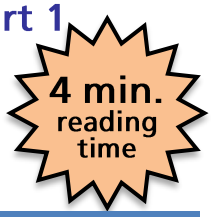
Inspections & Audits: Pitfalls and Criteria for Success – Part 1

A summary of the GMP DIALOGUE at the GMP-BERATER Tage 2017



by Sabine Rabus and Christine Gräßlin

The MRA between the USA and the EU has been in effect since November 2017. What is this resulting in? The results of our survey "GMP Compliance Index" show that audits are perceived differently from inspections. And almost everyone has experienced GMP inspections and audits either directly or indirectly. What are we learning as a result of this, and where do we need to make improvements? What is the best way to prepare for inspections and audits? What things need to be taken into account?

In the following, you can read a summary of the questions and answers that arose during the discussion at our GMP conference, the GMP-BERATER Tage 2017. GMP inspector Dr Petra Rempe and Annette Könemann, manager of the quality department at the laboratory L+S AG, responded to questions from interested GMP Publishing customers.

What right does a company have to prompt inspection reports? Will the relationship with the inspector worsen if they are requested? What is the situation regarding foreign inspections?

Every company to be inspected has the right to an appropriate inspection report. Since the issuing of a certificate by the German authority must take place within a 90-day period, it may be requested by the end of the time frame at the latest. In the case of foreign authorities in contrast, there is no legal basis for a specific time frame, and you need to have the appropriate patience.

How can such a situation be "defused"? The company can present an "action plan" to the authorities, for example, stating that although no inspection report is yet available, they have already prepared an action plan on a proactive basis. That gives the authorities the time to respond and compile an inspection report on a prompt basis.

How binding are oral agreements to an inspection in a case in which an inspection report still hasn't been received after three years? What approach should be taken if you are subject to another inspection in this period without the previous inspection report being available?

That's a difficult situation. The best approach in such a case is taking the "short official channel", i.e. asking directly what action the company itself can take. In this case, providing the authority with an action plan, for example, is also recommended. This shows that work on resolving the "areas of weakness" is under way and that the implementation has started without the provision of a report.

After a final audit meeting, at which all participants are in agreement, the company nonetheless fails to agree with the subsequent, identical report. What happens in such a case?

That is certainly a difficult situation for which there is no patent remedy. In the case of authorities, i.e. inspection reports, such situations do not arise. They arise more frequently during a customer audit. The following applies to inspection reports: according to the German Medicines Act (AMG, section 64 (3d), conducting supervision), an inspector must also provide the company with a first draft of his/her inspection report. What can be a trigger factor at the customer, however? In this respect, it is necessary to discuss the customer-specific company requirements that have to be taken into account. These are only acceptable if they comply with the EU GMP Guide, however. In general, however, an attempt is made to hold an enlightening discussion in the interests of arriving at a shared consensus.

GMP Experts: Annette Könemann and Dr Petra Rempe

The pharmaceutical manufacturer is responsible for ensuring that only GMP-compliant active ingredients are used. What is the situation with the supply chain, however? How exactly has the manufacturer to know it? What audits should the manufacturer or distributor carry out?

The supply chain must be known to the manufacturer and manufacturers of active ingredients have to be audited. Both manufacturers and distributors operate in a field of conflict. Is a trader also required to perform audits? "Collective audits" can take place on behalf of different customers, for example, whom the distributor contracts. From the legal perspective, the responsibility lies with the manufacturer.

Does an inspector have the right to view the results of self-inspections?

As a general rule, inspectors ask about the appropriate documents and the point in time of a self-inspection, in other words, "what was done and when". The inspector does not need to be shown more than a cover-sheet. The inspector does not have any right to view the documents. Self-inspection is the instrument of the company and not of the inspector.

"Pro forma SOPs" – how should these be approached? Are they really necessary?

Customers expect that for certain topics – e.g. CAPA or data integrity, – SOPs are available, and they make use of them to gain an overview. In this respect, superordinate SOPs are necessary, especially for the area of risk management. If the methods that are used in the company have been defined, specifying these once in superordinate SOPs and then providing an appropriate note in other SOPs is sufficient. In this way, these "superordinate" and/or "pro forma SOPs" also serve the purpose of defining themselves and their methods. They are also very helpful for inspections/audits. In general, this type of SOPs are also to be understood as being higher-level documents and not as an everyday working tool.

Are in-house audits necessary if a company has several sites?

There should be a global quality department which audits all the manufacturing sites on a centralised basis. There has to be a "responsibility matrix" which clarifies which site is responsible for what.

What about quality defects? Where are most of the inspection findings?

In this respect, the key topics are qualification, validation of testing methods and also the documentation in the laboratory. Qualification is often an area of conflict. Who qualifies and what should the qualification documentation look like? Are the user requirements specifications (URS) defined? Are the "responsibilities" clarified with the machine qualification, for example? Has

Annex 15 been correctly implemented? How are quality defects handled? All of these questions should be clarified in advance. This may be lacking at the practical level, however. It is frequently the case that these clarifications do not take place. If a systems manufacturer is not in a position to perform the qualification, the pharmaceutical company is responsible for the task. The URS should ideally be prepared by a multidisciplinary team. In this way, a transfer of know-how can also take place that all participants are able to benefit from.

The article will be continued next week in LOGFILE 14. In part 2 you'll read about auditing small-volume suppliers and typesetting studios, as well as about how you should approach known areas of weakness during an inspection.

Authors:

Sabine Rabus
Maas & Peither AG - GMP Publishing
E-Mail: sabine.rabus@gmp-publishing.com

Christine Gräßlin
Maas & Peither AG - GMP Publishing

