

# Inspection Readiness

From the Editors of

**THE FOOD  
& DRUG LETTER**

The Executive Briefing Series

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# Inspection Readiness:

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## A Guide to Preparing Subject Matter Experts to Face the FDA

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### About the Author

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# Introduction

FDA investigators are knocking at your door—are you ready? Your first thoughts may be of logistics—meeting space, document availability, the condition of your facility—but what about personnel? Are your employees prepared to face FDA investigators who are trained to thoroughly investigate a manufacturer’s entire operation?

The employees that know the most about your front-line operations are usually the ones who have the least experience with inspections and therefore are more likely to slip up. That’s why training of subject matter experts (SME) deserves at least as much attention in your inspection readiness plan as more tangible aspects like documentation and equipment function.

Putting unprepared SMEs in the same room as trained FDA investigators who are there to interrogate and interview them is clearly not a good strategy. No matter how intelligent, well-educated and capable your people are, they can slip up and lead investigators through doors you might prefer to keep closed. FDA investigators can draw conclusions from what your SMEs say, what they don’t say, even the way they do or don’t say it. The best way to guarantee those conclusions reflect positively on your business is to prepare your staff for their moment in the spotlight and make sure they practice, practice, practice.

This report offers guidance on developing an SME training plan, including selecting the best personnel to participate, assessing vulnerabilities and strengths, understanding common FDA interrogation techniques and testing readiness with simulated inspection interviews.

## Facts About FDA Investigators

It's as important to understand how the FDA investigators operate as it is to understand what systems they'll review, the techniques they use, the cues they look for in interviews, and how they prepare for the inspection, their mindset and motivation.

The first day on the job, FDA investigators take an oath of allegiance to the U.S. government and swear to uphold the Federal Food, Drug, and Cosmetic Act. They are officers of the government, just like an FBI agent or a U.S. marshal, and they take their jobs just as seriously.

FDA investigators serve as industry watchdogs—their goal is to protect the health of all people living in the U.S. They understand that they have a great responsibility to make sure that products are safe, effective and do not adversely affect the public. They understand that there is an implicit trust that the public places in the FDA and its investigators to ensure that every product says what it does and does what it says—every time. Investigators provide the FDA with reliable data from regulated manufacturers. In turn this information allows the agency to make decisions regarding the proper use of products for the public. It's about safety; it's about people's lives.

FDA investigators are very competent. They make sure that industry is compliant with regulations. They are highly educated and trained, not only in the tenets of good manufacturing practice but also in techniques for interviewing and eliciting information from individuals. They are motivated and extremely experienced in ferreting out trouble spots and violations.

# Preparation—Selecting and Training SMEs

Surviving an FDA inspection is all about managing risk—understanding your weaknesses, anticipating how investigators will perceive them and preparing your staff to respond. The human factor can make or break an inspection and may present the biggest risk of all if you are not fully prepared. You can't completely control what your employees will say, but careful consideration and preparation will minimize problems.

The first step is evaluating your SMEs to decide which ones will fare best in an inspection and which others may present too much of a risk to put in front of investigators. Several factors should be considered in this analysis.

1. **Competency in answering an investigator's questions.** Your SMEs must be ready to competently answer questions and provide clear explanations of your quality systems, processes and associated records. They also need to be ready to provide clear explanations related to any areas of risk you have identified.
2. **Performance under stress.** Consider how individual SMEs react to stress. Will they keep calm or will they panic? Are they likely to respond to investigators' challenges by passing the buck or pointing the finger at management? Needless to say, someone who may be a loose cannon should never be allowed to face an investigator.
3. **Demeanor and attitude.** Think about the kind of impression an individual may make on investigators. Does he or she appear professional, appropriately dressed and confident? Is his or her attitude one of openness and cooperation or hostility and fear? Can the SME make eye contact and speak clearly and with authority?
4. **Adaptability.** Can the SME handle unexpected requests and changes in the mood or direction of the inspection?
5. **New personnel.** If any of your key SMEs are new to their positions or to the company itself, they may need some extra coaching. They may require additional time to practice face-to-face, interpersonal inspection skills and learn how to work with an investigator.

## Some Common Pitfalls

There are some assumptions for selecting and preparing SMEs that companies should avoid. The first is the assumption that SMEs are prepared because they have previously participated in an inspection. Although some SMEs may be experienced due to prior participation, they still need to update their skills and have the chance to practice answering questions related to the current state of their subject matter, especially anything that is risk related. Second is the assumption that the SME should be the person who knows the most about the topic. This can be a problem if the individual does not have good communication skills and the ability to provide information in a clear and concise manner. A better strategy is to have the most knowledgeable personnel in the back room so that they can help to provide requested records and documentation.

Last is the assumption that job competence equals SME competence. The person who is very competent in performing his or her job does not necessarily possess the skills to engage in a successful encounter with an investigator.

## Training Subject Matter Experts

Next is the process of training the SMEs you have chosen to represent the company. Don't conduct training only in response to an impending inspection. Plan and carry it out well in advance of any potential inspections. Make SME training part of the company's standard operating procedures (SOP) so you can develop a thorough program, rather than rushing to meet a deadline.

Training for SMEs—in fact, any personnel involved in inspections—should go beyond the obvious topics of company policies, protocols, SOPs, and federal regulations and requirements. Trainees should learn about inspection etiquette, presentation skills; techniques investigators will use to elicit information, the types of questions they may ask and how to respond effectively.

As mentioned previously, FDA investigators are adept at finding out information, so SMEs should learn to recognize their methods and how to react to them. Investigators typically ask several different kinds of questions that present varying levels of risk.

