

Inspection readiness and successful execution

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Keywords

Inspection; Marketing authorisation (MA); Subject matter expert (SME).

Abstract

Inspections by competent regulatory authorities are a fact of life for manufacturers of pharmaceutical products and medical devices, to assure compliance, conformance and integrity of the finished product(s). Understanding what is required for a state of inspection readiness enables an organisation to be able to present itself in a positive and accurate manner. The necessary processes and roles in advance, during and after an inspection are presented and discussed.

Introduction

A manufacturer of a pharmaceutical product or medical device expects to be inspected by competent regulatory authorities, either routinely or as part of a product registration process. It is also possible that an inspection could be unexpected; a “For Cause” inspection resulting from a safety concern or adverse event, the outcome of an inspection on another part of the organisation or a whistle-blower. The guidance for what can be inspected and how the authorities go about this is publicly available.

Whatever the reason, the authority will broadly be looking to establish the following:

- Compliance to current good manufacturing practice (GMP)
- Conformance to current or proposed manufacturing authorisations – is the organisation doing what it says it does?
- Integrity of data and processes associated with the product and manufacturing process.

So, given their inevitability, when should companies start to prepare for an inspection from the authorities? Does it depend on the type of inspection, the reason for the inspection, and who the inspectors are? The short answer to these questions is no, it doesn't matter.

The type of inspection will determine the notice period given in advance of the inspection, but in the case of “For Cause” inspections, this could be very little; or none.

The panacea for the pharmaceutical sector is that of a state of constant inspection readiness, wherein any inspection can be successfully navigated at any time. Cutting across this aspiration is the reality of a dynamic business environment, where demands of costs, resource and time are balanced against constantly changing customer and regulatory expectations.

Establishing a state of constant inspection readiness requires a considerable investment of time and effort, and a supportive senior management philosophy. Sustaining it requires ongoing investment, coupled with a culture that looks to embed best practice in all areas of the business. The dividends of such a virtuous state of affairs are self-evidently wide-ranging, beyond the simple comfort of knowing that any inspection can be passed with flying colours at any time.

It is equally self-evident that no company should be totally unprepared for an inspection. The consequences of a “bad inspection” through lack of preparation for an otherwise adequate site could be far more disruptive and costly than that of the avoided preparation.

Most companies will opt for a middle ground, seeking a pragmatic balance for inspection readiness, as part of overall quality risk management. Systems and procedures will be in place to allow a rapid and proportionate response to the notification of an impending inspection.

From this position, assuming the site systems are fundamentally robust, with all employees trained and competent in their roles, as an approved site for manufacturing a licenced pharmaceutical product or medical device, then one should be comfortable that the company is largely prepared for an inspection. In that context, what then, should the steps for inspection readiness be?

There are some important practical preparations that will need to be done when you have notification of an inspection, and subsequently following receipt of specific information from the inspectors involved.

Inspection management process

To manage the inspection process, companies should do the following:

- Understand the roles that are needed to successfully administrate the inspection and assign (with deputies)
- Be aware of any recent site issues, remediation activities, particularly any which remain ongoing
- Ensure a single message is shared across the organisation, to avoid any self-generated surprises
- Review any areas of concern from previous inspections and identify any current trends or “hot topics” that could arise
- Understand the composition and background of the inspectors involved; who will act as the inspection leader and if there are any specialists as part of the team who will have areas of particular interest
- Understand the process following the inspection, should any issues be identified.

Communication

Aspects to consider with regard to communicating information to employees include the following:

- Inform the organisation what is happening, including any relevant company employees who might not be based on the site that will be inspected

- Share the timetable and agenda for the inspection, and any information regarding the inspectors, including “hot topics” or culturally significant information specific to the authority involved
- Reiterate the necessary behaviours of all employees and the requirement for full support and engagement, regardless of role. An important message is for everyone to assume that an inspector is listening to every conversation that takes place on the site
- Update the site with any changes of plan or issues highlighted, and arrange for updates to be sent around the site at the end of each day.

Logistics

The logistics of an inspection should be addressed, and include the following:

- Confirm the timetable with the inspectors
- Arrange for sufficient administration staff for the duration of the inspection (document request handling; scribes for all tours/interviews and meetings; escorts to accompany the inspectors to rest rooms, refreshment areas, etc)
- Ensure the availability of subject matter experts (SMEs). This might require reviewing holiday requests and checking the SMEs are available for possible earlier starts and later finish times than normal during the inspection
- General housekeeping, for example:
 - Securing sufficient room space (inspectors interview/reviewing room; a room large enough for the close-out meeting; a secure area for storing documents pre- and post- an inspector’s review; the back-room area)
 - Ensuring any dietary requirements of inspectors will be covered for meal and refreshment breaks
- Retrieve (and review) any documentation the inspectors have requested in advance for the start of the inspection
- Ensure that all staff who are involved with any recent issues are fully aware of the current situation
- Review the production/testing schedule.

Employees

The more challenging preparation is ensuring that all employees are inspection-ready; personnel are usually the most variable part of any organisation. Personnel must be prepared and trained to answer questions from the inspectors, so this will be the main focus of the rest of this article.

It is critical that all site employees, but especially those who could come into contact with an inspector (for instance, drivers, security, janitorial and catering staff), should have the information and training on the background, requirements and outcomes of the inspection.

