[14] The categories listed here are not intended to be exhaustive.

If a post-CRL meeting request is denied, the applicant will be notified in writing.

B. Meeting Granted

A post-CRL meeting request may be granted if:

- A post-CRL meeting request has not already been submitted for the same CRL.
  - FDA will grant one post-CRL meeting request (either teleconference or written response as requested by applicant) per CRL, covering only questions submitted in a single complete post-CRL meeting request package.
  - Applicants should include all questions in their complete post-CRL meeting request packages, rather than submitting questions on a rolling basis, as the Agency will not consider subsequently submitted questions.

- The proposed questions seek clarification concerning deficiencies in the CRL.
  - The GDUFA II Commitment Letter defines appropriate requests seeking clarification concerning deficiencies, considered *clarifying questions* for purposes of this guidance, as those posed by the applicant with the goal of gaining an understanding of specific deficiencies and expectations for resolution.[15]
  - The Agency interprets clarifying questions to include, for example, requests for clarification on requirements to address a deficiency (i.e., "Can the Agency clarify how the suggested limit of 1.1% for Impurity L was calculated by the Agency?").
  - To the extent a post-CRL meeting request contains both clarifying and nonclarifying questions, the Agency will grant the meeting, in part, and will only answer appropriate questions.

- A complete meeting package is submitted.
  - FDA will grant a complete post-CRL meeting request that satisfies the criteria outlined in section IV, to the extent the questions submitted are posed to clarify identified deficiencies.[16]
  - To the extent an applicant wishes to resubmit the meeting package correcting any missing elements, the applicant may do so. Goal dates, however, are only available for original, complete packages submitted within 10 calendar days of issuance of the CRL containing proposed questions that are within the scope of the CRL and otherwise meet criteria set forth in section IV. Thus, if a resubmitted post-CRL meeting request is granted, there will be no goal dates associated with scheduling and conducting the post-CRL meeting. Similarly, an otherwise complete post-CRL meeting request will be granted, but ineligible for a goal date assignment, if submitted outside the 10-calendar-day window.

If a post-CRL meeting request is granted, the applicant will be notified in writing. To the extent a post-CRL meeting request contains both clarifying and nonclarifying questions, the Agency

[15] GDUFA II Commitment Letter at 24.

[16] "Applicants may opt for a post-CRL teleconference to seek clarification concerning deficiencies identified in a CRL." See the GDUFA II Commitment Letter at 12.

will grant the meeting, in part, and will only answer clarifying questions. If the Agency grants a post-CRL meeting in part, it will notify the applicant in writing and identify the questions that are denied.

C. Written Responses

FDA will grant or deny a post-CRL meeting request for written responses within 10 calendar days of receipt of a written request, and the applicant will be notified in writing. If the post-CRL meeting request is granted, FDA will provide written responses within 30 days of receipt of a post-CRL meeting request requesting a written response. FDA will grant one post-CRL meeting request (either teleconference or written response as requested by applicant) per CRL, covering only questions submitted in a single complete post-CRL meeting request package.

VI. RESCHEDULING AND CANCELLING POST-CRL MEETINGS

Occasionally, circumstances arise that necessitate the rescheduling or cancellation of a post-CRL meeting. If a post-CRL meeting teleconference must be rescheduled, it should be rescheduled as soon as possible after the original date. A new post-CRL meeting request should not be submitted. The applicant and FDA should take reasonable steps to avoid rescheduling meetings. It will be at the discretion of the applicable review division(s) whether the meeting should be rescheduled depending on the specific circumstances. A meeting may be rescheduled if, for example:

- It is determined that attendance by additional FDA personnel not originally anticipated or requested is critical and their availability precludes holding the meeting on the original date.
- Essential attendees are no longer available for the scheduled date and time because of an unexpected or unavoidable conflict or an emergency situation.

A post-CRL meeting may be cancelled if, for example, the ANDA applicant withdraws the post-CRL meeting request or if the applicant submits a response to the CRL.

VII. PROCEDURES FOR THE CONDUCT OF POST-CRL MEETING TELECONFERENCES

Post-CRL meetings will be facilitated by the PM assigned to the ANDA and will begin with introductions and a statement of the agenda. FDA will strictly follow the agenda and will not entertain questions outside those submitted in the post-CRL meeting request package. Consistent with GDUFA I, post-CRL meetings are limited to 30 minutes. This 30-minute meeting period cannot be extended. To the extent questions on the agenda are addressed ahead of expiration of this 30-minute period, the teleconference will end upon the conclusion of discussions related to these questions.

Before the end of the meeting, FDA recommends that all attendees summarize discussion points, agreements, and clarifications to ensure that there is a mutual understanding of the meeting outcomes.

VIII. DOCUMENTATION OF MEETINGS

Documentation of meeting outcomes (responses to the questions and outcomes of any discussions regarding the responses), agreements, and disagreements is critical to ensuring that this information is preserved for meeting attendees and for future reference. FDA minutes are the official record of the meeting. FDA will aspire to issue the official, finalized minutes to the ANDA applicant within 30 days of the post-CRL meeting.

IX. RESOLUTION OF DISPUTES ABOUT MEETING MINUTES

On occasion, there may be disputes regarding the accuracy and sufficiency of the minutes of a post-CRL meeting. An ANDA applicant requesting additional clarification of the meeting minutes issued by FDA should contact the assigned PM for advice. This process addresses issues with the meeting minutes only. If an ANDA applicant needs to discuss additional issues that were not addressed at the post-CRL meeting, the ANDA applicant should contact the PM. FDA recommends that the ANDA applicant submit its concerns about the meeting minutes in writing to FDA within 10 calendar days of receipt of the meeting minutes.

If, after following up as described above, there are still significant differences in the ANDA applicant's understanding of the content of the official meeting minutes, the ANDA applicant should notify FDA in writing with respect to specific disagreements. The ANDA applicant should submit the correspondence to its application, with a copy to the point of contact describing the concern.

The ANDA applicant's concerns will be taken under consideration by the review division and the office director if the office director was present at the meeting. If the minutes are deemed to accurately and sufficiently reflect the meeting discussion, the PM will convey this decision to the ANDA applicant and the minutes will stand as the official documentation of the meeting. If, after discussions with the requester, FDA deems it necessary to effect a change to the official minutes, the changes will be documented in an addendum to the official minutes. The addendum will also document any continued requester objections.