

How to Manage an FDA Inspection

Ensuring the success of an FDA inspection can be a complex goal, even with an effective quality system. Attitude and preparedness can also affect the inspection.

By Mary Armstrong

For everyone involved, FDA inspections are time-consuming and labor-intensive processes, but they needn't be frustrating or mysterious if a company has prepared properly.

The most important preparation is complying with the pertinent laws and regulations, including developing safe and effective products and implementing an effective quality system. Although compliance is necessary to a good outcome, knowledge of the inspection process and preparation of key players can reduce anxiety and limit missteps associated with inspections.

This article serves as a guideline to help you prepare for an inspection, anticipate what FDA may be planning to do, and develop a procedure for handling FDA inspections.

Defining Roles

For large companies, there are numerous roles to be defined when getting ready for FDA. But in any company, a minimum of five roles must be delineated ahead of an inspection. In small companies, one person may hold several of these roles.

For any particular facility, there is a most responsible person. This is not a role that is chosen by the inspection team, but rather is defined by the hierarchy of the company. The *most responsible person* is the individual with the most accountability for the operations of the facility. In addition, the most responsible person is legally answerable to ensure that the facility is in compliance. Typical titles of the most responsible person are president, CEO, COO, general manager, or plant manager. The critical functions of this role are to provide leadership and to communicate to



FDA that the company intends to comply with all laws and regulations.

Another role, one that must be chosen by the inspection team, is the FDA escort. This role is key to the success of an inspection. The escort should be familiar with the everyday operation of the facility, know who will have the answers to FDA's questions, understand FDA's legal authority, and understand the company's policies regarding specific situations (such as signing affidavits). The escort should be prepared to accompany the investigator at all times. The escort's job includes meeting the inspector's needs, guiding the inspector to appropriate subject matter experts, and communicating internally how the inspection is progressing.

When FDA asks for something that the company is not prepared to provide, it is best to have defined ahead of time a person who can explain the company's policy on such matters. An example of an FDA request that is often denied is the reading and signing of affidavits by com-

pany personnel. Explaining a denial is best done by a person who has high ranking in the organization, but is not the most responsible person nor the FDA escort. Naturally, any denial of an FDA request should be reviewed ahead of time by legal counsel and is easiest to handle if the company's policy is contained in a written procedure.

In addition, one or more subject matter experts (SMEs) should be defined. These are the specific individuals who will be called upon to answer FDA questions. A list of all SMEs with their areas of expertise and authority should be created and updated as personnel change. Each expert must understand the expectations associated with participation and availability during an FDA inspection. Role-playing before the FDA inspection is helpful to prepare SMEs for the types of questions they are likely to be asked. Preparing SMEs and ensuring the list of SMEs is accurate are some of the most highly leveraged preparation activities a company can undertake.

It will also be necessary to have one or more designated FDA runners. Among other tasks, runners locate documents, find SMEs and tell them when to appear, and notify department managers if FDA is entering their areas. It is not hard to sell the role of FDA runner when the chosen persons understand they will be in the know about the FDA inspection.

Preannouncement of Inspections

FDA inspections can occur with or without prior notice. Both the length and the frequency of inspections are at the discretion of FDA. However, FDA will usually contact your company to set up a routine inspection if your company's last inspection was nonviolative. FDA will

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also generally contact you before conducting a preapproval inspection for a premarket approval (PMA) application. FDA will not contact a firm to preannounce an inspection when the firm has had a prior violative inspection, such as one resulting in a warning letter or other action.

When FDA contacts your company to notify it of an upcoming visit, understand that the start time of the inspection is not a negotiation point. However, you should let FDA know whether there is some extraordinary event about to occur, such as an all-day meeting that will have the entire management team off-site. FDA might then decide to change its plans, but be aware that it might not.

FDA may ask for the company's quality manual before the start of the inspection so the investigator can prepare. Such requests are normally granted, even though the Notice of Inspection (FDA-482) has not yet been given to the company.

FDA's Arrival

The receptionist is the first point of contact the investigator has with your firm. Make sure the receptionist is prepared for the inspector's arrival. When the investigator arrives at the facility, the receptionist should notify the most responsible person and the FDA escort. The investigator should be asked to wait in the reception area until the escort arrives.

In all cases, the receptionist should be briefed and should:

- Know whom to notify in priority order (most responsible person, or next-most responsible person if someone is out, etc.).
- Know who the FDA escort is and how to alert the escort to FDA's presence.
- Ask, but not insist, that the investigator sign the visitors' log.

- Ask the investigator to wear a visitor badge, assuming one is worn by other visitors to the company.

