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When an FDA inspection is imminent, it pays to have a plan. Start by getting your paper in order and your facility in a state of good repair. Train a team to manage interaction with inspectors. Coach your employees on how to answer questions. And don't forget to take notes.

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# Survival Guide to FDA Inspections

## Part 2, Conducting the Audit — Ready or Not, Here They Come

*It's late Friday afternoon, and you just got off the phone with FDA's district office. An FDA inspection in a few short weeks chases all other thoughts from your mind, which races with questions: "Are we prepared for an inspection? We need to create a project plan and to identify the right people to help; isn't the QA manager out of the country? A few weeks isn't enough time! What should we do?"*

An FDA inspection can be a nightmare that costs your company money, time, and reputation, or it can be an opportunity to understand the logic behind FDA regulations and to prepare accordingly. This article series reminds proactive managers of the preparation needed for inspections — whether those inspections are from FDA, a client, an investor, or a European agency. The first article in the series recommended that, before an inspection, companies examine their standard operating procedures (SOPs), monitoring systems, validation programs, and batch record management to ensure that they meet appropriate guidelines (1). If the guidance in Part 1 of the "Survival Guide" has been followed, your company has:

- invested the necessary resources toward understanding deviations and finding corrective actions to prevent them in the future,
- established change controls and documentation practices that are carefully followed so that your company can respond to any type of problem,
- and provided up-to-date training with training records in order, particularly for those functional units and those individuals who have been responsible for deviations, exceptions, or errors.

In this part of the series, we discuss what to do when notified by FDA that an inspection is imminent. Our purpose is to outline the common issues that companies

encounter during FDA inspections and to discuss how best to prepare your company for its response (2,3).

### One Month Before

FDA has just called to say that they will be conducting an audit of your facility within the next month. Before you panic, remember that there is still time to prepare for the inspectors' arrival and to ensure that everything is running smoothly. At this point, you don't have time to design or implement major initiatives. The goal is to put everything in its place.

Remember that some inspections are unannounced. So you must have your organization and plans in place, anticipating that an inspection might start at any time.

**Review previous inspections.** The first step is to take a close look at results from previous inspections. This is often where inspectors begin their investigations. Determine what commitments your company previously made from a corrective action perspective and whether or not those commitments have been addressed properly. If all commitments have been met, make sure the appropriate documentation is complete because inspectors may want to view the progress that has been made to date.

If previous commitments remain unaddressed, determine why, and identify what documentation has been completed. Create a new action plan providing details on how the company is addressing the issue and listing an anticipated deadline for resolution.

**Complete open items.** Next, complete any open item (activities that have been started but are not yet complete) documents and investigations. Determine which documents or activities need minor adjustments or approval signatures only. Those items must be approved and closed. Remember, if a document or investigation is incomplete, it is considered nonexistent and can be one reason for a citation.

**Institute an operation plan for the inspection.** An operation plan is an audit guide needed by every pharmaceutical and biotechnology company. Operation guides are the crucial — maybe the most crucial — method for ensuring that your company is prepared to respond to any issues raised by inspectors.

Preparing a list of internal contacts is the first action item in the operation plan (see the “Sample Contact List” box). The list should identify the person who is most knowledgeable in particular business areas or about particular projects (for example, the individual responsible for training programs or the person managing validation projects). For instance, if a new system has been validated and placed in service recently, identify the key individual or project manager on that system. Or if there has been an investigation because of a failure, identify the key person who followed through on that investigation and the person who prepared the appropriate documentation.

Once a complete list of internal contacts has been created, have each individual contact prepare a list of people they worked with who were responsible for specific project details. If a new system has been

implemented, the individual contact list would identify the project engineer, the QA person, and the validation person who implemented the project; or an investigation into a failure would identify the area manager for the unit in which the failure occurred, the QA individual who approved the plan of action, and any other staff who had either direct or indirect interaction with those activities. Substitutes should also be identified because some people may be unavailable on short notice.

Next, make sure that each person is alerted that an inspection is being conducted and that they may be needed to respond to questions. List and verify all contact information including work, home, cell, and pager numbers. Email addresses are also helpful. Request that those individuals identified outline their areas of responsibility, review the relevant documents, and remember major events such as lost batches or emergency shutdowns. If any documents are stored at an off-site facility (such as a corporate office or a storage center), transfer them or alert the other facility to have them available for quick access. The individual contacts must

be trained to handle an interview with an inspector. They should be instructed on what to say and how to say it. If two or more people were involved in resolving an issue or worked together on a particular project, interview them to make sure their stories coordinate with one another.