- *Close-ended questions* are narrowly focused and require only very brief answers, often a simple “yes” or “no” will do. They are usually employed to verify statements and address uncomplicated issues, for example, “Do you have a training program? Do you have a CAPA [Corrective and Preventive Actions] procedure? Is this your signature?” SMEs should avoid providing a broader response when they are asked a closed question. Doing otherwise can frustrate an investigator.
- *Open-ended questions* are designed to encourage the SME to talk and provide as much information as he or she wishes. They are very broad, such as “What can you tell me about ...?” or “What do you think about ...?” Investigators often use open-ended questions to obtain more detail while reviewing complicated or sensitive areas. Instruct SMEs to provide fact-based answers, not responses based on opinion. Train them to try and identify what the investigator is specifically looking for as opposed to giving very broad answers. The SME can offer to provide a system overview using a policy, procedure or diagram.
- *Leading questions* are phrased to suggest what kind of answer the investigator is seeking, such as “You don't believe that process is effective, do you?” An investigator may ask this type of question to see how the SME is going to react. For this type of question, the SME could answer that, “This process is monitored and when that information indicates that the process may have an issue, we take further action.” As mentioned above, SMEs should refrain from providing their opinion and respond with just the facts.
- *Nondirective or neutral questions*, such as “How do you like your job?” may appear in the early stages or throughout an inspection. Investigators often use these types of questions to establish basic facts and identify potential issues. Train your SMEs to keep in mind that their responses are never off the record during an inspection and they should always answer in an official manner. It is fine for casual conversation to occur during natural breaks throughout the day, but these should be kept to non-business issues, such as the latest books, movies and the weather.
- *Assumptive questions*—possibly the trickiest kind—are designed to put the interviewee at ease and imply that the investigator already knows and accepts the answer, so the SME feels free to provide information he or she might otherwise not have shared. An example of an assumptive question might be, “So your CAPA system does not require an investigation for all

non-conformances?” Notice how the question was phrased—it assumed that the CAPA system did not require an investigation. Instruct SMEs to listen very carefully to these types of questions to ensure that the investigator’s understanding is correct. Reinforce that although the investigator may seem more relaxed and casual, the inspection is an official, formal event and SMEs should not let their guards down.

- *Restatement of questions*—The investigator may ask the same question multiple times of the same SME or different SMEs. This is done to confirm facts and to ensure he or she is receiving consistent answers. SMEs can sometimes find this frustrating, but need to understand that this is part of the FDA investigator’s process. Make sure that other SMEs are kept aware of the content of previous discussions so that they do not make statements that contradict previous answers.

It’s just as important to pay attention to how the investigator is listening as it is to what questioning techniques he or she is using. The investigator may be using either the active listening or passive listening approach.

Active listening involves an effort to make sure the questioner understands the response. Investigators may paraphrase an SME’s answer to make sure what they heard is what the SME meant. Or they may ask an SME to clarify a response. Another active listening technique is to summarize the conversation at the end of each topic, again to verify that the questioner has understood the response.

When an investigator is in active listening mode, the SME has the opportunity to confirm the investigator’s understanding of answers provided and clarify any misconceptions. SMEs should be careful not to stray from the specific topic, open other lines of inquiry or unnecessarily expand on their responses.

The passive listening technique can be more difficult to handle. When an investigator asks an open-ended or leading question and then just sits back in silence, an SME may be tempted to fill the void with more information than is necessary. Train SMEs to just answer the specific question and then stop speaking once they have provided the answer, regardless of what the investigator does. This can be very challenging for SMEs because a 30-second pause in an inspection can feel like 30 minutes.

Knowing when to stop talking is one of the most important skills SMEs should learn. Trainers should also stress other response rules, such as “Tell the truth.” Lying to an investigator never pays off, and the damage to your company’s credibility will be long-lasting. SMEs also must allow the investigator to complete the question before responding. They should not assume they know where the question is heading. Just as important, once the investigator has finished asking the question, SMEs should ensure they have understood the question. If not, SMEs can repeat the question to verify that they have understood it. When in doubt, asking for clarification is important and necessary to ensure that SMEs provide accurate, correct answers to an investigator.

SMEs also need training on how to provide technical information or explanations. They should provide the information in a basic format and should not assume that an investigator already knows about their company’s specific technology and how it works. SMEs should avoid using jargon or acronyms without first defining them. Over all, they should be patient and respectful with investigators, keeping in mind that while investigators are highly trained, specific company information is new to them.

The use of the right terminology is just as important as how SMEs give an answer. As part of preparing for an investigation, employees need to understand definitions for FDA terms and language in

the regulations. If an investigator mentions “adulteration” or “misbranding,” it is important that those involved in the inspection understand the impact of those statements and take appropriate next steps in the discussion with the investigator.

Keep in mind that no matter how well trained and competent your SMEs are, issues are issues. If your company has failed to properly address a problem, you cannot expect an SME’s answer to make it a non-issue. This is why it is so important to identify your company’s areas of weakness in advance so that you can correct them. And if your company can’t eliminate a problem entirely, SMEs should know how to discuss it in a way that clearly represents how the company identified and addressed the issue or is in the process of addressing.

To address risks that have action plans still in process, SMEs should be prepared to show the timeline of actions and progress to date using the quality system record that documents this information. The FDA does not expect that a manufacturer will never experience problems. What it does expect is that problems are identified and appropriately addressed. One of the key points that the FDA has shared repeatedly when speaking at industry forums is that the agency expects industry to identify and correct problems on its own, without being prompted to do so by the FDA.

### **Interview Dos and Don’ts**

#### ***Do:***

- Answer all questions honestly;
- Say “I don’t know” or “I’ll get the answer for you;”
- Avoid such phrases as “I think,” “Sometimes/often/usually,” “never” and “next time;”
- Avoid qualifiers, such as “typically,” “normally,” “generally” and “usually;”
- Stop speaking once the question is answered;
- Ask for explanations or interpretations of what you do not understand;
- Maintain a friendly and cooperative attitude;
- Control your temper; remain courteous and professional; and
- Maintain eye contact.

#### ***Don’t:***

- Volunteer information or answer a question that hasn’t been asked;
- Be sarcastic;
- Guess answers;
- Attempt to answer “what if?” or hypothetical questions;
- Argue with an investigator;
- Philosophize, ramble or editorialize;
- Point out deficiencies or errors;
- Apologize for problems or comments made by an investigator;
- Feel the need to respond to every comment made;
- Become defensive or evasive;
- Look away, fidget or look nervous; or
- Make statements about your personal opinion of the FDA.

