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FDA proposes a process for receiving nonbinding feedback on an establishment's response to an FDA Form 483

Establishments should consider potential implications of utilizing the program

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On 19 February 2019 the U.S. Food and Drug Administration (FDA or the agency) released a draft guidance entitled, "Nonbinding Feedback After Certain FDA Inspections of Device Establishments" (draft guidance) for comment. The draft guidance, released in response to the FDA Reauthorization Act of 2017 (FDARA)[1], proposes a pathway for device and biologics manufacturers (regulated under device authorities) to receive nonbinding feedback on some or all of their proposed corrective action plans in their response to FDA Form 483 (Form 483) inspectional observations. This process, if implemented as described in the draft guidance, should be carefully evaluated depending on the circumstances, as discussed below.

Under the current draft guidance, in order to receive feedback, the establishment must declare that the inspectional observation(s) represent(s) a situation that: (i) if left unresolved, involves a public health priority; (ii) implicates systemic or major actions; or (iii) is related to an emerging safety issue(s). Should FDA decide that the establishment's request is eligible for feedback, the agency has up to 45 days from the receipt of the request to provide feedback on the action plan. Establishments seeking to obtain such feedback should consider the potential implications of the request. For example, making the required declaration on the observation(s) for which feedback is being sought could constitute an admission that is ultimately used against the company. In addition, by the time feedback is received (i.e., 60 days after issuance of the Form 483), companies may already have implemented or substantially completed certain corrective actions to address quality or safety issues.

Background

The FDARA required, among other things, that FDA provide timely nonbinding feedback to an owner, operator, or agent (collectively owner) of an establishment following an inspection, if issues are documented on a Form 483 that: (i) involve a public health priority; (ii) implicate systemic or major actions; or (iii) relate to emerging safety issues. However, by statute, FDA is

[1] FDARA, enacted on 18 August 2017, amended the Federal Food, Drug, and Cosmetic Act (FDCA).

the arbiter of whether issues documented on a Form 483 rise to a level that requires issuance of nonbinding feedback to the owner.[2]

Following an establishment inspection by FDA, while not required, owners historically have been strongly encouraged to provide a response in writing to the Form 483 regardless of the nature and severity of the observations. The response should outline the company's corrective action plan, including the actions the company has implemented or will implement to address the inspectional observations. If a response is submitted within 15 business days, the agency has committed, by its own policy,[3] to consider the owner's response in deciding whether to issue a warning letter.

FDA encourages the owner to begin implementation of their action plans without the benefit of FDA's feedback on the proposed actions. This implementation can be costly to the company and carries no certainty of adequately addressing the concerns raised in FDA's observations. Failure to adequately address FDA's inspectional observations can lead to repeat observations upon re-inspection, additional inspections, and/or the issuance of enforcement actions, such as warning letters, import alerts (for foreign establishments), or civil or criminal penalties.

As owners evaluate their options for responding to an FDA inspection, the feedback required under FDARA potentially could help owners avoid the unnecessary expense of solutions that ultimately will not resolve the observed deficiencies to the agency's satisfaction. The draft guidance identifies a standardized method for communicating and submitting requests for nonbinding feedback and further describes how FDA plans to evaluate and respond to such requests. It also highlights the sort of observations that will be eligible for nonbinding feedback. Owners should carefully consider the potential consequences before choosing to utilize this feedback mechanism.

Requests for nonbinding feedback

A request for nonbinding feedback must come from the person to whom the Form 483 was addressed or other individual who can adequately demonstrate to the agency that they represent the owner. FDA refers to this individual as the "requestor."

The requestor must submit the feedback request within 15 business days of the date the Form 483 was issued, and it should be directed to the FDA contact that is also indicated to receive the response to the Form 483 (in today's FDA regional office structure, this person is usually the Division Director for the region). If a Form 483 response is also to be submitted, FDA recommends that the response and request be submitted together, but as two separate documents.

The request for nonbinding feedback may pertain to a single observation, multiple observations, or an entire Form 483 and must explain why each observation for which feedback is requested meets at least one of the three statutorily defined eligibility criteria. Specifically, the request must explain why the observation(s):

- Involve a public health priority – such conditions have resulted in, or if unaddressed are likely to result in, the release of a violative product that may cause death or serious injury.
- Implicate systemic or major actions – the quality system or subsystem(s) deficiencies, when considering all pertinent factors, have resulted in, or would likely result in, the production of nonconforming, violative, and/or defective finished devices.

