PHARMACEUTICAL ONLINE

Guest Column | July 29, 2019

How To Prepare For An FDA Inspection

By Mark Durivage, Quality Systems Compliance LLC

Every organization that is regulated by the FDA must be ready at all times for a potential inspection. An FDA inspection is very different than an ISO certification or surveillance audit. Too often I see organizations "prepare" for scheduled ISO audits by playing catch-up on activities that have been neglected or otherwise overlooked. The catch-up strategy will be problematic for FDA inspections and will generally result in inspectional observations.

Why The FDA Conducts Inspections

The FDA conducts inspections for a variety of reasons, but the primary reason is to support its mission to "protect the public health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices; and by ensuring the safety of our nation's food supply, cosmetics, and products that emit radiation."

The FDA defines an establishment inspection as a careful, critical, official examination of a facility to determine its compliance with the laws and regulations administered by FDA.

The FDA uses establishment inspections to collect evidence to document violations, support regulatory actions, or to obtain information on new technologies, good commercial practices, or data for establishing standards or regulations.

Types Of Inspections

There are four types of FDA establishment inspections: pre-approval inspections, routine inspections, compliance follow-up inspections, and for-cause inspections.

Pre-approval inspections are conducted when an organization makes a submission to the FDA requesting to market a new product. The purpose of a pre-approval inspection is to verify the data included on the application and to confirm the facility is suitable for manufacturing the product.

Routine inspections are mandated by law and use a risk-based approach to determine inspection frequency. Organizations should conduct operations as though an inspection might be initiated on any given day, thus always are prepared and ready for an inspection.

Compliance follow-up inspections are used if the organization was issued significant 483 observations or other enforcement actions including warning letters or injunctions during a previous inspection. The FDA will inspect and verify the actions taken in response to those observations. The FDA is confirming the organization has responded adequately and corrected any previous violations. If the follow-up inspection reveals that the organization has not responded appropriately, the FDA will document current violations and may use the additional violations as evidence to support future regulatory actions.

For-cause inspections occur when consumers or employees report an issue to the FDA. Additionally, for-cause inspections can be triggered by reportable events that may have caused significant harm, death, or a product recall.

FDA Forms

There are three basic forms used by the FDA during an inspection: Form 482 (notice of inspection), Form 483 (inspectional observations, and Form 483 (inspectional observations).

When the FDA begins an inspection, a ***Form 482*** (notice of inspection) will be presented, along with contact information in the event a 483 response is issued. The 482 explains the agency's inspectional authority and provides expectations for the inspector and the firm. The 482 is issued to the organization's top management official or the most responsible person at the site at the time of the inspection.

The ***Form 483*** (inspectional observations) lists observations made by the FDA representative(s) during the inspection. These observations do not represent a final agency determination regarding compliance. The 483 formally notifies the organization's top management of objectionable conditions or practices relating to violations of the Federal Food, Drug, and Cosmetic (FD&C) Act that were observed during the inspection.

The ***Form 484*** (receipt for samples) is issued at the end of an inspection describing any samples obtained during the inspection. The 484 is given to the same individual who received the FDA 482.

During The Inspection

How your organization initially presents itself when the FDA arrives will generally set the tone for the inspection. Organization and confidence will project a favorable impression with the inspector(s). Upon their arrival, escort them to the "front roo" — usually a designated conference room where your organization's management representative will directly interact with the inspector(s). In addition to the management representative, your organization should have a "scribe" who will take minutes during the inspection and record all requests for documents and records requested by the inspector(s). Records of management reviews, internal audits, supplier evaluations, and financial data are considered confidential and generally not subject to FDA review.

At the beginning of the inspection, ask the inspector(s) if they would like an overview presentation of your organization. This is a great opportunity to show off your organization's competence and provide an overview of how the organization and its quality management system (QMS) is structured.

When the FDA inspector(s) requests documents or records, record the request in a log and forward it to your designated "back room" to complete the request. The back room is a second conference room or office where document and record requests are compiled and reviewed prior to submission to the front room. Best practice is to make three copies of each request — one for the official company record, one for the management representative, and the third for the FDA inspector(s). Each document and/or record should be stamped or watermarked **CONFIDENTIAL**. Once the back room has prepared the request, a "runner" will take documents or records and hand them directly to the management representative. The runner should never to hand anything directly to the FDA inspector(s); this provides the management representative a brief opportunity to review the documents and possible comment before handing them to the FDA inspector (s), potentially avoiding an embarrassing situation. If there is an issue with the documents or records being requested, the back room should inform the management representative

of the issue. The management representative should never be surprised. The scribe should make note of any records brought into the front room and if the FDA inspector(s) intends to take the documents with them.

When the inspector(s) requests a tour of the facility, the management representative and scribe should always accompany them. The scribe should record what is being reviewed and the individuals being interviewed. If the inspector(s) requests to take photographs, ensure management representative or scribe take similar photographs.

If the FDA inspector(s) requests to enter cleanrooms or other controlled environments, provide the training necessary to prevent microbiological contamination, including proper gowning requirements and techniques.

FDA inspectors are not required to sign your organizational documents, including:

1. Waivers exempting the organization from any responsibility or liability should an accident occur

2. Form letters concerning access to confidential information your organization does not want released

3. Training forms acknowledging training on personnel gowning procedures

4. Information/data requests

The only document that FDA inspectors are authorized to sign are sign-in and sign-out forms (paper or electronic) to comply with security measures, including documenting the removal/replacement of seals to inspect vehicles and containers.

Under normal circumstances, recording devices will not be used while conducting inspections. However, some organizations record and/or videotape the inspection and/or the discussion with management portion of the inspection. The FDA does not object to recording and/or videotaping; however, in such cases the FDA will also record the discussion to assure accuracy of the FDA records.

It should go without saying that you should always be truthful during an inspection. Also, ensure you fully understand any questions/requests the inspector(s) make, and remember it is OK to tell them you need to speak with a subject matter expert (SME) before providing a response.

The Keys To Inspection Preparation

The key to being ready for an FDA inspection is really simple:

1. Always instill a culture of compliance within your organization
2. Develop and document an external regulatory inspection procedure
3. Appoint a deputy management representative
4. Regularly practice mock inspections

Conclusion

Many firms are unprepared to manage an FDA inspection or to effectively respond to 483 observations. Perform mock FDA inspections annually and live each day as if the FDA was going to show up and begin an inspection. The approaches presented in this article should be used and are based upon industry practice, guidance documents, and regulatory requirements.

References:

1. *Investigations Operations Manual 2018*, https://www.fda.gov/downloads/ICECI/Inspections/IOM/UCM150576.pdf
2. "What Should You Do After An FDA Inspection?" March 2019, Life Science Connect https://www.pharmaceuticalonline.com/doc/what-should-you-do-after-an-fda-inspection-0001

About the Author:

Mark Allen Durivage has worked as a practitioner, educator, consultant, and author. He is managing principal consultant at Quality Systems Compliance LLC, an ASQ Fellow, and an SRE Fellow. He earned a BAS in computer aided machining from Siena Heights University and an MS in quality management from Eastern Michigan University. He holds several certifications including CRE, CQE, CQA, CSQP, CSSBB, RAC (Global), and CTBS. He has written several books available through ASQ Quality Press, published articles in *Quality Progress*, and is a frequent contributor to Life Science Connect. Durivage resides in Lambertville, Michigan. Please feel free to email him at mark.durivage@qscompliance.com with any questions or comments, or connect with him on LinkedIn.