Meeting with the Most Responsible Person

Upon meeting the most responsible person, FDA inspectors must show their credentials. Credentials look something like a driver's license and include a name and number to identify the investigator. Investigators may also show an FDA badge. Some investigators are officers of the Public Health Service and may be in uniform.

At the meeting with the most responsible person, FDA issues a Notice of Inspection (also called an FDA-482). The investigator will state the purpose of the visit. The most common reasons for a visit are for-cause, pre-PMA, or routine inspection using the quality system inspection technique (QSIT). In turn, the most responsible person should introduce the investigator to the escort, express the company's desire to cooperate with the inspection, and ask to be alerted if there are any issues the investigator wants to discuss.

The most responsible person should also ask whether FDA will meet at the end of each day and review findings. If such a meeting is not possible or is impractical, it is appropriate to ask to be briefed if FDA finds anything significant. FDA may decline both of these requests; however, when the most responsible person displays an interest in the progress of the inspection, it signals an interest in rectifying any possible deficiencies.

It is also important for the most responsible person to ask that the closeout of the inspection be at a time when he or she is available. At this point, the investigator is forming an opinion of the company and its leadership. This is the company's first and most opportune moment to make a good impression.

The Tour

FDA generally asks for a quick tour of the facility first. Although it may seem premature to the company for FDA to jump right into the inspection, this is an important task for the investigator. Make sure that someone familiar with giving plant tours is available to lead the investigator and FDA escort on the tour. Guard against including too many people in this tour. A cast of thousands hinders the main objective, which is to move through the plant efficiently. Answer FDA's questions as they come up during the tour, but table questions for later discussion if they require a longer explanation or if the SME is not available. Be sure the investigator understands that he or she can come back to any area as necessary when the SME is available.

Dealing with Logistics

If possible, get a conference room or office for the entire time FDA will be present at the facility. Alert all who should know of FDA's presence, both internal personnel and external contacts. External personnel to notify may include a regulatory lawyer or the company's board members.

Once the tour is concluded, it is a good idea to take the inspector to the designated meeting room to go over logistics. For the company's part, you'll want to ensure that the investigator understands the company's business hours, when manufacturing or other operations of interest are occurring, times for shift changes, and whether lunch is available to the investigator at the facility or close by.

The investigator may tell you what he or she plans to do next or for the next day or two. If the investigator isn't providing specifics, ask. Some investigators will share their thoughts and plans and others won't, but it is appropriate to get as much detail as you can up front in an effort to

ANSWERING QUESTIONS AND OTHER INSPECTION TIPS

alert SMEs and others responsible that they may be called on to answer questions or provide documentation.

Inspection Process: What to Expect

If the inspection is routine, it will follow the QSIT program. If it is a preapproval inspection for a PMA device, there is a compliance program for this type of inspection. FDA's procedures for these types of inspections are available on its Web site and should be familiar to the FDA escort. If FDA is there for the purpose of following up on a warning letter, then the direction of the inspection should generally be clear. The investigator will be looking for evidence of the company's compliance with a plan of action made in the response to the warning letter.

For-cause inspections are the most unscripted from the company's perspective. The investigator may have specific directions for the inspection that are not publicly available. You may ask to see these instructions, but the investigator may or may not be willing to share them. Obviously, the more you can anticipate what the investigator is going to ask for, the better you'll be able to answer questions in a timely fashion.

There are several tips that can help a company get through an inspection process. See the sidebar: "Answering Questions and Other Inspection Tips" for more information on significant dos and don'ts associated with the inspection process.

Closeout Meeting

The investigator will request a meeting to close the inspection. At the meeting, FDA should provide a written list of significant observations on a form called the FDA-483. FDA may also orally detail less-significant observations during the meeting. This meeting is crucial and should be attended by the most responsible person (or the person next in the chain of command), the FDA escort, and those responsible for taking corrective actions.

The investigator will discuss each of the objectionable conditions observed and provide the company an opportunity to agree or disagree. The investigator will take notes, including what is said and who says it.

Always tell the truth. This statement needs to be a part of your procedure for inspections, and anyone answering FDA's questions needs to be trained on the procedure.

Don't offer more than asked. Think first before answering a question to be sure you understand it and know how you're going to answer. If you're not sure what is being asked, clarify with the investigator. If the FDA investigator doesn't respond, just wait until he or she does. If the investigator doesn't comment after you're done answering a question, wait for a comment. The normal rules of social interaction don't apply during an inspection. Frequently, an investigator will allow an uncomfortable pause during questioning to try to prompt you to talk more. Don't take the bait.

