ALSTON & BIRD

WWW.ALSTON.COM

FDA Compliance & Enforcement ADVISORY ■

SEPTEMBER 8, 2023

FDA Issues Draft Guidance on Post-Warning Letter Meeting Requests Under GDUFA

By Cathy Burgess, Anthony Fanucci , and Krupa Zachariah

On September 1, 2023, the Food and Drug Administration (FDA) published a draft guidance, Post-Warning Letter Meetings Under GDUFA for Industry, detailing the post-warning letter meeting request process for certain drug manufacturing facilities. The process was outlined in the GDUFA III commitment letter, which contains the performance goals and program enhancements for the Generic Drug User Fee Amendments (GDUFA) third reauthorization (for fiscal years 2023–2027).

Summary and Purpose

The draft guidance describes the factors a facility should consider before submitting a post-warning letter meeting request on the facility's ongoing efforts to remedy current good manufacturing practice deficiencies described in a warning letter; how to prepare and submit a complete meeting request package; and how the FDA intends to conduct the post-warning letter meeting.

The draft guidance describes a post-warning letter meeting as an avenue to obtain preliminary feedback from the FDA on the adequacy and completeness of corrective and preventive action (CAPA) plans and to aid the facility in resolving the inspectional deficiencies that the FDA identified in the warning letter. The draft guidance emphasizes that during a post-warning letter meeting, the agency does not consider any "application-related discussions" appropriate, even if the agency application assessors attend the meeting.

While the GDUFA III commitment letter describes the processes to submit both a post-warning letter meeting request or reinspection request, the draft guidance covers only post-warning letter meeting requests.

GDUFA III Performance Goals

The draft guidance highlights the GDUFA III performance goals associated with the post-warning letter meeting requests, as indicated in Section VII(D)(10) of the GDUFA III commitment letter. Notably, the FDA restated its performance goal to issue decisions on post-warning letter meeting requests for "50 percent of eligible requests within 30 days of requests" in fiscal year 2024.

Who May Submit a Request and Request Timing Considerations

For eligible facilities, as defined by section VII(D)(3)of the GDUFA III commitment letter, the draft guidance clarifies that the FDA intends to only accept a post-warning letter meeting request from the "facility, parent company, or authorized legal representative." Applicants (unless the applicant and the facility are the same legal entity), customers, or other third parties should not submit post-warning letter meeting requests.

The draft guidance further suggests that the FDA would deny a post-warning letter meeting request if the facility files the request with or around the same time it submits its warning letter response. Specifically, the FDA states in the draft guidance that "reasonable progress toward remediation is unlikely" if a facility files a request for a post-warning letter meeting around the same time the firm submits its warning letter response. The FDA notes that the facility should request the meeting "in a separate and subsequent submission from the firm's warning letter response."

Preparing a Meeting Package and Content Requirements

The meeting package should clearly indicate that the facility is requesting a post-warning letter meeting "under the terms of the GDUFA III commitment letter and include adequate information for FDA to assess the potential utility of the meeting." The draft guidance then describes how firms should prepare the meeting package and outlines recommendations for its contents. Specifically, the draft guidance mentions that the meeting package should:

- Describe the facility's principal areas of interest. The request "may include discussion of remediation activities for all deviations identified during the inspection, whether or not those issues were included in the warning letter."
- Include for each deviation or violation described in the warning letter "a description of the root cause analysis and a retrospective evaluation of the impact of each deficiency on product quality and other systems at the same facility and systems at different facilities (e.g., operational design, quality system flaws) for all planned or implemented CAPAs as well as a CAPA plan timeline."
- Reference each warning letter response and supporting documentation.
- Provide a summary of any additional CAPAs not related to issues specifically cited in the warning letter but nonetheless related to the associated inspection. Further, the FDA notes that if previous or post-warning letter inspections were also classified as official action indicated (OAI), the meeting package should include a summary and completion status of those CAPAs.

We note that the FDA's recommendation to include a description of the root cause analysis and a retrospective evaluation of the impact of each deficiency on product quality and other systems at the same facility and systems at different facilities highlights what the agency expects to see in inspection-related correspondence. Arguably, if a facility follows the FDA's recommendation as part of an initial inspection response, it could potentially avoid a warning letter, obviating the need to request a post-warning letter meeting.

Regarding formatting, the draft guidance indicates that the meeting package should include a table of contents, appropriate indices, appendices, cross-references, bookmarks differentiating sections, and should be sequentially paginated.

The draft guidance includes a proposed agenda containing sections requesting specific information. The proposed agenda should address relevant information, including facility information, meeting logistics, a table or section including CAPA summaries, status reports, and facility questions. The FDA recommends using tables to organize the information in the meeting package. Further, the agency notes that it may request clarifying information during its review of the meeting package.

Assessing Meeting Requests: Grant, Deny, or Defer

In the draft guidance, the FDA restates its intention to grant a post-warning letter meeting request only if the facility has submitted a "thorough and complete CAPA plan that addresses all items cited in the warning letter, and reasonable progress has been made toward remediation." A facility can expect to receive a notification of a decision to grant a request from the FDA by email.

The draft guidance describes several reasons that the FDA may deny a request for a post-warning letter meeting, including "if the CAPA does not include a retrospective evaluation of the scope of issues, address whether other systems or facilities are affected by the problem or include supporting documentation." When it has denied a request, the FDA intends to provide a written notification to the facility, including an explanation of the reasons for the denial.