## Practice—Simulating Investigator Interviews

The culmination of all this training should be “mock” inspection interviews. One of the most effective methods to prepare SMEs is to conduct simulated inspections. These are practice sessions designed to prepare SMEs to respond to both specific and general topics. This is the arena where they can practice their skills before facing the real inspection. Ideally, they should participate in a minimum of two or more simulations before participating in an actual FDA inspection.

Who should conduct this simulated inspection? Best practice is to use independent personnel. For example, if your company has multiple sites or separate corporate groups that are not related to your division, you may be able to ask some of their key staff to serve as objective observers and participants in your simulated inspection. You may be able to bring in someone who is independent from within your company. Ideally, you can also bring in independent third-party consultants who have both in-depth experience with FDA inspections and have extensive industry experience. Such consultants not only understand FDA trends and are attuned to what investigators require, but are also sensitive to a manufacturer’s business pressures. In essence, they are sensitive to and understand how regulations impact your business and can help ensure that you are compliant and that the processes that are in place are practical and sustainable. The independent consultant/mock investigator should also be very experienced with quality systems.

So what methods are used? During a simulated inspection, the mock investigator will ask both common and more challenging questions that FDA investigators would typically ask. Your SMEs should answer as they would during an actual inspection. This provides your SMEs an opportunity to experience what it’s going to feel like to sit in that hot seat across from someone they don’t know and what it will be like to experience some of the investigator questioning techniques they learned during training. One of the many benefits of this approach is that SMEs learn in a “safe” environment. They have a chance to experience and understand what the results are when they give a less than optimal response, and they learn to improve on the accuracy of incomplete or incorrect responses.

Before conducting simulated inspections, a company will need to identify the topics that it wants to cover. SMEs need to know how to competently explain basic information about your system as well as how the company identified and remediated any vulnerability. Therefore, companies should plan to cover general topics and issues associated with vulnerabilities. Field recalls or corrections, late medical device reporting (MDR) or significant investigations related to complaints are some examples of risk-based topics you may want to select when preparing for a simulated inspection. The benefit of including risk-based topics in preparation is that both the topic and associated documentation are reviewed at a very high level of detail. This minimizes or prevents any surprises in verbal responses or document content that may contradict your strategies and conclusions.

The process also gives you a chance to assess your SMEs’ performance. You can see how they will react when they are pressured by an investigator. When the simulated inspection is complete, the SMEs receive feedback on their responses regarding the potential risks of incomplete or incorrect responses as well as any other actions that may be necessary to reduce compliance vulnerabilities. Conduct multiple sessions until you are confident that SMEs are prepared for responses on all topics. You may find you need to make adjustments after conducting simulated inspections.

The individual who acts as the investigator can provide feedback to help you determine whether an SME's performance can improve with additional coaching and practice, or that you may need to bring in another person to work with the FDA investigators. Failing to adjust and address poor performance from an SME is a common mistake that manufacturers make. Remember there are no egos when it comes to inspections, and although members of your team may be very competent in performing their jobs, they may not possess the skills to interface with an investigator.

### **Best Practices for Conducting Simulated Inspections**

Best practice is to plan to test the support process during simulated inspections. To prepare for an inspection you need to ensure that you have a back room operation leader or coordinator who is well versed in all site operations. Good examples are senior quality or operations leaders. It's also important to make sure that you have an organized process to document an investigator's requests accurately and to fulfill them in a timely manner. Once you have done this you can test your processes and how the personnel perform during simulated inspections.

Understanding how the process holds up during times of stress, (i.e., heavy requests loads and pressure), is necessary to manage risk. This will help you avoid unnecessary backroom errors and prevent incorrect or unsatisfactory information from coming into the inspection room. Some common errors to avoid are failures to:

- Control documents brought into the room;
- Verify that the request was filled correctly;
- Review the document for unknown issues;
- Understand the direction and intent of the investigator/inspection; and
- Retrieve documents from the inspection room when finished.

# Case Study #1: Setting Up the Team

Below are two hypothetical situations facing a diagnostic company and a pharmaceutical company that are preparing for respective inspections. Read each company's scenario and then answer the questions on the selection of SMEs.

## **XYZ Diagnostics SMEs**

XYZ Diagnostics is an innovative company with great products. The organizational structure at the manufacturing site consists of a site director, to whom all resources report. The senior staff consists of directors for each of the main areas (operations, quality, research and development, field service and human resources). A manager reports to each director. The director of quality reports to the vice president of quality for the business (located at headquarters).

The managers for the following departments report to the quality director:

- Operations quality – QA support for manufacturing;
- Complaint handling – Complaint evaluation and investigation;
- Field quality – Medical device reporting, Device corrections;
- Quality systems – CAPA oversight, Management review;
- Incoming quality – Inspections and testing of incoming raw materials; and
- Compliance – Internal audit program.

The director of operations reports directly to the site director, has been on the job for six months and was not present for the most recent inspection.

Six managers for the following departments report to the director of operations:

- Technical product support
- Warehouse
- Kitpack
- Conjugation (by product line)
- Rare reagents
- Bulk solutions

For the most part, the current management team is the same team that was in place during the last inspection. New team members include the new director of operations, new manager in the production area for HIV and the manager for conjugation.

## **ABC Pharmaceuticals SMEs**

At ABC Pharmaceuticals, the entire management team at the manufacturing site reports to the senior site director. Most of the senior level managers have been in their positions for less than one year,

including the senior site director. The director of human resources and director of product development have been in their jobs for three years and were both present during the last inspection. There is a senior staff consisting of directors for each of the main areas (operations, warehouse and distribution, quality, product development, human resources). A manager reports to each director.

The managers who report to the quality director are:

- Operations quality – QA inspections and support for manufacturing;
- Complaint handling – Complaint evaluation and investigation; recalls, adverse event reporting;
- Incoming QA – Sampling and testing of incoming raw materials;
- Laboratory testing – In process and final release testing;
- Document management – Review and approval of procedures and batch records; and
- Compliance officer – Internal audit.

The director of operations has been on the job for about four months and has the following managers as direct reports:

- Bulk drugs;
- Compressing and coating;
- Finishing – Packaging and labeling;
- Validation;
- Product support–product investigations;
- Engineering–Facility and equipment maintenance; and
- Warehouse and distribution.

