Post-Complete Response Letter Clarification Teleconferences 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)

October 2022
Generic Drugs

Revision 1

Contains Nonbinding Recommendations

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

Guidance for Industry

Additional copies are available from:
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
https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm

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

October 2022
Generic Drugs

Revision 1

TABLE OF CONTENTS

Contains Nonbinding Recommendations

Post-Complete Response Letter Clarification Teleconferences 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) teleconferences (post-CRL clarification teleconferences) 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 clarification teleconference is a meeting that is requested in writing by an ANDA applicant pursuant to the procedures described in this guidance following receipt of a CRL.[3]

It is important that there are efficient, consistent procedures for the timely and effective conduct of post-CRL clarification teleconferences. This guidance will assist applicants in generating and submitting a request for a post-CRL clarification teleconference and the associated meeting package to FDA as contemplated in the Generic Drug User Fee Amendments of 2022, reauthorizing the Generic Drug User Fee Amendments (GDUFA III) for Fiscal Years 2023-2027. This guidance is intended to provide procedures that will promote well-managed post-CRL clarification teleconferences and help ensure that such meetings are scheduled and conducted in accordance with the time frames set forth in the GDUFA Reauthorization

[1] This guidance has been prepared by the Division of Policy Development in the Office of Generic Drug Policy in the Center for Drug Evaluation and Research at the Food and Drug Administration. You may submit comments on this guidance at any time. Submit comments to Docket No. FDA-2017-D-5928 (available at https://www.regulations.gov/docket/FDA-2017-D-5928).

[2] For purposes of this guidance, *ANDA* means the original application including all amendments and supplements to the application.

[3] Post-CRL clarification teleconferences have a different purpose and different eligibility criteria than post-CRL scientific meetings. For additional information on post-CRL scientific meetings, see the guidance for industry *Formal Meetings Between FDA and ANDA Applicants of Complex Products Under GDUFA* (October 2022). 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.

Performance Goals and Program Enhancements Fiscal Years 2023-2027 (GDUFA III commitment letter).[4]

This guidance revises the guidance entitled *Post-Complete Response Letter Meetings Between FDA and ANDA Applicants Under GDUFA* issued in December 2018. This revision is being issued to incorporate the performance goals outlined in the GDUFA III commitment letter that FDA has agreed to meet, and clarifies how FDA will conduct post-CRL clarification teleconferences subject to the GDUFA performance goals.

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)[5] amended the FD&C Act to authorize FDA to assess and collect user fees to provide the Agency with the resources[6] to help ensure patients have access to quality, affordable, safe, and effective generic drugs. GDUFA fee resources 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 Generic Drug User Fee Amendments of 2022. As described in the GDUFA III commitment letter applicable to this latest reauthorization, 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, the purpose of a post-CRL clarification teleconference is for applicants to seek clarification concerning deficiencies identified in a CRL.[7] Under the GDUFA III commitment letter, post-CRL clarification teleconferences are available for both major and minor CRLs issued in the first cycle or in subsequent assessment cycles. FDA will grant any complete post-CRL clarification teleconference request that satisfies the criteria outlined in section IV of this guidance. FDA will only grant post-CRL clarification teleconference requests that pose questions to clarify identified deficiencies. Other issues, including questions requiring further Agency review, disputes about classification of complete

[4] The GDUFA III commitment letter is available at https://www.fda.gov/media/153631/download.

[5] Title III of the Food and Drug Administration Safety and Innovation Act, Public Law 112-144.

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

[7] GDUFA III commitment letter at 16.

response amendments,[8] or new information submitted by the applicant, will not be addressed in a post-CRL clarification teleconference. If applicants have non-clarifying questions in relation to a CRL, they can consider requesting a post-CRL scientific meeting[9] or submitting a controlled correspondence,[10] as appropriate. An applicant may have a post-CRL clarification teleconference prior to requesting a post-CRL scientific meeting.[11]

III. GDUFA III PERFORMANCE GOALS

In accordance with the GDUFA III commitment letter, FDA agreed to certain goals and procedures for the scheduling and conduct of post-CRL clarification teleconferences for all ANDAs.[12]

FDA has committed to providing a scheduled date for 90 percent of post-CRL clarification teleconferences within 14 calendar days[13] of receipt[14] of a written request.[15] FDA has further committed to conducting 90 percent of post-CRL clarification teleconferences, held on an FDA-proposed date, within 30 days of receipt of a written request. In the event FDA proposes a post-CRL clarification teleconference date within 30 days of receipt of a written request, but the teleconference is ultimately scheduled outside of the 30-day window at the applicant's request,

---

[8] See the draft guidance for industry *Requests for Reconsideration at the Division Level Under GDUFA* (December 2017) (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* (July 2018) for further information on disputing the classification of a complete response amendment.