In the draft guidance, the FDA once again highlights its discretion to defer a post-warning letter meeting if it has "determined that a re-inspection is the most appropriate next step (i.e., defer the meeting in favor of re-inspection)." The FDA's ability to do so is consistent with our understanding that some within the agency interpret the commitment letter to require applicants to submit a post-warning letter meeting request before submitting a request for reinspection. While neither the commitment letter nor the draft guidance contains an explicit requirement stating so, that interpretation is consistent with FDA testimony before Congress on the user fee reauthorization hearings and with our understanding of the commitment letter negotiations.

Rescheduling and Canceling Post-Warning Letter Meetings

Section VIII of the draft guidance addresses the factors that the FDA considers when a meeting is canceled or rescheduled. The FDA lists several reasons why the agency or facility may reschedule a meeting and notes that the agency will make every effort to ensure the meeting occurs within a reasonable time. Further, the draft guidance clarifies that if a post-warning letter meeting is canceled by a facility, the FDA intends to consider a subsequent request to schedule another meeting to be a second and final post-warning letter meeting request. The draft guidance states that a facility may cancel a post-warning letter meeting if it withdraws the meeting request or determines that any preliminary written comments from the FDA have adequately answered its questions.

Format of Post-Warning Letter Meetings

The final section of the draft guidance covers the procedures for the conduct of meetings. The FDA will generally schedule post-warning letter meetings for one hour, and the draft guidance notes that facilities should submit materials to the FDA 30 calendar days before the scheduled meeting date. The FDA emphasizes that "presentations should be brief to maximize the time available for discussion." The FDA recommends the following post-warning letter meeting format in the draft guidance:

- Introductions.
- FDA opening remarks.
- Facility presentation of the CAPA plan progress and questions.
- FDA and facility discussion of the CAPA plan progress and facility questions (allowing for at least 30 minutes).
- Action items and next steps.

- Closing remarks by corporate or facility senior leadership.
- FDA closing remarks and discussion of any action items.

While the draft guidance clarifies many aspects of the process and considerations of requesting a post-warning letter meeting, the FDA omits a few key issues. For instance, the FDA does not address whether it has a backlog of post-warning letter meeting requests. Additionally, the draft guidance does not update stakeholders on the agency's progress towards meeting its commitment in fiscal year 2024 to issue decisions regarding post-warning letter meeting requests for 50 percent of eligible requests within 30 days of requests.

The draft guidance is available for public comment for 60 days, due November 6, 2023. Interested stakeholders may submit comments electronically and should identify their comments with the draft guidance's docket number: FDA-2023-D-3370. Please contact us if you require assistance in drafting and submitting comments to this draft guidance.

Alston & Bird can advise clients that are evaluating whether to request a post-warning letter meeting, and we can assist clients in preparing meeting packages and presentations. If you have any questions or require assistance, please let us know.

You can subscribe to future *Food, Drug & Device/FDA* advisories and other Alston & Bird publications by completing our **publications subscription form**.

If you have any questions, or would like additional information, please contact one of the attorneys on our **FDA Compliance & Enforcement Team**.

ALSTON & BIRD

WWW.ALSTON.COM

ATLANTA: One Atlantic Center ■ 1201 West Peachtree Street ■ Atlanta, Georgia, USA, 30309-3424 ■ +1 404.881.7000 ■ Fax: +1 404.881.7777
BEIJING: Hanwei Plaza West Wing ■ Suite 21B2 ■ No. 7 Guanghua Road ■ Chaoyang District ■ Beijing, 100004 CN ■ +86 10 8592 7500
BRUSSELS: Rue Guimard 9 et Rue du Commerce 87 ■ 3rd Floor ■ 1000 Brussels ■ Brussels, 1000, BE ■ +32.2.550.3700 ■ Fax: +32.2.550.3719
CHARLOTTE: One South at The Plaza ■ 101 South Tryon Street ■ Suite 4000 ■ Charlotte, North Carolina, USA, 28280-4000 ■ +1 704.444.1000 ■ Fax: +1 704.444.111
DALLAS: Chase Tower ■ 2200 Ross Avenue ■ Suite 2300 ■ Dallas, Texas, USA, 75201 ■ +1 214.922.3400 ■ Fax: +1 214.922.3899
FORT WORTH: Bank of America Tower ■ 301 Commerce ■ Suite 3635 ■ Fort Worth, Texas, USA, 76102 ■ +1 214.922.3400 ■ Fax: +1 214.922.3899
LONDON: 4th Floor, Octagon Point, St. Paul's ■ 5 Cheapside ■ London, EC2V 6AA, UK ■ +44.0.20.3823.2225
LOS ANGELES: 333 South Hope Street ■ 16th Floor ■ Los Angeles, California, USA, 90071-3004 ■ +1 213.576.1000 ■ Fax: +1 213.576.1100
NEW YORK: 90 Park Avenue ■ 15th Floor ■ New York, New York, USA, 10016-1387 ■ +1 212.210.9400 ■ Fax: +1 212.210.9444
RALEIGH: 555 Fayetteville Street ■ Suite 600 ■ Raleigh, North Carolina, USA, 27601-3034 ■ +1 919.862.2200 ■ Fax: +1 919.862.2260
SAN FRANCISCO: 560 Mission Street ■ Suite 2100 ■ San Francisco, California, USA, 94105-0912 ■ +1 415.243.1000 ■ Fax: +1 415.243.1001
SILICON VALLEY: 755 Page Mill Road ■ Building C - Suite 200 ■ Palo Alto, California, USA 94304-1012 ■ +1 650.838.2000 ■ Fax: +1 650.838.2001
WASHINGTON, DC: The Atlantic Building ■ 950 F Street, NW ■ Washington, DC, USA, 20004-1404 ■ +1 202.239.3300 ■ Fax: +1 202.239.3333