The managers reporting to the directors of operations and quality have been in their positions for some time, and the validation manager has been with ABC Pharmaceuticals for 25 years; including 10 of those years as validation manager.

### Case Study #1 Exercise

#### XYZ Diagnostics

1. Would you recommend preparing any SMEs for the upcoming inspection?
  - a. Yes
  - b. No

2. If you answered yes to #1, which SMEs would you prepare?  
If you answered no to #1, provide your rationale for not preparing SMEs.

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3. What type of preparation would you recommend? (Choose best answer.)
- a. Provide a training presentation on inspection Dos and Don'ts.
  - b. Review the scope of the inspection and anticipated content.
  - c. Conduct simulated audits by topic to prepare SMEs.
  - d. All of the above.
  - e. None of the above, the SMEs do not require any preparation.

**ABC Pharmaceuticals**

1. Would you recommend preparing any SMEs for the upcoming inspection?
- a. Yes
  - b. No
2. If you answered yes to #1, which SMEs would you prepare?  
If you answered no to #1, provide your rationale for not preparing SMEs.

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3. What type of preparation would you recommend? (Choose best answer.)
- a. Provide a training presentation on inspection Dos and Don'ts.
  - b. Review the scope of the inspection and anticipated content.
  - c. Conduct simulated audits by topic to prepare SMEs.
  - d. All of the above.
  - e. None of the above, the SMEs do not require any preparation.

## Case Study #2: Reviewing Support Processes

During the last inspection in 2010, XYZ Diagnostics used a back room, which was run by the previous director of operations. However, that director has moved on and the company now has a different director who has been in the job for six months. The director of quality was in the inspection room with the investigator during most of the inspection in 2010 and remembers that there were some incorrect documents brought into the room and sometimes the information provided was not what the investigator wanted. She talks to the personnel who were in the room during the last inspection to get their perspective on how the inspection went. The information the back room team shared is as follows:

- It was difficult to pull an electronic list of all CAPA and complaints;
- Sometimes the atmosphere was very chaotic, the director of operations told each person what to do, but would become very stressed when things got busy and would yell at the personnel in the room. They had to wait for instructions from the director to do anything;
- The copier broke down;
- The room was very small and it was hard to move around and keep track of the documents;
- Requests were documented on paper and tracked on a spreadsheet; and.
- The other directors at the site came into the room and all offered advice.

The director of quality also remembered that at times there were decisions made that were different than the ones that she had made with the previous director of operations. It was not always clear why or how those decisions were made because they were so busy, and she never seemed to have the time to follow-up on these discrepancies.

Based on this analysis, XYZ decided that it wanted to practice the “support process” during the simulated inspection. The management team identified the following activities to improve and test the support process during the simulated inspections:

- **Define roles:** Each function needed in the support process is defined so it is clear who is responsible for each function. This will help to avoid some of the chaos and confusion that occurred during the last inspection;
- **Train the team:** The support team will receive training on the defined roles;
- **Prepare equipment:** The support room equipment will be set up and tested during the simulated inspections;
- **Practice requests:** The simulated inspections will include requests that are likely to be made during an inspection. This will ensure that the team can respond to common requests, such as electronic listing of CAPA and complaints efficiently and accurately; and
- **Name a leader:** Define responsibility and decision-making rights for management to prevent the problem of different leaders providing conflicting directions.

Our pharmaceutical company from Case study #1 is also looking at its support process, and has also done some analysis:

### **ABC Pharmaceutical Support Process**

*Review the analysis performed by ABC Pharmaceutical below and then answer the questions*

During the last inspection in January 2011, ABC used a back room which was run by the operations quality manager. The director of quality has been in his job for six months and was not present during the last inspection and neither was the current site senior director or operations director. The quality director met with the operations quality manager, who was in charge of the back room during the last inspection to see how the inspection was handled. The operations quality manager provided the following information:

- They were able to keep up fairly well with the investigator’s request;
- They did have some incorrect information in some of the documentation that was brought into the room (i.e., a procedure had a missing page and another document had pages out of order);
- They were able to easily pull the electronic lists requested for nonconformance and deviations, but there were new IT systems that were recently implemented and they were not sure how to pull data or generate reports from the new system;
- They had a problem with the copy paper in the last inspection; they ran out of paper and had to send someone to an office supply store to purchase some more paper. This delayed requests for about an hour;
- They have a database that is used to document requests, and this is done directly from the inspection room; and
- Many of the requests coming from the inspection room were difficult to understand, and were being sent by different people.

The operations QA manager believed that the inspection room appeared to be a bit disorganized during the last inspection. In addition, it appeared that no representative from ABC Pharmaceutical was clearly in charge of the inspection room.

#### **Case Study #2 Exercise**

1. Would you recommend preparation related to the support process prior to the upcoming inspection?
2. If you answered yes to # 1, list all activities you recommend for preparation.  
If you answered no to #1; provide your rationale for why no preparation is required.

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## Case Study #3: Setting the Stage

Let's look at a hypothetical scenario for a simulated inspection. A leader on the management team—let's say, the director of quality—gets the ball rolling. This individual is responsible for working with the management team and site staff to ensure that everyone is ready just as they would be for an actual FDA inspection.

As she begins to organize, she contacts the manager of the compliance department and asks him for current information on FDA enforcement trends and also for the results of internal audits. He may tell her, for instance, that there have been a lot of warning letters issued by the FDA related to complaint procedures and that the company's own internal audits found some similar observations.

Armed with that information, the director of quality assembles her team of operations and quality together and asks them to identify some of the compliance risks that might surface during an inspection. In this instance, the team looked at:

- Warning letters for the past and current years;
- Internal audit results;
- CAPA, nonconformance and complaint trending;
- Field actions; and
- Process monitoring.

The team found a few issues, including an elevated complaint rate for a particular product and an internal audit observation for its complaint handling procedure not requiring the evaluation for further investigation to be documented. That ties to one of the top issues in recent warning letters from the FDA.

The quality director takes the information from the inspection readiness team and meets with the senior leadership team at the site to review the inspection readiness plan including simulated inspection(s). Members of the management team add their perspectives. The management team is aware the action plan to address the complaint handling issue is in process, but it's overdue. They share the fact that there is a new operations manager in the manufacturing area and that corrective actions are still in process.