**Prepare work environments.** With any FDA inspection, two rooms need to be designated for the audit. The first room is the *inspectors’ room*, in which the inspectors conduct the audit. Make sure that room is clean and has general office supplies, a phone, coffee, access to a rest room, and a place for the inspectors to take a break. The room should be comfortable, but don’t go overboard providing amenities. Inspectors are not allowed to accept gifts. When selecting the location for the inspectors’ room, don’t choose one too close to the manufacturing facilities. That will help prevent interruption of day-to-day activities and operations. Inspections can be interruptions, but employees should be encouraged to continue to be productive.

The second room is often referred to as the *war room*. The war room is typically an assigned area beside or across from the

## Sample Contact List

Part of the Operation Plan is a list of key contacts. Here is a sample list of the information that should be available for contacts regarding the water systems.

Water System Contacts							
	Name	Phone	Email	Cell Phone	Home Phone	Personal Contact	Vacation Schedule
<b>Engineering contact</b>							
Back-up contact							
<b>Maintenance contact</b>							
Back-up contact							
<b>Validation contact</b>							
Back-up contact							
<b>Quality control contact</b>							
Back-up contact							
<b>Regulatory contact</b>							
Back-up contact							

**Inspection Request Form**

For every request that an inspector makes, the inspection reporter completes a form like the one below. As an inspector's request is met, each item requested is checked.

**Inspection Request Form**

**Date:** \_\_\_\_\_

**Reporter name:** \_\_\_\_\_

**Inspector name/ID number:** \_\_\_\_\_

**Subject:** \_\_\_\_\_

**Requests:**

**Item 1:** \_\_\_\_\_

**Item 2:** \_\_\_\_\_

**Item 3:** \_\_\_\_\_

**All requests complete**

**Print Name:** \_\_\_\_\_

**Signature:** \_\_\_\_\_

**Date:** \_\_\_\_\_

**Note: Check  when complete**

inspectors' room. The war room is a staging area in which employees can respond to the inspectors' requests for information quickly and effectively. The purpose of this room is also to control traffic into and out of the inspectors' room. Anyone going into the inspectors' room must first pass through the war room. It should be equipped with the same supplies as the inspectors' room with the addition of a copy machine, computer equipment, and a printer.

**Identify and train key personnel.** Three roles are necessary to guarantee an inspection runs smoothly. We will call them the *war room commander*, the *war room clerk*, and the *inspection reporter*.

*The war room commander* is responsible for overseeing all activities in the war room. At any one time, there can be several different requests (for documentation or to speak with different employees, for instance). It is the sole responsibility of the war room commander to contact employees and to collect documentation in response to those requests. When employees arrive in the war room, the commander reviews their documentation and provides last minute coaching on the types of information that the inspector will be asking for.

*War room clerks* are responsible for assisting war commanders with their duties. War room clerks are typically administrative support personnel. It is their responsibility to make copies and track all documents

entering the inspection room. They also conduct other general administrative tasks such as answering the phone and maintaining a meeting calendar to ensure all necessary personnel are available for sessions with the inspectors. Depending on the size of the company, there might be one or more war room clerks assisting with an inspection.

*The inspection reporter* is essentially an observer and a note taker. The reporter is responsible for recording everything that is said and requested by the inspectors. As the reporter records information, requests are relayed to the war room. Depending on the size of the inspection and the number of inspectors present, there can be many requests made each day. A good rule of thumb is one reporter for each inspector.

These three necessary roles ensure an accurate and efficient response to inspector requests. Remember, one thing an inspector is measuring is how quickly and thoroughly the audited company responds. Inspectors document everything, and they do not forget that a requested document or person was not supplied by the time the audit concluded.

**Preparing inspection documentation.** Everything that occurs during an inspection should be documented. Invest some time in preparing forms to make the process easier. Once those forms have been created, they can be reused during future inspections.

A *request form* is the primary form that should be created for an inspection (see the "Inspection Request Form" box). Request forms keep track of what an inspector is requesting, when it was requested, who was contacted, and what documents or items were inspected. The inspection reporter is typically the person who initiates the form. The form can be preprinted, emailed, or printed out and is usually sent to the war room. In the war room, the war room commander and clerks complete the request.

**Remember to clean.** Clean offices and work environments are a simple way of making a good impression. Employees should be informed of an inspection and instructed to straighten their offices and organize their files. They need to make sure nothing is left in the open that could cause an issue for inspectors. The sidebar, "Preparing the Manufacturing Area for an Inspection," has further details.

## During the Inspection

An inspection can be stressful. Before an employee meets with an inspector, there are some dos and don'ts to make sure that the inspection runs smoothly.

**Do not panic.** Be responsive and courteous. Act professionally and provide the courtesy that should be offered to any visitor. Focus on answering inspector questions and on presenting the facts.

