Assuring a Successful Inspection

How to Effectively Deal with Challenging Inspectional Issues

VICKY STOAKES, INTEGRX
DAVID CHESNEY, PAREXEL CONSULTING
ELAINE MESSA, NSF HEALTH SCIENCES CONSULTING
STEVEN NIEDELMAN, KING & SPALDING LLP

What is an Inspection?

A careful, critical, official examination of a facility to determine its *compliance with laws*.

Inspections may be used to *obtain evidence* to support *legal actions* when violations are found.

(Source: FDA Investigations Operations Manual)

What is a Successful Inspection?

- The investigator has been provided with ***correct information*.**
- The investigator has no erroneous perspectives or conclusions.
- The investigator understands the context of any adverse findings, and the company understands the findings
- The company's operations have been represented as positively as the ***truth*** allows.
- Interviewers have established a ***professional*** and ***respectful*** relationship with the investigator.
- The inspected firm has successfully demonstrated its ***responsiveness*** and ***commitment*** to a robust quality system.

FDA's Inspectional Authority

21 USC 374 (Section 704 of the FD&C Act)

Upon presentation of credentials and Notice of Inspection (FDA-482) - FDA has authority to:

- Conduct inspections without an inspection warrant.
- Inspect, ***at reasonable times*** (this would include any time the facility is in operation), and ***within reasonable limits, and in a reasonable manner*** any factory, warehouse, or establishment in which devices are manufactured, processed, packed, or held for introduction into interstate commerce or after introduction into interstate commerce.

The term "reasonable" is not defined!

FDA's Expectations

- FDA expects:
  - Investigators to conduct inspections in a reasonable manner
  - Industry to welcome the investigator professionally and do all they can to facilitate an efficient inspection
  - Minimal delays to occur at the beginning of unannounced inspections; no delays for pre-announced inspections
  - Investigators to conduct efficient inspections with as little disruption to operations as possible

FDA Expectations (con't.)

- FDA expects:
  - Information to be provided to investigators as swiftly as possible without delay; if you don't know the answer state so – get the right person who does know
  - Records and copies thereof to be provided in a timely manner
  - Parties being inspected to be nervous and anxious (it's Ok – the investigator is as well!)
  - Access to all locations and records related to the manufacturing process – which means every step of the way (no secret or hidden rooms)

FDA Expectations (con't.)

- FDA expects:
  - Courtesy and respect to be shown by all parties
  - Investigators to openly communicate the scope of the inspection, and share findings at least daily
  - Contentious issues may arise and there be an open dialogue to avoid misunderstandings
  - Industry to have procedures in place for inspections/audits
  - There will be a "war room" or "backroom" providing inspectional support

Inspectional Issue # 1

A computer system application with a back-end database is used to perform a regulated activity

- How would you handle:
  - Request to present the “live” system during the Inspection
  - Requests for custom ad-hoc queries
  - Request for e-copy of the database, in whole or in part

Inspectional Issue # 2

Investigator requests to review and obtain copies of company audit reports

- Does the FDA have authority to have access?
  - How would you handle such a request during an inspection?
  - Is there a distinction between internal audits and third party audits?
  - What strategies would you use to respond to the request?

Inspectional Issue # 3

How would your firm handle:

- Collection of Documentary Samples
- Affidavit issuance
- Office of Criminal Investigation participation
- Seizure by the US Marshall

Inspectional Issue # 4

FDA issued *Guidance for Industry: Circumstances that Constitute Delaying, Denying, Limiting, or Refusing a Drug Inspection*, dated 10/2014

- How would your firm address questions raised during an inspection about
  - Delay in scheduling a pre-announced inspection
  - Delay in producing records
  - Limiting photography
  - Limiting facility access

Inspectional Issue # 5

The Investigator asks "Are you refusing me permission to [enter that area]/[see that record]/[take a photograph]/other request"

- How would you best respond?
- If you refuse access, what options does FDA have?
- How can this conflict be best avoided?

Inspectional Issue # 6

- **Your inspection host suggests using a system of verbal and hand signal "prompts" to cue interviewees when they are "volunteering too much information"**
  - Good idea? Why?
  - Bad idea? Why?

Inspectional Issue # 7

FDA Investigators arrive at your manufacturing facility after public access hours. Upper management is not present at your facility. They issue a Notice of Inspection (FDA-482) to the only Manager who will speak to them and they insist on immediate admittance to the production area.

How does your firm handle this situation?

- Is FDA within its rights?
- What do you do?

Inspectional Issue # 8

How does your firm prepare for an inspection? Are you always "*inspection ready*"?

- Are there documents that should be readily available in advance of an inspection?
  - If so, which?
- Does everyone know who shall attend the opening meeting ?
  - Is it a good idea to have Senior Management present?
- Do you have an inspection/audit SOP?
  - What logistical information does it provide to ensure an efficient inspection?

Inspection Issue # 9

During an inspection, how would your firm handle Investigator Requests that are "off the mark", such as:

- Investigator presents (on blank paper) a list of documents received by the investigator & requests the company to sign the list
- Lead Investigator and other Investigator are clearly not in agreement; seen arguing in the parking lot
- Investigator says, "*No electronic communication with the backroom or he/she will not be able to be "up-front"* with the firm

Inspectional Issue # 10

How would you handle unusual requests or questionable investigator behavior?

- What steps should you take to address behavior issues?
- How do you distinguish between behavior issues and personality differences?
- At what point during the inspection would you raise unreasonable requests or unacceptable behavior?
  - Would you do outside the response to any FDA-483 or Warning Letter?

In Summary…

- A successful inspection has a positive impact on your business activities – a poor outcome can be very disruptive, costly and affect your firm's reputation and brand loyalty
- For those findings that are easily corrected, take the necessary action to correct them while the inspection is ongoing – and whenever possible, have the investigator verify the corrective action was completed
- Three most important words to remember and implement – Document! Document! Document!. In FDA's eyes if it isn't documented – it didn't happen
- Conduct mock audits of the overall process from the receptionist who will greet FDA, to the CEO, and the SME's. Test the backroom, and assure IT support stands ready.
  - Make sure your opening presentation is current – as well as all organizational charts
  - Ensure everyone knows their roles – and especially those in the backroom whose roles are critical to the outcome of a successful inspection

Questions?

THANK YOU!