After meeting with management, the quality director finalizes her plans, identifying key risk topics. They include:

- The complaint-handling CAPA, which has a missing element and is late; and
- The documentation and associated investigation and CAPAs.

The quality director also identifies topic areas for SME preparation. Two SMEs who are considered essential are the new operations manager and the manager of complaint handling, because of the issue with the complaint CAPA.

So let's take a look at examples of simulated inspections between the mock audit investigator and the SME. Each interview should focus on a topic that needs preparation for inspection. In this case the topic is on the complaint handling procedures.

## Scene One: Just the Facts

*Investigator:* Do you have a procedure for complaint handling?

*SME:* Yes, we have a procedure for complaint handling. It's been recently updated because of an internal audit observation.

*Investigator:* I see. Could I see a copy of the updated procedure, the associated change record, the internal audit report and the CAPA associated with this observation?

*SME:* Sure, we'll get you that information.

*Investigator:* While we are waiting for the documents I requested, can you tell me what the observation was?

*SME:* Sure. The observation was that the procedure didn't require that we document the evaluation we perform to determine whether a further investigation is required.

*Investigator:* What are the actions that you have taken?

*SME:* One of the actions is overdue. We updated the procedure to require that the evaluation is now documented; a rationale for why we're not going to perform further investigation, if that's the case, and the signature of the individual who performed the evaluation. We're making a change to the software to accommodate this.

**Feedback**—The investigator notes that the SME made some mistakes that should be avoided in a real inspection:

- **Providing extra information.** In this case, the SME provided extra information that was not required to answer the question. When asked about the procedure, she said, "We changed it because of an internal audit observation." The investigator didn't ask if the procedure had been updated, only if there was a procedure. The SME also stated that corrective actions were overdue. And then the SME included the details of that internal audit finding, which the FDA is not entitled to see.
- **Offering documents the investigator is not entitled to receive.** The SME agreed to provide an internal audit report. The FDA is not entitled to see internal audit reports, although an investigator can request the resulting CAPA report. This mistake opened up issues for the investigator to probe even further. In fact, this led the investigator to ask what the observation was, when really none of this information should have entered into the inspection. The SME again offered up extra information when she stated that the actions were overdue. The investigator had asked only what the actions were, not whether they had been completed on time.

**Recommended follow-up**—As part of these simulated inspections, the person acting as the investigator provides coaching and feedback. In this case, the external expert recommended that the site develop a procedure that outlines the company policy for providing documentation to regulatory agencies and that all personnel who will be involved in the inspection are trained on the procedure. The procedure would specify items that the company would not normally provide in an inspection, such as internal audits, pictures, video recordings and personnel or financial information. By outlining this information in a policy, and training personnel on the content, it's easier to prepare your SMEs to provide the proper response if an investigator asks for these items.

Best practice is to have a company policy that outlines how the company handles an inspection in general, from the receiving of an investigator upon arrival, to the support process, inspection team and how to handle requests for documentation that an investigator is not entitled to see. The policy should provide instructions for an elevated approval by the company's legal or corporate quality organization for possible exceptions, as there may be occasion when the company may need to grant an exception. This also gives SMEs some latitude as opposed to refusing an investigator's request.

Having a sound policy and ensuring everyone is trained on it, helps manage risk when issues arise, and to maintain an effective, positive relationship with the investigator, which is crucial to success.

## Scene Two: Hold Your Temper

*Investigator:* When will the actions be complete?

*SME:* I think they may be done in about a month.

*Investigator:* How late are they?

*SME:* I believe a month or so.

*Investigator:* A month or so? Why is this OK? (Investigator leans forward and takes an aggressive tone.) Do you think it's OK to continue to not appropriately evaluate complaints?

*SME:* Well, no. (SME folds arms.) But management didn't assign somebody to the validation right away.

*Investigator:* How long did it take management to assign someone? Don't they think this is important?

*SME:* I don't know. (SME sounds irritated.) You'll have to ask them.

*Investigator:* All right. Let's bring in the manager who was responsible to assign the resources and ask them.

*SME:* OK. (SME sighs.)

**Feedback**—After this exchange, the investigator pointed out several problem areas.

- **Avoid the phrase “I think” and other qualifiers.** Advise your SMEs to stay away from qualifiers like “I think,” “I believe,” “I suppose” or “To be honest.” They may be common phrases in our everyday speech, but they give an indication the SME is not sure of his or her answer or that something else may be wrong.
- **Don't answer a question if you don't have the necessary information.** The proper response is, “I don't know, but I'll get you the answer.” A lot of times people are afraid to do that, but it's really the best case if you don't know the answer.
- **Make sure your SMEs know important facts about your operation.** From its research, the inspection readiness team deduced that CAPA would be an area of risk. The SME should have been briefed on the details of the CAPA and its current status.
- **Stay cool under stress.** When the investigator took an aggressive tone, it shook the SME's composure. In fact, the SME implicated the management team when she responded that managers

hadn't assigned someone to perform the validation work on time. The SME was advised not to get into this type of commentary with an investigator. Sometimes these comments can end up in the establishment inspection report (EIR), in which the investigator documents the events of the inspection, including key statements from personnel who were interviewed. The comment could also lead the investigator to conclude that management isn't appropriately engaged or performing their duties. So, stay away from such commentary.

- **Keep your attitude positive.** The SME also used an inappropriate tone of voice when pressed by the investigator. She became argumentative and defensive, folded her arms, which is classic negative body language. Investigators will observe body language and listen to the tone of voice for clues that there may be a problem. In fact, all FDA investigators receive training on interview techniques and interpretation of nonverbal body language and verbal queues. In addition, it is important to build trust and rapport with an FDA investigator, a positive relationship will contribute to building trust. It is never a good idea to argue with an investigator, you are not going to win!
- **Don't open the door to new issues.** When the SME said, "You'll have to talk to management," she opened the door for the investigator to bring management in, which is exactly what happened. There may be appropriate times to call in management, but you want to be thoughtful and purposeful about how and when that occurs.

**Recommended follow-up**—The investigator recommended that all SMEs understand how to handle difficult discussions, including how to:

- Maintain a calm tone of voice;
- Maintain positive body posture; and
- Be respectful and listen.

