Post-Complete Response Letter Meetings Between FDA and ANDA Applicants Under GDUFA

Guidance for Industry

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

December 2018
Generics

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Office of Communications, Division of Drug Information
Center for Drug Evaluation and Research
Food and Drug Administration
10001 New Hampshire Ave., Hillandale Bldg., 4th Floor
Silver Spring, MD 20993-0002
Phone: 855-543-3784 or 301-796-3400; Fax: 301-431-6353
Email: druginfo@fda.hhs.gov
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Contains Nonbinding Recommendations

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

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 office 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 FDA Reauthorization Act of 2017, reauthorizing the Generic Drug User Fee Amendments (GDUFA II) 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

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[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] Public Law 115-52, Title III.

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

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

GDUFA was reauthorized (GDUFA II) on August 18, 2017 in order to facilitate timely access to high 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.[6] 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."[7] 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,[8] 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.[9]

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[6] See Generic Drug User Fee Act Program Performance Goals and Procedures, available at https://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM282505.pdf

[7] GDUFA II Commitment Letter at 12.

[8] Please see the draft guidance for industry *Requests for Reconsideration at the Division Level Under GDUFA* (when final, this guidance will represent FDA's current thinking on this topic) and the guidance for industry *ANDA Submissions – Amendments to Abbreviated New Drug Applications Under GDUFA* for further information on disputing the classification of a complete response amendment. 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.

[9] GDUFA II Commitment Letter at 12.

FDA has committed to providing a scheduled date for 90 percent of post-CRL meetings within 10 calendar days[10] of receipt[11] of a written request.[12] FDA has further committed to conducting 90 percent of post-CRL meetings held on an FDA-proposed date within 30 days of receipt of a written request.[13] 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 participate in the requested meeting from the applicant's organization and consultants.[14]

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

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[10] See the GDUFA II Commitment Letter at 12. See also the GDUFA II Commitment Letter at 25, stating that, as used in the Letter, "[d]ays – unless otherwise specified, means calendar days."

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

[12] GDUFA II Commitment Letter at 12.

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

[14] The applicant should notify their point of contact (POC) immediately if the list of meeting participants from the applicant's organization and consultants changes. In this situation, FDA may reschedule the meeting if the revised list of meeting participants requires additional FDA personnel. In the event this meeting is ultimately scheduled outside of the 30-day window, FDA will consider its GDUFA II goal of conducting the meeting within 30 days of receipt of a written request met.

- A proposed agenda outlining how the 30-minute[15] 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.

V. ASSESSING POST-CRL MEETING REQUESTS

The applicant's point of contact (POC)[16] 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 non-clarifying questions to include those that fall under the following categories:[17]
    - 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 non-clarifying 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?

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

[16] For purposes of this guidance, the applicant's POC will generally be the regulatory project manager (RPM). However, the appropriate discipline project manager will be the applicant's POC in lieu of the RPM for post-CRL meeting requests for labeling only supplements or chemistry, manufacturing, and controls (CMC) only supplements.

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

- 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 additional FDA assessment of information (e.g., data) to develop a response. Clarifying questions should not require an expenditure of significant FDA resources.
- 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).
- A post-CRL meeting request was previously granted for the same CRL.

If a post-CRL meeting request is denied, the applicant will be notified in writing. To the extent an applicant wishes to resubmit the meeting package and provide any missing elements, the applicant may do so. GDUFA II 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 the criteria set forth in section IV. Thus, if a resubmitted post-CRL meeting request is granted, there will be no GDUFA II goal dates associated with scheduling and conducting the post-CRL meeting.

B. Meeting Granted

A post-CRL meeting request may be granted if:

- A post-CRL meeting request has not already been granted for the same CRL.
  - FDA will generally grant only one post-CRL meeting request (either teleconference or written response as requested by the applicant) per CRL, covering only those clarifying questions submitted in a single complete post-CRL meeting request package.

- 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.[18] Clarifying questions should not require additional FDA assessment of information (e.g., data) to develop a response or require an expenditure of significant Agency resources.
  - The Agency interprets clarifying questions to include, for example, requests for clarification on requirements to address a deficiency (e.g., "Can the Agency clarify how the suggested limit of 1.1% for Impurity L was calculated by the Agency?").

- A complete meeting package is submitted.

[18] GDUFA II Commitment Letter at 24.

- 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.[19]
- 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.
- Goal dates 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 the criteria set forth in section IV. If an original, complete post-CRL meeting package is submitted outside the 10-calendar-day window, the meeting request will be granted but will be ineligible for a goal date assignment.

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 non-clarifying questions, the Agency 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 a written response within 30 days of receipt of a post-CRL meeting request requesting a written response. FDA will generally grant only one post-CRL meeting request (either teleconference or written response as requested by the 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 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 discipline(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.

[19] "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.

- 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 applicant's POC 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.[20] To the extent questions on the agenda are addressed ahead of the 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 participants 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. If an ANDA applicant has concerns with the meeting minutes issued by FDA, or would like additional clarification of the meeting minutes, the ANDA applicant should contact the assigned POC in writing within 10 calendar days of receipt of the meeting minutes. The ANDA applicant's concerns will be taken under consideration by the review discipline and senior management if senior management were present at the meeting. If the minutes are deemed to accurately and sufficiently reflect the meeting discussion, the applicant's POC 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 ANDA applicant, FDA deems it

[20] In consideration of the time constraints of post-CRL meetings, FDA encourages applicants to carefully consider the order in which they would like FDA to address their questions.

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 objections from the ANDA applicant.