Writing An Effective 483 Response

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A well-reasoned, complete, and timely 483 response is in your best interest.

The 483 response

- There is no regulatory requirement to respond to the 483….

…..however, it’s in your best interest to respond in writing.

Writing an effective 483 response Topics to be covered:

- Regulatory framework and FDA policies and procedures for the FDA 483;
- Four reasons for submitting a well-reasoned, complete, and timely 483 response;
- Eight suggestions for an effective 483 response.

Form FDA 483 Inspectional Observations

- Under what authority does FDA issue 483s?
  - "The observations of objectionable conditions and practices listed on the front of this form are reported:
    1. Pursuant to Section 704(b) of the FFD&C Act
    2. To assist firms inspected in complying with the Acts and regulations enforced by the FDA"

Form FDA 483 Inspectional Observations

- Clarification:
  - What is a Form FDA 483?
  - What is it not?

Form FDA 483 Inspectional Observations

- List of inspectional observations
- 483 language
  - *“This document lists observations made by the FDA representative during the inspection of your facility. They are inspectional observations, and do not represent a final Agency determination regarding your compliance.”*

(Form FDA 483 & FDA Investigations Operations Manual (IOM) 5.2.3.1.4 http://www.fda.gov/ora/inspect_ref/iom/)

FDA’s expectations during an inspection

- *“…investigators should make every reasonable effort to discuss all observations with management… as they are observed, or on a daily basis to minimize surprises, errors, and misunderstandings when an FDA 483 is issued.”*
- IOM 5.2.3

FDA’s expectations during an inspection (2)

- *“Industry may use this opportunity to ask questions about the observations, request clarification, and inform the inspection team what corrections have been or will be made…”*
  - IOM 5.2.3

FDA activities following the inspection

- Investigators prepare the Establishment Inspection Report (EIR) & recommend classification of the inspection
- Supervisory review
- Classification of inspection: NAI, VAI, OAI
- If OAI, referral to district's Compliance Branch for further review & action

Why submit a 483 response?

Four reasons for submitting a well-reasoned, complete, and timely 483 response

1. Could possibly mitigate an FDA compliance decision for further action, e.g. untitled letter, Warning Letter

Four reasons for submitting a well-reasoned, complete, and timely 483 response

1. (cont)

- "As a general rule, a Warning Letter should not be issued if the agency concludes that a firm's corrective actions are adequate and that the violations that would have supported the letter have been corrected."
- Regulatory Procedures Manual, http://www.fda.gov/ora/compliance_ref/rpm/pdf/ch4.pdf

Four reasons for submitting a well-reasoned, complete, and timely 483 response

2. Demonstrates to the FDA (and other stakeholders) an understanding and acknowledgement of the observations

Four reasons for submitting a well-reasoned, complete, and timely 483 response

3. Demonstrates to the FDA (and other stakeholders) a commitment to correct, i.e. the intent to voluntarily comply

Four reasons for submitting a well-reasoned, complete, and timely 483 response

4. Establishes credibility with FDA

Suggestions for addressing 483 observations

Following an Inspection – Suggestions:

- Assess each observation
  - Focus on specifics
  - Focus on system-wide implications
  - Focus on global implications
  - *Consider affected products*
  - Consider root-cause analysis
  - Focus on the regulatory requirement(s) associated with the observation

Following an Inspection – Suggestions (cont):

- Develop action plan to achieve immediate, short-term, and long-term correction and to prevent recurrence
- Know when to seek outside assistance

Eight suggestions for an effective 483 response

Eight suggestions for an effective 483 response:

1. Include a commitment/statement from senior leadership
2. Address each observation separately
3. Note whether you agree or disagree with the observation

Eight suggestions for an effective 483 response:

4. Provide corrective action accomplished and/or planned; tell FDA the plan
   - Be specific (e.g. observation-by-observation)
   - Be complete
   - Be realistic
   - Be able to deliver what you promise
   - Address affected products

Eight suggestions for an effective 483 response:

5. Provide time frames for correction
6. Provide method of verification and/or monitoring for corrections
7. Consider submitting documentation of corrections where reasonable & feasible
8. BE TIMELY

To summarize

- There is no regulatory requirement to respond to the 483….

…..however, a well-reasoned, complete, and timely 483 response is in your best interest.

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“The safest way to double your money is to fold it over once and put it in your pocket”

Kin Hubbard