If an investigator is emotional while expressing a concern, that is an important time to listen carefully and remain respectful. In such a case it's best to defuse the situation and let the investigator know that you understand what he or she is telling you; or if you don't, then ask for clarification. This doesn't mean promising corrections. When it comes to any corrective actions, that's best handled outside the inspection and according to company procedures. Promising a corrective action or correction to an investigator can also be included in the EIR, and it is very important that any actions taken to address an investigator's concern are thoroughly comprehended, investigated and developed. SMEs should be taught under what circumstances they should defer to another, more qualified individual within the company for resolution of a problem.

SMEs must also understand that they should refrain from making statements about the inspection in general, such as, "I had to miss lunch yesterday because of your request" or "I had to cancel my vacation because you started this inspection." While those statements could be true, that is not relevant to the inspection and does not contribute to establishing positive rapport with the investigator.

Additionally, you should make sure to notify all personnel at your company when an inspection is taking place and instruct them not to discuss company matters in hallways, restrooms, the cafeteria or other public areas.

### Scene Three: Silence is Golden

*Investigator:* Let's look at the CAPA and the procedure update.

*SME:* Here they are.

*Investigator:* What is the change that you made?

*SME:* We added this section here which requires the evaluation of the need for further investigation to be documented, along with a signature of the person who did it.

*Investigator:* Do you have an effectiveness check?

*SME:* Yes, the records are checked by another person to ensure that this has occurred.

*Investigator:* I do not see it here.

*SME:* Well, we are performing this check. I could show you the records.

*Investigator:* (Pauses.)

*SME:* Since this will now be a required field in the software, you can't proceed without entering this information. It's a very nice system. Would you like to see it?

**Feedback**—The pregnant pause is a very effective tool in an interview. Train your SMEs to stop talking when they have finished answering a question. Instead, they should wait until the investigator asks the next question. This is one of the hardest things to handle during an inspection. This can certainly feel very awkward, but it's definitely the correct behavior in this situation.

In this simulation, the SME kept talking, providing extra information and offering to show the investigator the computer system.

Investigators employ a variety of techniques, and it's important for SMEs to be prepared and not fall into any traps. For instance, they may face an investigator who asks questions very quickly. An investigator may phrase a question in a manner that makes it sound like something is wrong, when actually it's just a way to see what kind of responses it will elicit. An investigator may want to see if there's going to be a calm, confident answer or if somebody becomes rattled.

**Recommended follow-up**—The investigator cautioned the SME against defending something once an issue becomes evident, such as in this example where the effectiveness check wasn't documented. It's better in that situation to simply acknowledge that you understand the investigator's concern. The investigator also recommended that the company update the CAPA record to include the effectiveness check criteria and documentation, prior to an actual inspection, thereby avoiding an issue. Additionally, the investigator recommended that the company confirm the procedure for CAPA provides adequate instructions for effectiveness checks.

### Scene Four: No Guessing

*Investigator:* Have you looked at your historical complaint records to ensure an investigation was performed where required?

*SME:* No.

**Investigator:** *How can you be sure that you have?*

**SME:** *Well, we evaluate all of our complaints. It just wasn't documented before.*

**Investigator:** *What about the corrective action to make a software change? This document shows it was due one month ago.*

**SME:** *Well, I've looked into this, and we should be done with this within a week.*

**Investigator:** *Is management aware of this?*

**SME:** *I'll follow-up on that question.*

**Feedback**—The CAPA for updating the software was late. However, there was nothing to indicate management knew this. The SME answered correctly by saying she did not know if management was aware of the situation, that the information wasn't in the record and that she would follow-up on the question. In addition, the CAPA record was incomplete because it did not include any analysis into the historical effects of the missing requirement.

**Recommended follow-up**—The investigator made recommendations to address the late CAPA and lack of historical review. A review and approval by management to extend the CAPA is one option to address the late CAPA. Another option is to demonstrate how CAPA information is tracked and provided to management. For the lack of historical review the investigator recommended that the company consider performing a “look back” or review of complaints to ensure that there were not any other important product issues that the manufacturers failed to appropriately investigate. This may seem like a daunting task, but you can apply a risk-based approach to a historical review and provide assurances that the company has addressed all field issues.

### **Completion of Simulated Inspection—Closing Statements**

With the simulated inspection complete, it's time for a debriefing with the management team. The independent investigator should meet with managers, such as the quality director, and go over the results.

Together, they should review what happened in the simulated inspection and the list of follow-up actions. That may include specific actions, such as those required for the CAPA, but also the recommendations for individual SMEs and what additional work is required to better prepare them. In this case, the independent investigator said the SME who was involved in the complaint handling topic was not a lost cause and likely would improve with additional simulated inspection practice sessions. In addition, regular debriefs should take place as simulated inspections continue to inform management about the SME's progress and any needed follow-up actions.

## Case Study #4: Responding to Validation Concerns

The next hypothetical situation is a simulated audit discussion related to the topic of validation. The discussion is between a mock investigator and the manager of validation. After reviewing the discussion, write down the feedback that you would give to the SME, feedback related to the topic and any recommended follow-up actions.

**Investigator:** *I am going to review how you at ABC Pharmaceuticals handle validation. Can you answer my questions?*

**SME:** *Yes, I can answer your questions. I am the manager of validation. If you ask me a question that I cannot answer, we will get the answer for you.*

**Investigator:** *Good. Let's start with an overview of how you handle validation. So how do you do validation here? Help me understand how that works.*

**SME:** *A good way to walk you through how we handle validation would be to start with the procedures, I will ask for them.*

(The procedures are brought to the audit room quickly. The SME looks at them and notices that there is a red-line version and change record of the document that was made as an action to address the 483 on validation.)