Clarify what is being asked. If you don't understand what was asked, clarify the meaning or purpose of the question. If the question seems overly broad, ask for specifics. Most importantly, if the implication of the question seems wrong, clarify the context of the question or the reason for it.

Try to limit fishing expeditions. FDA often asks broad questions. Try to narrow the scope of the response. For example, if the investigator says, "I'd like to see your complaint file," you could respond, "For what year?" or "For what product?" or, "Are you looking for a particular type of complaint?" Responding with a question helps your situation in two ways. First, you show you want to assist FDA in looking at complaint files. Second, the investigator cannot respond with a yes or no answer. Keep in mind that the investigator has the right to ask for all the files, but more often than not, a question will help refine the request.

If you do not know the answer to a question, say so. It is all right not to know the answer. The best response is to find the person who does know the answer or to find the answer, if it's appropriate for you to do so.

Refer to written procedures as you are answering questions. Rather than looking like you don't know what you're supposed to do, referring to procedures shows that you use them on a daily basis as you go about your work. When you don't refer to them, it can send a message that they're unimportant and are seldom used.

Don't argue, but rather, discuss. On the same note, don't be afraid to question the investigator. If you are the subject matter expert or the person responsible for a department, explain your company's procedures and practices without apology. If the investigator finds fault with your company's procedures, ask for an explanation of the concern to be sure you understand it.

Ask the investigator whether he or she sees anything of concern. FDA may or may not answer. Understand that the investigators are human. Some will share what they're thinking and others won't.

If FDA asks for a copy of something, make a duplicate copy for the inspection file. It's usually easiest to keep copies filed by the date they were provided. Don't destroy the inspection file when the inspection is over. Your record retention policy should dictate how long the inspection file is kept.

If FDA takes a physical sample, take a duplicate physical sample. Although it is not common during medical device inspections, be prepared if FDA does take a sample.

If the investigator is willing to do a daily debrief, take advantage of it. During a debriefing, make sure you understand what the investigator is observing. If you think the investigator has misunderstood something, offer to provide additional information or explanation. If the company has decided that a corrective action is necessary based on what the investigator has found, let the investigator know that the company agrees and is planning corrective action.

For each written observation, make sure you understand the observation. If you don't, ask for clarification. If you agree with the observation, and a corrective action has been determined, explain what will be done. If you agree with the observation, but don't know what the correction will be yet, say so. If you don't agree with the observation, explain your concern and discuss it with the investigator.

- Don't promise to make a correction if you don't agree with the observation.
- Don't promise a specific correction if you're not positive you will be able to follow through.
- Do display a willingness to correct problems.

For each oral observation, make sure you understand it and have an employee write it down so it can be considered for corrective action after the meeting is over.

Promise to respond to the 483 in writing to the district office, and ask the investigator for any other comments or suggestions.

Written Responses

Respond to the 483 as soon as possible, preferably within five working days. Include a short cover letter emphasizing the company's intent to com-

ply with the law and regulations. Cite each written observation followed by the company's response. If the firm agrees with the observation as written, explain how and when it will correct the problem. If it doesn't agree, explain why and ask for a meeting with the FDA district office to discuss the issue. If a corrective action is complete and you can supply evidence of completion, do so.

Devising a Written Procedure to Manage Inspections*

It is advisable to formulate a written procedure detailing how to manage inspections. Preparing a procedure and training on it ensures consistency throughout your organization in managing inspections and representing the company.

As you develop your company's procedure regarding inspections, include in its scope that your company intends to fully comply with regulations and cooperate with regulatory agency representatives. As you train on this procedure, make sure employees understand that they are expected to act in a professional, courteous manner; be honest in their responses; and answer questions to the best of their ability. A written procedure is a good place to define and detail the roles mentioned in this article,

how the inspection will be conducted from a company perspective, and how the results of the inspection will be handled: It may be an appropriate place to describe company policy with respect to photography, signing affidavits, or other issues that may be of concern.

Conclusion

Inspections are by their nature difficult and stressful processes. The more prepared you are, the less intimidating they may seem. If a company has done its best by the time of the inspection, it can be proud and confident in its quality system and take any FDA observations as opportunities to mend deficiencies and produce better, safer products.

About the Author

Mary Armstrong is a Senior Regulatory & Quality Consultant at Reglera Inc. Prior to this, as a biomedical engineer at FDA, Ms. Armstrong performed inspections of medical device manufacturers.

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GMP Labeling®, Inc.

525 West Remington Drive
Sunnyvale, CA 94087

Phone **800-637-4487**
408-522-3200
Fax 408-522-3212
E-mail sales@gmplabeling.com
Web www.gmplabeling.com

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