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Is FDA Moving the Goalposts on 483 Responses? What the New Draft Guidance Means for Your Company

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The US Food and Drug Administration (FDA) has issued new draft guidance giving drug manufacturers – for the first time – formal guidance on how the agency expects firms to respond to a Form FDA 483 following a drug current Good Manufacturing Practice (cGMP) inspection. The guidance is broad in scope and applies to both foreign and domestic facilities that manufacture human or animal drugs regulated by the Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER) or Center for Veterinary Medicine (CVM), extending to combination-product manufacturers when CDER or CBER is the lead center. Until now, companies have largely relied on experience and institutional knowledge to determine what a "good" response looks like. This draft guidance puts structure around the process, signaling that FDA now expects 483 responses to follow a more consistent structure and be clearly tied to the strength and reliability of a facility's broader quality system.

FDA also explicitly asks manufacturers to identify the response preparer and, if the preparer is not the company itself, to provide a letter of authorization from the consultant or outside counsel who prepared the response on the manufacturer's behalf. Moreover, FDA is specific in its requests for large-scale compliance efforts, such as reports covering global pharmacovigilance investigations. In this way, the new guidance articulates what FDA insiders have often advised: FDA wants to see that a company has not only addressed, or is actively addressing, the observations in a 483, but is also fully assessing and correcting any underlying systemic issues.

Recommended practices

The draft guidance highlights several elements FDA views as important for a robust response. Several of these elements relate to format or other logistical requirements – a table of contents, a copy of the 483, identity of the response preparer and letters of authorization if the company retained a consultant or outside counsel. More substantively, FDA recommends an executive summary of all remediation activities followed by a more detailed description of each observation and associated remediation plans, including risk assessments of the observations, detailed investigation reports and signed attachments to support the company's response.

Disagreements

FDA recommends that companies seek clarification and address disagreements related to scientific or technical issues during an inspection with FDA investigators. If a significant disagreement is not resolved before issuance of the 483, companies should communicate these concerns in their 483 response. Companies will want to describe the contested facts and provide scientific data and supporting information to allow FDA to better evaluate the concern. Moreover, companies should reference applicable laws, regulations and guidance that support their position.

Preliminary results and interim reporting

FDA recommends that, if there are remediation activities that are not complete at the time a company submits its response (which is often the case), the company should submit preliminary results with a timeline for completion. Companies should also highlight interim measures put in place until the corrective actions and preventive actions (CAPAs) are complete. FDA expects CAPA plans to be measurable and verifiable, and companies can expect such plans to be evaluated by FDA in a future inspection to ensure the planned actions were effectively implemented.

Importance of timing

The 15-business-day time frame for a 483 response is critical. Although a company is not required to provide a response within this time frame, timely submission improves a company's likelihood of avoiding a compliance or enforcement action. That said, some corrective actions, particularly those of the holistic nature FDA expects, cannot be accomplished in a 15-day time frame. Moreover, FDA states in the draft guidance that it will not typically delay a regulatory action, such as issuing a warning letter, particularly if FDA observed significant deficiencies concerning product quality or patient safety during the inspection. This leaves companies in the hard position of promising comprehensive corrective actions on a broader scale and wanting to submit complete responses within the 15-day time frame that reflect the actions the company has taken in that time period. In this way, the guidance may not actually achieve FDA's goals, leaving manufacturers to determine the best strategy for the 483 response in light of their specific timelines for corrective actions.

See the big picture

While the draft guidance clarifies what FDA expects to see in an individual response, it also makes clear that the agency is looking for companies to conduct systemic investigations and assess observations in the context of their overall quality system. Specifically, FDA encourages companies to explain "conditions or systemic issues that led to the observations," and to include information about "the scope of the issue, effect on other drugs, and whether the observation is an isolated incident or is systemic in nature." Put simply, FDA wants to understand whether a finding reflects a one off problem or evidence of a broader breakdown. The guidance also notes that firm management plays an important role in ensuring the quality system can support this kind of evaluation and in maintaining the overall effectiveness of the system.

Manufacturers should be prepared for FDA to continue to take a broad view of their operations as it evaluates the response. FDA will consider not only the observation itself, but also what the company's assessment and supporting information reveal about the strength and effectiveness of its quality system.

Practical concerns

The guidance raises some practical concerns that may warrant submission of comments for the agency's consideration. For example, as discussed above, the tension between the 15-business-day response window and the breadth of information FDA expects in the initial response, coupled with the agency's position that it will not ordinarily delay regulatory action to review late-submitted responses, could disadvantage many small and mid-size companies. Although the guidance encourages interim reporting, it does not expressly commit FDA to consider such submissions in its enforcement decision-making. This dynamic could encourage companies to rush comprehensive investigations to avoid having their assessments and corrective actions disregarded.

Bottom line: Companies should continue to prioritize submitting as comprehensive a response as possible within the 15-business-day window. A timely, well-organized submission that acknowledges ongoing remediation efforts can demonstrate good faith and may position a company more favorably if FDA initiates further enforcement action. This is particularly important in the context of more serious enforcement tools, such as injunctions. To obtain injunctive relief, FDA must show, among other things, a likelihood of recurring violations, and that the company is unwilling or unable to comply with the law. A company's documented efforts to investigate and remediate 483 observations –including interim reports and CAPA implementation timelines – may be directly relevant to that analysis and could undermine FDA's ability to satisfy this standard. In addition, the guidance appears to take an expansive view of quality investigation requirements. It recommends that companies prepare an investigation plan that includes a detailed protocol and methodology, a scientifically justified and risk-based scope, and justification for excluding any part of an establishment's operations from the investigation.

These recommendations – together with the guidance's recommendation that a comprehensive investigation plan be prepared to address FDA's 483 observations by including identification of any related trends, linking any connected FDA 483 observations, assessing risks and analyzing root cause – appear to go beyond what is currently required under existing regulations. Thus, this particular area seems to merit industry comments, as the guidance's detailed recommendations concerning the form and substance of the 483 response may set a higher bar than current regulations warrant.

Looking ahead

In short, while the draft guidance provides a helpful framework,[1] it leaves important questions unanswered, including the role of interim submissions and how FDA will weigh ongoing remediation efforts in its enforcement decision-making.

The Cooley team, including former FDA enforcement attorneys, is available to help you assess how this draft guidance may affect your operations and prepare for evolving FDA expectations. FDA is accepting public comments on the draft guidance through May 8, 2026, and submitting by that date will ensure your feedback is considered as the agency works on the final guidance. Please reach out with any questions or if you would like assistance preparing comments.

Note

1. This draft guidance does not apply to medical devices and, thus, device companies should continue to follow 21 CFR Part 820 and related guidance concerning device inspections. However, some key points from the draft guidance, including the importance of submitting a 483 response within 15 business days and developing comprehensive, risk-based CAPA plans with root-cause analysis, provide useful guidance for device firms as well.

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