**Investigator:** *Is that the procedure?*

**SME:** *Yes, but it is not the one that I wanted to show you.*

**Investigator:** *Well that's ok, since it's here let's take a look at it anyway (investigator puts hand out).*

**SME:** (Pauses while trying to decide what to do.) *Here you go.*

**Investigator:** *This looks like a markup. Is this an official procedure?*

**SME:** *It is part of a change record related to a change we made to the procedure. There is also a description related to the changes.*

**Investigator:** *I see. I know you had a 483 related to validation.*

**SME:** *Yes, this is one of the actions we took to address the observation. In addition to this we also performed a gap analysis of other validations.*

**Investigator:** *Good, and what were the results of that?*

**SME:** *We documented the outcome in our CAPA investigation.*

**Investigator:** *Ok, let's get that CAPA. So did you find any other validations that had problems?*

**SME:** *We documented our follow-up in the MVP. (Looks to side and does not make direct eye contact.)*

**Investigator:** *MVP?*

**SME:** *Master Validation Plan.*

**Investigator:** *What is a master validation plan?*

**SME:** *That is where we document planned validation work and approach.*

**Investigator:** *I would like to look at the master validation plan and the associated gap analysis in the CAPA.*

About 15 minutes go by and the documents have not arrived yet. The investigator looks impatient, the SME sits silently.

**Investigator:** *Will the information I requested be coming soon?*

**SME:** *Let me go check on that.* (SME steps out of the room and comes back in with the records.)

*Here are the documents.*

**Investigator:** *Ok, I want to look at the validation plan.* (Pauses and looks at the plan.) *There are a lot of items listed on here. When will all this work be done? What is the risk to your products that are in the field? Why is it ok for you to continue to manufacture and distribute products while you are doing this work?* (Investigator speaks rapidly, with a very concerned tone.)

**SME:** *The work is going to take us 18 months; you can see the dates here.*

**Investigator:** *What about the risk to your products? How have you addressed this?*

**SME:** *We are not having any failures when we perform release testing on our products.*

**Investigator:** *That is not adequate to address this issue. Just because you meet the release specification does not ensure your products performance.*

SME says nothing, looks down.

**Investigator:** *This is far worse than what I expected to see given the observation from last year. These gaps are pretty serious.*

**SME:** *We have prioritized the validation work according to risk, and the most important items are being completed first.*

**Investigator:** *Can you show me how you performed that assessment and where it is documented?*

**SME:** *Yes, this is part of our CAPA. The risk prioritization is shown here.* (SME points out in the document.)

**Investigator:** *Why is it ok for you to continue to distribute your products with these gaps? Have you assessed that?*

**SME:** (Pauses.) *No, we have not assessed that, but we certainly could. We can prepare an assessment while you are here.*

**Investigator:** *At this point I am very concerned and really need to look at this very closely to understand the risk to your products.*

**SME:** *We will start working on the assessment of risk to distributed product.*

**Case Study #4 Exercise**

	<b>Feedback</b>	<b>Follow-Up Actions</b>
<b>SME</b>		
<b>Topic</b>		
<b>Support Process</b>		

## The Feedback—SME

The feedback that the simulated investigator provides to the SME should reinforce the positive behaviors and areas for improvement.

### *The positives*

- **Developing positive rapport:** Initially, the SME did a good job of establishing positive rapport when he indicated he could answer the investigator’s questions, and if he couldn’t he would get the answer for the investigator. The SME also explained who he was and his role in the organization.
- **Narrowing down a broad request:** Another positive was how the SME narrowed down the very broad question when the investigator asked, “How do you do this here?” The SME suggested using the procedure on validation to illustrate how the organization handles a process. It is always good to point to your procedures and use them to reinforce your process and demonstrate that you follow it.
- **Checking progress of requests:** The records took a while to be brought to the room and the SME handled it well by going to check on the status of the records. Fifteen minutes is probably not a terribly long period of time, but in this case the investigator was waiting for this information—so it was important to expedite obtaining it—there is also a related process element here that needs to be addressed.

### *Areas for Improvement*

- **Offering extra information:** The SME offered extra information when he stated that there was a gap analysis.
- **Lack of direct answer:** When asked when the validation work would be completed and whether a risk analysis had been performed, the SME did not directly answer the question.
- **Use of jargon:** The SME used an acronym, MVP, without defining it for the investigator. Train SMEs to provide definitions of acronyms and other terms that may be specific to the company or the product.
- **Body language:** The SME exhibited poor body language when he did not make eye contact with the investigator. It is important for SMEs to make eye contact when providing answers, as the investigator could interpret this as evasive or non-cooperative.
- **Rapid fire questions:** When the investigator asked questions rapidly, the SME did not respond well as he did not answer all the questions. SMEs should be instructed to ensure they understand all the questions that have been asked when an investigator takes a “rapid fire” questioning approach. Ideally, they should paraphrase each question to make sure that they understood each one. This slows the conversation down and ensures that they understand what the investigator asks and that they provide the investigator with the information he or she was looking for.
- **Committed to take an action:** The SME committed to performing a risk assessment in response to the investigator’s concern that one had not been performed. While it may have been the right action to take, he should not have committed to it on-the-spot without the appropriate analysis and preparation.

### **Recommended Follow-Ups**

Follow-up recommendation for this SME would be to receive some general coaching that emphasizes answering questions directly, avoiding offering extra information, clearly communicating technical information, watching body language and handling rapid fire questions. Coach the SME on how to handle issues that are of concern to an investigator. In addition, share this type of coaching with all SMEs who will participate in the inspection.

### **The Feedback—Topic**

The problem with the topic is that there was no documented risk assessment to address the validation gaps and their potential effect on product performance. The recommendation is to complete a risk analysis of the validation gaps. Based on the results of the risk analysis, a manufacturer should prepare a rationale for continued manufacturing that includes any needed containment measures until it can complete validation work.

### **The Feedback—Support Process**

The incorrect document was brought into the room when the change request was provided instead of an approved procedure. There was also an issue with the time that it took for the request to get to the inspection room.

Recommended follow-up is to pre-stage documentation that an investigator is highly likely to request. In this case the manufacturer can prepare the CAPA, Master Validation Plan and associated procedures and have them ready to provide to the investigator so that time is not taken during an actual inspection to prepare them. The company should also share this example with the support team so that they can understand how the mistake was made and take action to ensure that it is not repeated.