[2] *See* FDCA section 704(h)(2)(B)(ii).
[3] *See* 74 Fed. Reg. 40212 *available here* (last visited 19 February 2019); *See also generally* U.S. Food & Drug Regulatory Procedures Manual, Chapter 4 – Advisory Actions (September 2018) *available here* (last visited 19 February 2019).

- Relate to emerging safety issues – an emerging safety issue that, if unresolved, is likely to result in the release of devices that are likely to cause death or serious injury.

The request should detail the company's proposed response to each observation on which feedback is sought, including a detailed description of the actions intended to be taken, the timeframe for implementation of those actions, and supporting documentation, as appropriate.

FDA's nonbinding feedback

If the agency determines that none of the criteria are met, the requestor will be notified within 45 calendar days that the requested feedback is unavailable. However, if one of the justifications is deemed to be satisfied, the agency must respond to the feedback request within 45 calendar days of its receipt.

According to the draft guidance, FDA's feedback will assume that the proposed action will be implemented fully in the manner described by the owner. Under this assumption, FDA's feedback will indicate whether the proposed corrective action appears to be adequate, partially adequate, or inadequate to address the cited observation. If the proposed action does not appear to be fully adequate, FDA will explain its reasoning and provide a recommendation for how the deficiency may be corrected. However, it is important to emphasize that there is no guarantee that implementing FDA's feedback will adequately address the problems that resulted in the Form 483 observation, and implementing FDA's feedback does not preclude or limit any further regulatory action by the agency.

The owner is not required to adhere to FDA's nonbinding recommendations and may use an alternative approach to correct the inspectional observations, but this approach is not without risk and careful consideration should be given to any such strategy.

Hogan Lovells analysis

The press release accompanying the draft guidance included commentary from Jeff Shuren, M.D., director of the Center for Devices and Radiological Health that, "it's important for communications between the agency and manufacturers to be clear and efficient so companies can address safety and quality issues as quickly and as adequately as possible to help them come into compliance with our regulations," and the draft guidance "proposes a standardized process for providing this type of timely, efficient, and nonbinding feedback to manufacturers with respect to proposed corrective actions in response to our inspectional observations."

While the agency's intent in developing the program is laudable, owners should consider the following when deciding whether to seek FDA feedback.

FDA feedback under the program may not be timely

FDA has 45 days to respond to the company's request for nonbinding feedback, meaning that the feedback would be provided up to 60 days after the Form 483 was issued. In practice, many actions are initiated or even completed in the 15 business day Form 483 response deadline, or shortly thereafter. Thus, companies may not significantly benefit from FDA feedback on these short term actions. Action plans that require multiple months to implement could benefit from the FDA feedback as there would likely be time to adjust the action plan before it is fully implemented, but manufacturers should be cautious about delaying necessary actions while awaiting FDA feedback as such delays may not serve the best interest of addressing important quality or safety issues.

In our experience, FDA has historically provided feedback on the adequacy of a company's Form 483 response through formal correspondence and/or, to some extent, by how the inspection is

ultimately classified by FDA. However, there is no timeline for issuance of this feedback nor are there criteria to be satisfied in providing feedback. The draft guidance appears to suggest that the nonbinding feedback provided through the proposed program may be more substantive than what has historically been provided. As noted above, the nonbinding feedback may explain why proposed actions may be inadequate or partially adequate and may include FDA recommendations for developing an adequate action plan.

It is not clear whether FDA's response to a request for nonbinding feedback will provide enough additional information in a timeframe that significantly benefits a particular requestor. Formalizing the requirement for feedback could be a positive development for industry in some cases, particularly for those companies undertaking large remedial actions that could require months to complete the work.

Potential liability in making declarations

In order for a request for nonbinding feedback to be eligible for a response, companies will need to explain and concede (or even advocate) that a particular issue involves a public health priority, implicates systemic or major actions, or relates to emerging safety issues likely to cause death or serious injury. To satisfy the statutory requirements, the company will need to provide an explanation that could be interpreted as an admission of violation or that the product presents an unreasonable risk of harm to patients. Further, neither the statute nor the draft guidance provides any protection to companies to limit the agency's use of that information at a later date or as a basis for enforcement action. In addition, such declarations potentially could be used against a company in civil actions. The legal liability implications of an owner taking the position that its Form 483 observations meet one or more of the criteria for receiving informal feedback could very well outweigh the value of receiving such nonbinding feedback in many cases. Companies may alternatively benefit from third-party experts' and regulatory counsel's insight into what has satisfied the agency in the past or what industry best practices are for remediating certain types of issues before responding to the Form 483.

FDA is accepting comments to the draft guidance under docket number FDA-2018-D-4711 through 20 April 2019.

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