U.S. FOOD & DRUG ADMINISTRATION

A Deep Dive into the New GDUFA III Meeting: Post-Complete Response Letter (CRL) Scientific Meeting

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A Deep Dive: GDUFA III Scientific Meetings

May 15, 2023

Outline

- Introduction
- Purpose
- Grant/Deny Decision Criteria
- Meeting Process and Timeline
- Current State/General Advice
- Challenge Questions

GDUFA III Meetings

*PSG: Product-Specific Guidance

**CRL: Complete Response Letter

Purpose

- *Purpose of* ***ANDA Assessment Meeting Program*** - Provide or continue to provide targeted, robust advice to ANDA applicants as they work to meet the standards for ANDA approval.

- *Purpose for* ***Post-CRL Scientific Meeting*** - Provide an applicant scientific advice on possible approaches to address deficiencies identified in a CRL related to establishing equivalence.

GDUFA III Commitment Letter

GDUFA III Commitment Letter

Does not have to have had a post-CRL teleconference prior to requesting this meeting

An applicant can request a Post-CRL Scientific Meeting.

Does not have to have had a Product Development Meeting

A meeting request must discuss:

- a new equivalence study needed to address the deficiencies in the design identified in the CRL
- an approach that is different from that submitted in the ANDA, e.g., a change in study type from in vivo to in vitro
- a new comparative use human factors study
- a new approach to demonstrating sameness of a complex active ingredient

and

it is a complex generic product, or in FDA's judgment the request raises issues that are best addressed via this meeting process and cannot be adequately addressed through Controlled Correspondence

FDA agreed to grant or deny the Post-CRL Scientific Meeting request within **14 days** after receipt of the request.

FDA agreed to hold the Post-CRL Scientific Meeting within **90 days** after the date the meeting is granted.

GDUFA III Commitment Letter IV. C.

Will Grant

Meet both criteria below:

- Complex generic product, and

- Relates to one or more of following four topics:
  - a new equivalence study needed to address the deficiencies in the design identified in the CRL;
  - an approach that is different from that submitted in the ANDA, e.g., a change in study type from in vivo to in vitro;
  - a new comparative use human factors study, or
  - a new approach to demonstrating sameness of a complex active ingredient

May Grant

In FDA's judgment the request raises issues that are best addressed via this meeting process and cannot be adequately addressed through Controlled Correspondence

Relates to one or more of following four topics:

- a new equivalence study needed to address the deficiencies in the design identified in the CRL;
- an approach that is different from that submitted in the ANDA, e.g., a change in study type from in vivo to in vitro;
- a new comparative use human factors study, or
- a new approach to demonstrating sameness of a complex active ingredient

May Be Denied Scenario

A post-CRL scientific meeting request may be denied because

- The product does not meet the criteria for a complex product, or
- In FDA's judgment the request raises issues that can be adequately addressed through controlled correspondence, or
- The meeting request does not discuss one of the following as it relates to establishing equivalence:
  - a new equivalence study needed to address the deficiencies in the design identified in the CRL;
  - an approach that is different from that submitted in the ANDA, e.g., a change in study type from in vivo to in vitro;
  - a new comparative use human factors study, or
  - a new approach to demonstrating sameness of a complex active ingredient

Timeline

ANDAs in CR status that meet eligibility requirements

Grant/Deny Decision Issued to Applicant	• Within 14 days after receipt of the Meeting Request
Meeting/Teleconference Held or Written Response Issued	• Within 90 days after the date the meeting is granted
Preliminary Responses to Applicant's Questions	• Issued no later than 5 days prior to the external meeting with applicant
Meeting Minutes	• Issued within 30 days of the meeting or teleconference

If a due date falls on a weekend or federal holiday, it will be moved to the preceding business day

After Grant/Deny Decision is Made…

- **Denial Letter** –
  - Justification for the denial

- **Grant Letter** –
  - Meeting time/date, or goal date for providing written responses
  - Preliminary list of FDA attendees
  - Meeting format (i.e., in-person face-to-face, videoconference, teleconference, or written response only)

Expectations of the Meeting Package…

- The cover letter should clearly identify that it is a "*Post-Complete Response Letter Scientific Meeting Request*"
- Clearly state if it is a complex/non-complex drug product, and include any rationale or justifications for why the product meets the criteria for a complex product, if applicable
- Clearly state which of the four criteria (in the GDUFA III Commitment Letter) relating to establishing equivalence the meeting request (potential discussion) is focusing on
- Clearly state the requested format (i.e., in-person face-to-face, videoconference, teleconference, or written response only)

A Post-CRL Scientific Meeting May Be Cancelled If …

- The applicant withdraws the meeting request, or
- The applicant informs FDA that its questions have been adequately answered by preliminary written comments, or
- FDA issues product-specific guidance on establishing bioequivalence to the reference listed drug (RLD), which addresses the questions in the meeting package.

Related to Preliminary Response…

- FDA intends to issue no later than 5 days prior to the meeting
- The meeting may be canceled if the applicant finds the preliminary written comments are adequate to address their questions
- If a meeting is still to be held, the applicant should provide an updated agenda with its list of questions and any proposed presentation materials, no later than 48 hours before the meeting

Presentations and Additional Questions

- Presentations by applicants are not generally needed for post-CRL scientific meeting. If an applicant decide to have a presentation, the presentation material should be shared with FDA no later than 48 hours prior to the meeting

- FDA may not be able to provide comments on any new questions raised in the presentation

After the Meeting is Held…

- FDA will issue meeting minutes within 30 days of the meeting
- FDA meeting minutes are the official minutes of the meeting
- If the applicant believes there is a discrepancy in the minutes, they should submit their concerns in writing within 10 calendar days of the receipt of the official meeting minutes

Current State

As of 4/28/2023,

- FDA has received 11 Post-CRL Scientific Meeting requests
- FDA has granted 7 Post-CRL Scientific Meeting requests

General Advice for Questions Included in the Meeting Package

- FDA will not pre-review any specific scientific data submitted in the meeting package

- Typically, the eventual acceptability of any proposed new approach/new study will be assessed upon submission of an ANDA amendment containing the relevant information

References

- Formal Meetings Between FDA and ANDA Applicants of Complex Products Under GDUFA Guidance for Industry (October 2022) (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/formal-meetings-between-fda-and-anda-applicants-complex-products-under-gdufa-guidance-industry)

- FDA GDUFA III Reauthorization Page https://www.fda.gov/industry/generic-drug-user-fee-amendments/gdufa-iii-reauthorization

Challenge Question #1

Is following statement true or false?

A post-CRL scientific meeting request can only be submitted after first submitting a post-CRL teleconference to the agency.

- True
- False

Challenge Question #2

My application was submitted prior to October 1st, 2022 but now is in CR status, is my application still eligible to request post-CRL scientific meeting?

- Yes
- No