## Lessons Learned

Even when SMEs are well prepared there are some things that can go wrong if the whole team does not stay focused. The following are steps that SMEs can take to keep the investigation on track:

- **Listen, listen, listen.** Those who are present in the inspection room should actively listen to feedback and information relayed during conversations with investigators. It is crucial that the team does not inadvertently miss picking up on their concerns. A company can think that an inspection is going well because the investigator is not contentious and can completely miss signals that something is wrong.
- **Seek to understand.** It is imperative that when an investigator expresses concern over an item that SMEs take the time to truly understand the content of the expressed concern. If they do not understand, SMEs may come across as ignoring an investigator's concern, which can result in the investigator searching and finding additional examples to illustrate his or her point.
- **Keep it positive.** Establishing a positive rapport with an investigator can make or break an inspection. It is up to SMEs and management to convey and demonstrate a cooperative attitude to an investigator. Establishing and maintaining an atmosphere of cooperation and open communication will go a long way and make it easier to discuss concerns should they come up.
- **Business practice.** Integrating inspection preparation into the way you do business can be a competitive advantage. Maintaining a program and conducting practice two to three times a year can prevent a distracting, time consuming fire drill preparation effort when inspection is announced. You can formulate your preparation and schedule around anticipated inspection activity, depending on your product type and whether you are introducing new products to the market that require pre-approval inspection.
- **Plan, do, check, act.** After each inspection have the full team assess what went well and what did not and take action where necessary to improve.

## Conclusion

The benefit of this risk-based approach to preparing your SMEs for inspection is that it gives you a chance to look at your areas of weakness, address those vulnerabilities, prepare documentation, and get your key people ready to represent themselves and the company confidently.

Keep in mind that experiential learning is more effective in training SMEs than classroom instruction. With simulated inspections you've provided a realistic environment in which to prepare them. When you have people that go into an inspection room who have been properly prepared through simulated inspections, they understand what happens during an inspection and they will become more confident in their encounters with an investigator.

Most people that work through this process are much more confident and perform much better than those who do not prepare in this manner. It makes a huge difference in the inspection room and contributes to building a positive rapport with the investigator, which in turn contributes to your company's reputation. Preparing SMEs through simulated inspection requires an investment in time and resources. However, all the time and resources that are spent in advance of an inspection will definitely pay dividends in the end.

## Appendix A: Answer Key

## Answers to Case Study #1

### XYZ Diagnostics

1. Would you recommend preparing any SMEs for the upcoming inspection?
  - Yes
  - No
2. If you answered yes to #1, which SMEs would you prepare?  
If you answered no to #1, provide your rationale for not preparing SMEs below.
  - **HIV conjugation area manager**
  - **Complaint handling manager**
  - **Field quality manager**
  - **Technical product support for wack-a-do analyzer**
  - **Technical product support for HIV assay**
  - **Technical product support for troponin**
  - **Manager of quality systems**
3. What type of preparation would you recommend? (Choose the best answer)
  - a) Provide a training presentation on inspection Dos and Don'ts
  - b) Review the scope of the inspection and anticipated content
  - c) Conduct simulated audits by topic to prepare SMEs
  - d) All of the above**
  - e) None of the above, the SMEs do not require any preparation

### ABC Pharmaceuticals

1. Would you recommend preparing any SMEs for the upcoming inspection?
  - a. Yes**
  - b. No
2. If you answered yes to #1, which SMEs would you prepare?  
If you answered No to #1, provide your rationale for not preparing SMEs below.
  - a. Validation manager**
  - b. Complaint handling manager**
  - c. Product support manager**
  - d. Bulk drugs manager**
  - e. Finishing manager**
3. What type of preparation would you recommend? (Choose the best answer)
  - a. Provide a training presentation on inspection Dos and Don'ts
  - b) Review the scope of the inspection and anticipated content
  - c) Conduct simulated audits by topic to prepare SMEs
  - d) All of the above**
  - e) None of the above, the SMEs do not require any preparation

## Answers to Case Study #2

1. Would you recommend preparation related to the support process prior to the upcoming inspection?

- Yes
- No

2. If you answered yes to # 1, list all activities you recommend for preparation below.

If you answered no to #1, provide your rationale for why no preparation is required.

- **Ensure that there are defined roles for the inspection and support rooms.**
- **Train inspection team and management on defined roles.**
- **Prepare the support room and equipment, test during simulated inspections.**
- **Define process for pulling electronic data and ensure reports are verified or validated.**

Answers to Case Study #4

	Feedback	Follow-Up Actions
SME	<p><b>Positive behaviors</b></p> <ul style="list-style-type: none"> <li>• Developing positive rapport</li> <li>• Narrowing down a broad request</li> <li>• Checking on records that were delayed</li> </ul> <p><b>Areas for improvement</b></p> <ul style="list-style-type: none"> <li>• Offered extra information</li> <li>• Did not directly answer the question</li> <li>• Used jargon (MVP)</li> <li>• Body language – did not make eye contact</li> <li>• Rapidly asked questions</li> <li>• Committed to take an action</li> </ul>	<p><b>General coaching on interactions during inspections</b></p> <ul style="list-style-type: none"> <li>• Answer questions directly</li> <li>• Avoid offering extra information</li> <li>• Learn how to clearly communicate technical information</li> <li>• Be aware of body language and eye contact</li> <li>• Learn how to handle rapid fire questions</li> </ul> <p>Learn how to handle issues when they arise during inspections.</p> <p>Share this coaching and information with all SMEs</p>
Topic	<p>No documented risk assessment for validation gaps</p>	<ul style="list-style-type: none"> <li>• Complete a risk analysis for validation gaps</li> <li>• Prepare a rationale for continued manufacturing                             <ul style="list-style-type: none"> <li>○ Containment measures</li> </ul> </li> </ul>
Support Process	<ul style="list-style-type: none"> <li>• Incorrect document was brought into the room                             <ul style="list-style-type: none"> <li>○ Change request instead of approved procedure</li> </ul> </li> <li>• Timeliness of fulfilling requests</li> </ul>	<ul style="list-style-type: none"> <li>• Include pre-staging of documentation that is highly likely to be requested                             <ul style="list-style-type: none"> <li>○ CAPA</li> <li>○ Master Validation Plan</li> <li>○ Associated procedures</li> </ul> </li> <li>• Share procedure example with back room, reinforce process</li> </ul>