**Listen carefully** to what you are asked, and respond directly to the question. If the inspector's question is unclear or could be interpreted in different ways, ask for clarification. It is okay to repeat questions back to the inspector. For example, "Do I understand you correctly? You want to see the SOP for cleaning a test tube."

**Do not guess.** If you don't know something or are unsure of the answer to a question, say so; don't guess. It is perfectly fine to ask the inspector for more time to review the details surrounding the question. The reporter will make a note and keep track of what details still need to be communicated. Moreover, there may be other people who can more appropriately respond to the question. In that situation just say, "Please give us some time to contact the right person for you to talk to, and we will get back to you on your request." The reporter again makes a note and informs the war room to contact the right person to address the need. This is why creating an operation plan and identifying the right people is so crucial.

**Do not be confrontational.** When an inspector asks a question, the employee answering needs to keep a level head. If the question feels threatening or accusatory, try to reword it. For instance, an inspector might ask, "Why did you write this SOP?" Turn that question around and ask, "So, you want to know why the company's policies dictate that this SOP be written like this?" Turning the question around to reflect a neutral perspective can often alleviate tension and help return focus to the issue. Stick to the facts, and do not allow emotions to come into play: In this situation, they can have negative results.

**Do not play games.** Sometimes, when staff do not know the answer or are unsure of an answer, they begin to play games with the inspector. They might try to confuse the inspector by responding to something that has not been asked or by providing

## Preparing the Manufacturing Area for an Inspection

Clean offices and manufacturing facilities are a simple way to make a good impression. Inform employees of the inspection, and ensure the following tasks are implemented.

**Start with visual inspection.** Pay special attention to gowning rooms, supplies, and personnel behaviors. This is an excellent opportunity to provide training courses to refresh employees' skills.

**Label everything.** Make sure that equipment and signs, displayed properly, identify the manufacturing equipment and operational processes.

**Remove all items or equipment that are out of service.** If it is impossible to remove items, make sure an "out-of-service" sign is displayed.

**Repair damaged areas.** There should be no cracks on the walls or floors. Take time to repair and paint damaged areas and to clean the facilities.

information that is not relevant. Inspectors become suspicious about staff that try to mislead them, and they may begin to think that the company is trying to hide something. In a situation like this, it is best to respond by saying, "Let me get back to you on that," or "I need more time to review the details."

**Respond quickly and accurately.** Because inspectors keep track of what they ask for, the efficiency and effectiveness of the inspection reporter and of the war room personnel can ensure that order is brought to the inspection. A quick and accurate response to an inspector query can leave a favorable impression. Have validation protocols, reports, batch records, SOPs, and other documents available. Pay special attention to documentation relating to deviations, changes, rejected batches, failed tests, and to decision-making processes (such as R&D reports and memos). Inspect file rooms, and make sure they are in order. Locate missing or borrowed documents, and temporarily limit document removal from the file room.

**Provide documentation.** The inspectors should be provided with the requested documents only. In the war room, review documents to make sure information is complete and accurate. Also, remove from the document given to the inspectors any miscellaneous items like Post-It notes, hand-written comments, or extra pages.

Make two copies of each document you intend to submit to the inspectors. Mark each set "copy," and keep the originals nearby until they can be filed and stored properly. One set of documents should be

kept in the war room, and the other set should be given to the inspector. This way, the company has an accurate record of what they provided to the inspectors.

**Work with FDA.** Too many companies view FDA as a threat. Working with FDA and not against it gives companies an advantage. Treat inspectors as human beings, instead of the enemy. Taking these steps makes the inspection easier for both organizations.

Although no one has a crystal ball and can anticipate any and all requests or issues that might arise during an inspection, being prepared and organized can make your experience a positive one. Hopefully, this article shows that you can organize your interaction with the agency when they are on your site using the same methodical approach you take to the rest of your daily activities. The last article in this "Survival" series discusses how to prepare follow-up documentation after the inspectors have left. It is designed to ensure that you maintain positive ongoing relations with FDA for any future activities in which you might both be involved.

## References

- (1) Lavian M. and Allen P.W., "Survival Guide to FDA Inspections: Part 1, To Prepare or Not to Prepare, There Is No Question," *BioPharm* 15(8), 20-26, 49 (August 2002).
- (2) FDA, "Electronic Records; Electronic Signatures," *Code of Federal Regulations, Food and Drugs*, Title 21, Part 11 (U.S. Government Printing Office, Washington, DC, revised 1 April 2001).
- (3) FDA, "Food and Drug Administration," FDA website (Health and Human Services, Rockville, MD, accessed June 2002). Available at [www.fda.gov](http://www.fda.gov). **BP**