Qualio

5 considerations for responding to an FDA 483

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Getting to market with your medical device or drug in the United States is impossible without the FDA paying very close attention.

You must have FDA approval or clearance to sell your product, and once you've secured approval your interactions with the Agency aren't over. An FDA inspector will arrive to check your facilities (or your contract manufacturing facility) on a periodic basis, and they will fully expect to see a robust and functioning quality system in place to support your product and, more importantly, the safety of your patients.

If they don't like what they see, you'll receive a Form 483. Here's what to do if that happens.

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Introduction to FDA inspections and the 483 process

The best FDA inspections are always open and collaborative, and produce actionable feedback in a short period of time. It's an opportunity for an unbiased, independent set of eyes to interrogate your QMS and ensure you're doing (and documenting!) everything required to ensure the safety of your patients and the integrity of your product. Being well prepared with a solid, well-organized quality system will reduce the stress levels of the entire process.

Nevertheless, your inspector may not like everything you show them. They'll keep detailed notes in their EIR, or Establishment Inspection Report, and you're entitled to a copy of this document if you ask for it. When the inspector has findings they consider 'non-conformances', these will be detailed in a **Form 483.**

These findings should be addressed immediately during the inspection if possible. A simple example would be an information gap in an SOP, and your inspector will note that you've corrected the item on the 483.

If the issues can't be corrected simply and immediately, you'll need to pursue a medium-term action plan. Keep the following 5 things in mind:

1. Don’t ignore it

You aren’t legally obligated to respond to 483 observations, but if you choose not to, you’re borrowing trouble in the future. Inspectors always review the EIR and any 483 findings from the last audit and will ensure they cover those topics specifically.

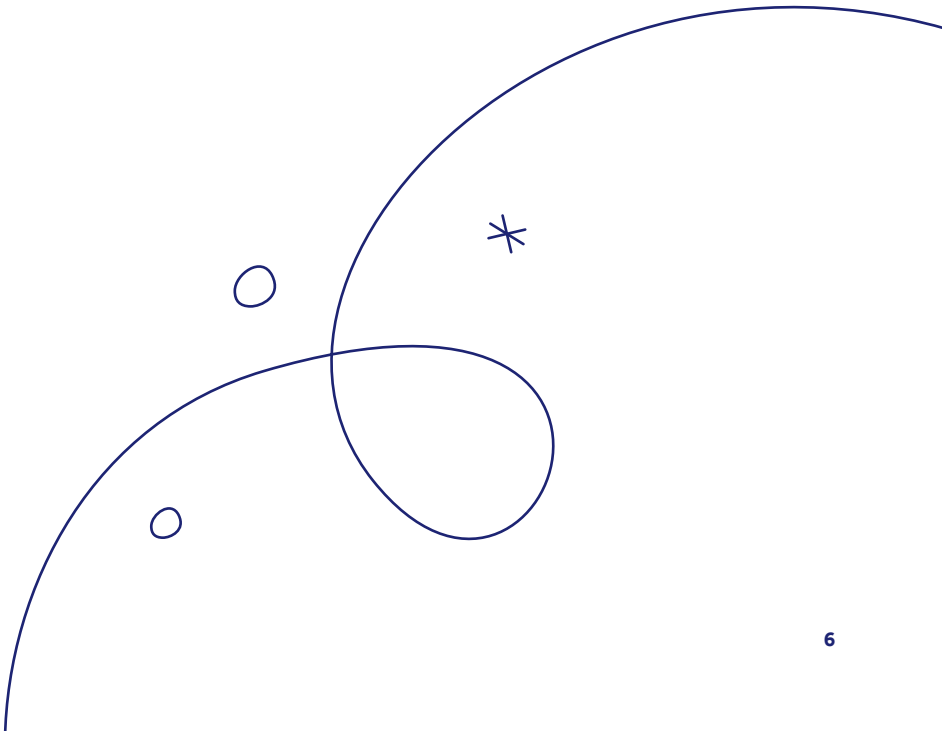
Repeat findings are a sure way to a warning letter, as they represent systemic breakdowns and a huge lack of commitment to quality and continuous improvement on the part of the organization.

2. Speak up

Ask questions of the inspector during the inspection. Ask more questions at the close-out meeting. Ensure you clearly understand the issue they have identified, from their perspective. You may not agree with them, but the responsibility to correct the identified problem is clearly with you.

It is rare for an inspector to not come around if you truly are meeting the intent of the regulations, and your documented process or records are just unclear to them. Arguing with them is fruitless and just changes the tone of the inspection for the worse. But ensuring clarity before they leave your facility is critical to correcting the issues identified.