[9] The purpose of a post-CRL scientific meeting is to provide an applicant scientific advice on possible approaches to address deficiencies identified in a CRL related to establishing equivalence. An applicant's post-CRL scientific meeting request must discuss one or more of the following: (1) a new equivalence study needed to address the deficiencies in the design identified in the CRL; (2) an approach that is different from that submitted in an ANDA (e.g., a change in study type from in vivo to in vitro); (3) a new comparative use human factors study; or (4) a new approach to demonstrating sameness of a complex active ingredient. GDUFA III commitment letter at 28-29. For more information on post-CRL scientific meetings, see the guidance for industry *Formal Meetings Between FDA and ANDA Applicants of Complex Products Under GDUFA* (October 2022).

[10] The purpose of the controlled correspondence process is to provide a mechanism for a direct inquiry on FDA's position with respect to a particular element of generic drug development or post-approval submission requirements and for the Agency's direct, brief, timely response. For example, an ANDA applicant may submit a controlled correspondence to seek regulatory and/or scientific advice after issuance of a CRL or to request evaluations of alternative bioequivalence approaches (e.g., pharmacokinetic, in vitro, clinical). GDUFA III commitment letter at 11, 46. For more information on the controlled correspondence process, see the guidance for industry *Controlled Correspondence Related to Generic Drug Development* (December 2020).

[11] GDUFA III commitment letter at 26.

[12] Ibid at 16.

[13] Ibid. See also the GDUFA III commitment letter at 47, stating that "[d]ays – unless otherwise specified, means calendar days."

[14] For purposes of meeting the commitments outlined in this guidance, post-CRL clarification teleconference 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 clarification teleconference request is closed.

[15] GDUFA III commitment letter at 16.

FDA will consider its goal of conducting the teleconference within 30 days of receipt of a written request met.

IV. POST-CRL CLARIFICATION TELECONFERENCE REQUESTS

To make the most efficient use of FDA and industry resources, any post-CRL clarification teleconference request should include the information specified in this section. If FDA determines that the post-CRL clarification teleconference 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 a post-CRL clarification teleconference. The cover page should identify the submission as a **"Post-Complete Response Letter Clarification Teleconference Request."** A complete post-CRL clarification teleconference request package should include the following information:

- A list of proposed questions seeking clarification of the deficiencies identified in the CRL, grouped by assessment discipline and describing the reason why such deficiencies are not clear.[16]

- A list of all individuals, with their titles and affiliations, who will participate in the requested teleconference from the applicant's organization and consultants.[17]

- The requested format—teleconference[18] or written response only.[19] If the requested format is a teleconference, the post-CRL clarification teleconference request package should also include the following information:

    - A proposed agenda outlining how the 30-minute[20] time allotted for the post-CRL clarification teleconference should be apportioned to each proposed question.

---

[16] Ibid.

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

[18] Teleconference means a verbal communication by telephone, and not a written response unless otherwise agreed to by the applicant. GDUFA III commitment letter at 48.

[19] Written response only responses are sent in lieu of a teleconference when requested by or otherwise agreed to by the applicant. If an applicant requests or otherwise agrees to written responses only, the written responses only count toward meeting the GDUFA goal.

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

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

V. ASSESSING POST-CRL CLARIFICATION TELECONFERENCE REQUESTS

The applicant's point of contact (POC)[21] assigned to the ANDA, in collaboration with the assessment disciplines, as necessary, will determine whether to grant or deny the post-CRL clarification teleconference request and will respond to the applicant as described below.

A. Teleconference Denied

If a post-CRL clarification teleconference 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 clarification teleconference 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:[22]
    - 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).
    - Requests for Agency input on a proposed alternative approach to address a deficiency.
    - Disputes regarding the relevance of a deficiency.
    - Disputes regarding the determined scale-up and postapproval changes (SUPAC) level.
    - Disputes regarding guidance documents.
    - Disputes regarding facility assessment scheduling/timing or tools used.
  - 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?
- 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).

