Responding to the FDA & Basics of Remediation

"Tales from the Dark Side"

5WS CONSULTING
For the FDA Regulated Industry

Setting the Tone

You just received an FDA-483 with *Data Integrity Observations*

"Records were Fabricated, Altered, Concealed or Missing."

Now what??

Overview

Tales from the Dark Side

- Response Timing
- Response Content
- Follow-Up on Response
- FDA's Steps/Actions
- Requesting a Meeting
- Remediation Choices
- Remediation Reminders
- Closing Summary

Response Timing

Response - Timing

You have 15 working days for initial response to 483:

- **Do** have consultant/advisor with FDA compliance experience review response
- **Don't** send it to consultant/advisor last minute

(Multiple revisions may be required)

Response Timing

NOTE:

This is only a preliminary response!

Response Content

Response Content

- **Be positive and professional!**
  - **DO NOT denigrate the FDA investigator.**
  - **Acknowledge the finding.**
  - **Give explanations, not excuses.**
- **Give evidence as attachments**
- **Use professional language and grammar**

Response Content

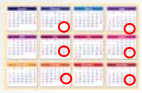
- **Introduction/Summary**
- **FDA Finding, followed by:**
  - **Explanation of facts about finding**
  - **Company practices, SOPs, results of preliminary investigations**
  - **Proposed actions/Risk assessment based on preliminary investigations and impact assessment**
- **Table**
- **Exhibits**

Response Content

Example of table:

CAPA Plan				
Observation	CAPA	Responsible Person(s) or Departments	Proposed Completion Date	Actual Completion Date

Response Content



- **Include timeframe for sending follow-up to response to FDA**
- **DO NOT tell FDA your remediation is complete if it isn't.**
- **CAPAs should be global/systematic**

Follow-up to Response

Follow-up to Response

What should a follow-up look like?

Follow-up to Response

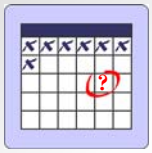
- Mimic initial response format
- Follow-up by timeline specified in initial response
- Be clear in steps taken between follow-ups

COMPLETED

FDAs Steps/Actions

FDA's Steps/Actions

When should you hear back from FDA?



FDA's Steps/Actions

- How necessary and available is your product?
- Opportunity to make global changes
- Other plants?

Decision

Research/Discussion

Review of Response/EIR

Establishment Inspection Report (EIR)

Audit/FDA 483

Warning Letter Excerpt:

If you are considering an action that is likely to lead to a disruption in the supply of drugs produced at your facility, FDA requests that you contact CDER's Drug Shortages Staff immediately, at drugshortages@fda.hhs.gov, so that FDA can work with you on the most effective way to bring your operations into compliance with the law. Contacting the Drug Shortages Staff also allows you to meet any obligations you may have to report discontinuances or interruptions in your drug manufacture under 21 U.S.C. 356C(b) and allows FDA to consider, as soon as possible, what actions, if any, may be needed to avoid shortages and protect the health of patients who depend on your products.

"If you are considering an action that is likely to lead to a disruption in the supply of drugs produced at your facility, FDA requests that you contact CDER's Drug Shortages Staff immediately at drugshortages@fda.hhs.gov so that FDA can work with you on the most effective way to bring your operations into compliance with the law…"

Requesting a Meeting

Requesting a meeting

When should you request a meeting with FDA?

Requesting a Meeting

A meeting is not always the best option, but might help to:

- Meet the face
- To provide updates on commitments made
- To discuss short supply Impact if plant is shut down
- Clarify FDA expectations

Requesting a Meeting

Preparing for meetings:

- **Detailed agenda with:**
  - Attendees/Titles
  - Topics
  - Offer Dates & Times
  - Limit it to 1 to 2 hours
  - Send in advance

Keep to the agenda and timeline!!

Remediation

Remediation: Components

- **Investigation and risk assessment**
- **Retroactive data review**
- **Further testing**

- **Communication with customers & vendors**
- **Recalls**
- **Personnel move/remove**
- **Other CAPAs**

- **SOP review, rewriting and creation**
- **Training**
- **Verification of training effectiveness**

Remediation - Choices

Who will perform remediation?

1. Consultants
2. DIY (Do It Yourself)
3. Combination of both

Remediation - Choice #1

Select Consultants if:

- You don't have the people
- You don't have the expertise
- FDA strongly suggests it
- Your customer requires it

Warning Letter Excerpt:

Data Integrity Remediation

Your quality system does not adequately ensure the accuracy and integrity of data to support the safety, effectiveness, and quality of the drugs you manufacture. We strongly recommend that you retain a qualified consultant to assist in your remediation.

"Your quality system does not adequately ensure the accuracy and integrity of data to support the safety, effectiveness, and quality of the drugs you manufacture. We **strongly recommend** that you retain a qualified consultant to assist in your remediation."

Remediation - Choice #1

Considerations:

- Contract requirements
- Lack of ownership
- Can be costly
- Not always a guarantee of success

Remediation - Choice #2

DIY if:

- You have enough people
- You have enough expertise
- You have the choice

Benefit – Ownership

Remediation - Choice #3

Use consultants for some things:

- CAPA and plan help/review
- Help with retrospective review
- Progress audits

NOTE: Use appropriate expertise and be prepared to share CV of consultant

Remember…

- Don't tell FDA you're ready until you've verified.

COMPLETED

- Make changes globally
  Verify globally!

- Consider transparency

Remediation

As you go through remediation…

- **Integrity is about perception**
- **Each auditor is different**
- **Kaizen** *(continuous improvement)*

In Closing…

In Summary:

FDA Responses:

- Be positive and professional
- Provide explanations, not excuses
- Don't try to fix everything before the initial response

In Summary:

Remediation:

- Choose your level of involvement (if you can)
- Make changes globally
- Don't tell the FDA you're ready until you have verified.

Thank you!

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