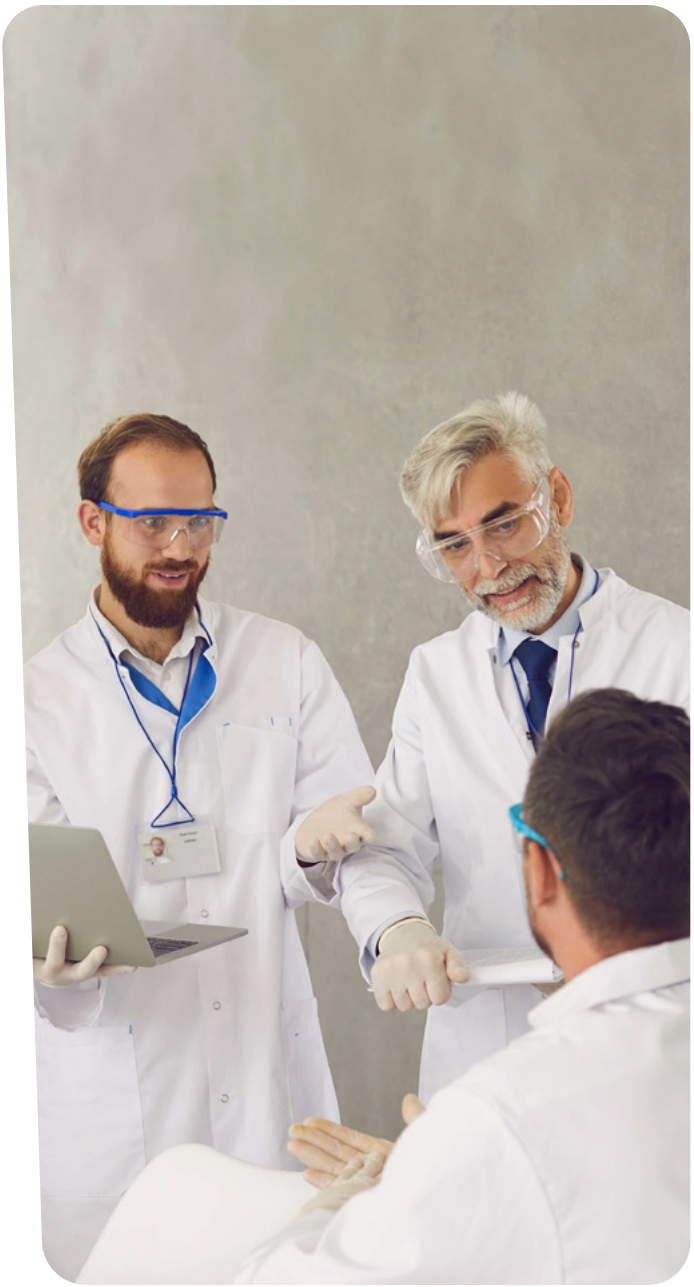
The FDA's Operations Investigations Manual is a helpful tool in learning what they look for and how they expect organizations to adhere to quality standards.



3. Assemble your response team

Once you have the 483 in hand with the list of non-conformances, immediately assemble cross-functional teams to assess the issues. Sometimes, the different items can be grouped together to be addressed.

Use your CAPA system and thoroughly investigate root causes. Consider if the issue might touch other systems also. Resist the urge to jump to an immediate conclusion before a thorough root cause investigation can take place. A solid CAPA system will ensure you don't miss the boat with your corrections.



4. Stick to the program

Establish and stick to solid timelines. The ideal response time to a Form 483 is **30 days**. If you can correct items within that timeframe with meaningful corrections that truly address the issue identified, then summarizing the corrections made in your response to the agency is ideal.

If the issues are bigger and more systemic in nature, then respond with:

a. the immediate corrective/containment action taken,
b. a summary of the investigation findings (or that the investigation is ongoing), and
c. a timeline for completion of the investigation at least should be provided.

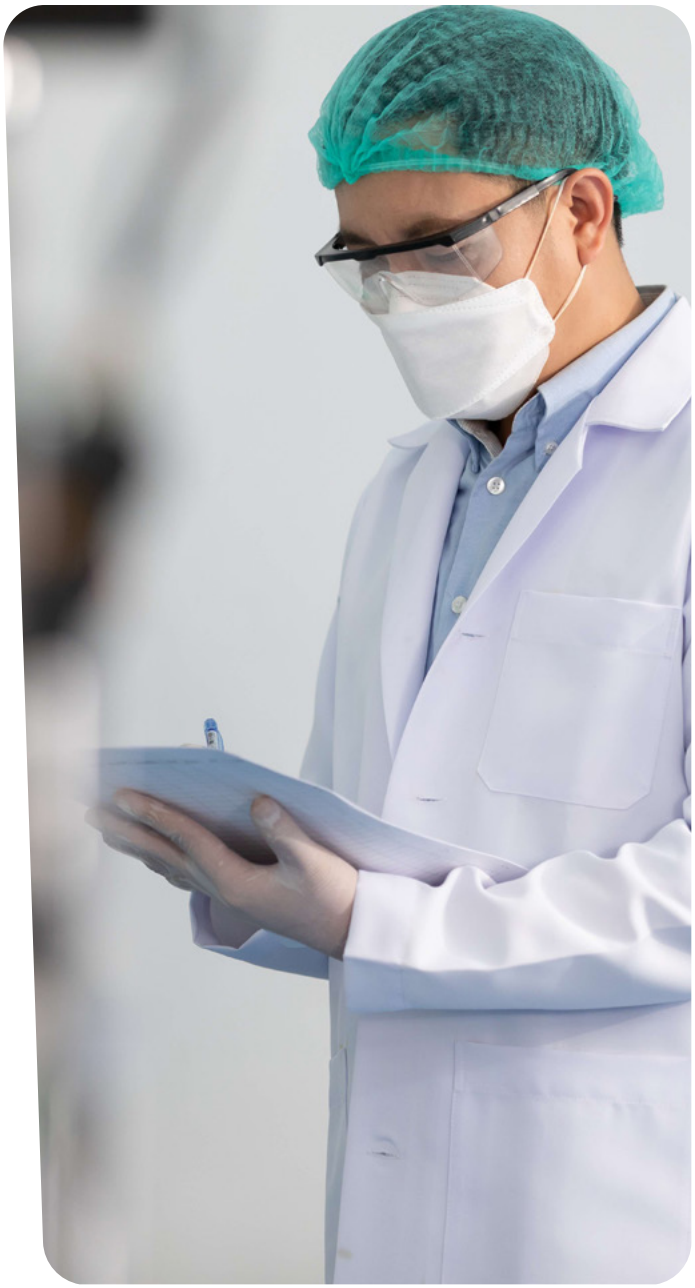
If you've identified corrections, but the implementation timeline is going to be longer, then report that. Keep in mind that any commitments you make in this response letter will be followed up on. You shouldn't pad the timeline unnecessarily, but be realistic and don't overcommit.