[21] 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 clarification teleconference requests for labeling only supplements or chemistry, manufacturing, and controls (CMC) only supplements.

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

- 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 proposed questions are within the scope of questions that are appropriate for a post-CRL scientific meeting.[23]
- The post-CRL clarification teleconference request is not submitted post-CRL (i.e., it is submitted during the assessment cycle, post-Information Request/Discipline Review Letter, or after the applicant has already submitted a CRL response).
- A post-CRL clarification teleconference request was previously granted for the same CRL.

If a post-CRL clarification teleconference request is denied, FDA will notify the applicant in writing. To the extent an applicant wishes to resubmit the meeting package and provide any missing elements, the applicant may do so. GDUFA III 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 clarification teleconference request is granted, there will be no GDUFA III goal dates associated with scheduling and conducting the post-CRL clarification teleconference.

B. Teleconference Granted

A post-CRL clarification teleconference request may be granted if the following criteria are satisfied:

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

- The proposed questions seek clarification concerning deficiencies identified in the CRL.
    - The GDUFA III commitment letter defines appropriate requests as ones that clearly identify the specific deficiencies to be discussed and the reason why such deficiencies are not clear, considered *clarifying questions* for purposes of this guidance.[24] 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.

[23] See footnote 9.

[24] GDUFA III commitment letter at 16.

- A complete meeting package is submitted, as outlined in section IV.

Applicants should include all questions in their complete post-CRL clarification teleconference 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 clarification teleconference package is submitted outside the 10-calendar-day window, the teleconference request may be granted but will be ineligible for a goal date assignment.

If a post-CRL clarification teleconference request is granted, the applicant will be notified in writing.

Post-CRL clarification teleconference requests that contain clarifying questions and non-clarifying questions may be granted in part for the clarifying questions and denied in part for the non-clarifying questions.

If applicants have non-clarifying questions, they can consider requesting a post-CRL scientific meeting[25] or submitting a controlled correspondence,[26] as appropriate, to obtain the Agency's feedback on those non-clarifying questions.

C. Written Responses Only

FDA has agreed to grant or deny an applicant's post-CRL clarification teleconference request for written responses only within 14 calendar days of receipt of a written request, and the applicant will be notified in writing. If the applicant's request is granted, FDA has agreed to provide written responses only in lieu of a teleconference within 30 days of receipt of a post-CRL clarification teleconference request requesting written responses only.[27] FDA will generally grant only one post-CRL clarification teleconference request (either teleconference or written response only as requested by the applicant) per CRL, covering only clarifying questions submitted in a single complete post-CRL clarification teleconference request package.

[25] See footnote 9.

[26] See footnote 10.

[27] GDUFA III commitment letter at 16.

VI. RESCHEDULING AND CANCELLING POST-CRL CLARIFICATION TELECONFERENCES

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

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

Post-CRL clarification teleconferences 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 the clarifying questions submitted in the post-CRL clarification teleconference request package. Consistent with GDUFA I and GDUFA II, post-CRL clarification teleconferences are limited to 30 minutes. This 30-minute teleconference period cannot be extended.[28] 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 teleconference, FDA recommends that all attendees summarize discussion points, agreements, and clarifications to ensure that there is a mutual understanding of the teleconference outcomes.

VIII. DOCUMENTATION AND MEETING MINUTES

Documentation of teleconference outcomes (responses to the questions and outcomes of any discussions regarding the responses), agreements, and disagreements is critical to ensuring that

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

this information is preserved for teleconference participants and for future reference. FDA meeting minutes are the official record of the teleconference. FDA intends to issue the official, finalized minutes to the ANDA applicant within 30 days of the post-CRL clarification teleconference.

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 clarification teleconference. An ANDA applicant requesting additional clarification of the meeting minutes issued by FDA should contact the applicant's POC in writing within 10 calendar days of receipt of the meeting minutes. This process addresses issues with the meeting minutes only and not additional issues that were not addressed at the post-CRL clarification teleconference.

The ANDA applicant's concerns will be taken under consideration by the assessment discipline and senior management if senior management were present at the teleconference. If the minutes are deemed to accurately and sufficiently reflect the teleconference discussion, the applicant's POC will convey this decision to the ANDA applicant and the minutes will stand as the official documentation of the teleconference. If, after discussions with the ANDA applicant, 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 objections from the ANDA applicant.[29]

[29] Any addendum will be shared with the ANDA applicant by FDA.