All trained staff should be competent and confident to be able to explain what their job entails, how they perform that job and why they need to perform their role. However, often training plans do not necessarily cover what to expect during an inspection and, perhaps more importantly, how to respond to questions from the inspectors.

Whether being asked questions in the document review area or during a site tour, this can be a daunting experience, especially for staff who may not have experienced an inspection previously. This is fundamental preparation for employees and SMEs should therefore be part of ongoing targeted training and not be “fast-tracked” as soon as an inspection is imminent.

The training for the preparation of staff for an inspection can be done by undertaking self-audits/inspections on a regular basis, and to complement this, a programme of audits should be planned on a regular basis, which should be a mix of system audits (eg, of specific

phases of manufacturing and testing) and “on the spot” inspection (eg, reviewing a completed manufacturing record with the operator). Self-inspection is of course a GMP requirement.

This training by itself will not be sufficient preparation for a regulatory authority inspection as there will always be an element of familiarity between the auditor and the auditee. Therefore, using consultants to perform mock inspections is an ideal method to prepare employees. Often consultants are available who were previously inspectors, which adds to the authenticity of the situation. While the main purpose of the training should be preparation of the employee, the consultant could also highlight issues with processes or systems that have not been exposed previously and therefore can be added to a risk log to be managed by the normal process.

The outcomes from both training audits and inspections should be reviewed and lessons learnt. All activities must be appropriately documented.

The role of the subject matter expert

It is important to recognise that a specific set of skills and training is required to successfully and accurately present the organisation to the inspection team. An advantage that is sometimes overlooked ahead of an inspection is the fact that the organisation and its employees are in the position of being by far the most knowledgeable about its products and processes. A prepared SME should therefore be in a position to address any question in their field of expertise, and back it up with appropriate documentation and data. The role of the back-room (discussed later) is to support the SME in this endeavour.

It should be recognised that the best SME to interact with the inspectors may not necessarily be the most knowledgeable individual, if they are not temperamentally suited for the role. However, these individuals can play a valuable role, to back up the SME and anticipate the direction of questioning to allow pre-emptive preparation.

SMEs must ensure they are equipped with a set of skills and behaviours to enable them to engage with inspectors who are equally well-trained in asking questions and evaluating the answers that they receive. SME skills and behaviours include:

- Thorough knowledge of their subject, plus site systems and processes
- Awareness of any current issues and risks
- Confidence and good personal presentation skills
- Ability to perform under stress.

There are additional skills required to listen, comprehend and answer any questions from the inspector:

- If you don’t know the answer to the question asked, state this and where possible, suggest a person who may be able to answer
- If unsure of what the inspector is requesting, be ready to ask for clarification
- Awareness of body language and facial expressions, which can convey far more than the actual words spoken
- Adhere to facts only and do not offer personal opinions
- Only answer the question asked; provide no additional information
- If asked a closed question, then answers of “Yes” or “No” are acceptable and no further explanation should be required or given
- Be aware, and be comfortable with silence. If the inspector is silent after an answer, there is no need to fill the silence with further information
- The inspectors might be unfamiliar with the processes on site, therefore make no assumptions about their knowledge, but also don’t stray away from the question
- For answers or clarifications that require detailed explanations of

a site system, request the documentation and allow the inspector to review the system, answering further questions if asked

- Avoid the use of jargon, undefined technical terms or acronyms
- Avoid using the commercial name only for equipment; use the generic name, adding further information if required to ensure the inspector knows exactly which equipment is being described
- Understand that the inspectors are always working. If they happen to chat to you informally, such as during breaks, this informality ends when the break ends. The inspectors have a job to do.

The role of the back-room team

An organised and efficient “back-room” enables the hosts and SMEs in the Interview Room to concentrate on the task of answering the inspectors’ questions and presenting any requested information. The specific roles and processes of the back-room team should be identified in advance and assigned appropriately, but may vary dependent on the type and size of the inspection. Generally, the back-room team should comprise and be equipped with:

- A thorough knowledge of past and current issues and risks
- A defined process to identify, retrieve, log and provide information and documents to the Interview Room
- The ability to anticipate questions and request and prepare documentation and SMEs in advance of inspectors’ requests
- The experience to predict concerns that an inspector might have, based on the questions being asked. This may include being able to recognise when a question is being repeated by different inspectors, or variants of the same question are being used. A real-time, electronic scribe system provides a means for the

back-room team to be able to ascertain what is happening in the Interview Room

- A process by which any identified issues can be remediated before the completion of the inspection, offering an opportunity to take them “off the table”
- A process of feeding back at the end of each day of the inspection, so that the following day can proceed without delay. This may need resource to work non-standard hours.

At the completion of the inspection, it is important to communicate the outcomes to all necessary stakeholders. Action plans should be agreed and implemented to resolve and respond to any issues that have been identified, within the required timelines. Even following a successful inspection, there will be opportunities to identify areas for improvement, both within the wider business and the inspection management process itself. Such outcomes should be built into continuous improvement programmes to enhance readiness for the next time.

Conclusion

To achieve a successful inspection by a regulatory authority requires the coordination of a great number of processes and individuals. A state of inspection readiness, including defined management processes, communication plans, trained employees, a culture of good practice, and rehearsal, enables an organisation to be able to present itself in the best possible light. When properly effected, any inspection, while possibly never enjoyable, can be undertaken with minimum disruption and in the knowledge of a positive outcome. ■