5. Get a second opinion if needed

If you truly disagree with the finding, an external, independent opinion should be sought. Sometimes, the company is too entrenched in their existing systems to be able to see, from an outsider's perspective, that things are unclear or incomplete.

Your initial 483 response can be that you're investigating further, buying some time. But outright dismissing their finding is a dangerous move for a company to make, and puts you well on the path to bigger issues in the future. Once you've had that independent assessment, and are in agreement that the intent of the cited regulation is met, you can clearly explain your position.

There are formal processes in place should you be unable to resolve the issue with your inspector directly.



Conclusion

A robust QMS, underpinned by the right quality tools and engagement, is the best way to prevent major issues from being identified during FDA regulatory inspections. But even the best planned and executed quality systems have opportunities to improve, and thorough scrutiny from an independent third party can be a helpful way to throw light on issues you've overlooked.

Always treat your FDA interactions as opportunities to improve patient outcomes and your business practices. In this light, your 483 can be a positive experience which opens a new exciting chapter for your business.

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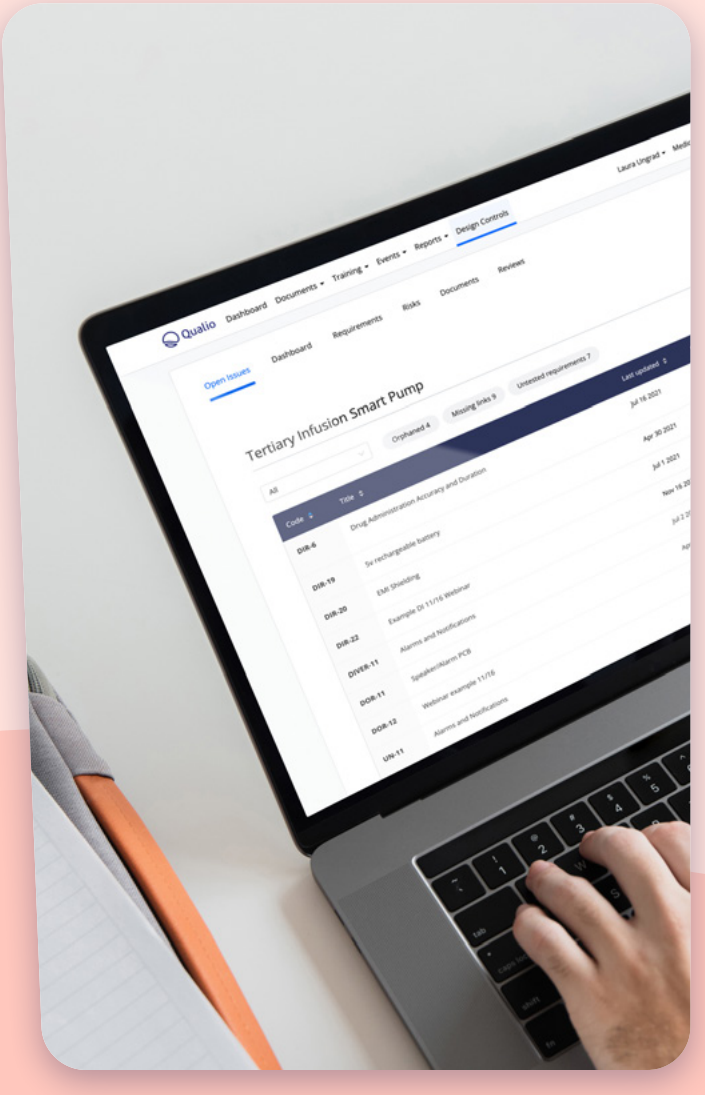

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