Questionnaire for preparing GMP-inspections

More than 650 typical questions related to audits and inspections

Each question with reference to the current EU GMP Guide Part I/II and the 21 CFRs 210/211/11

For auditors and manufacturers of drugs and APIs

Audit Questionnaire

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Questionnaire for preparing GMP-inspections

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Here you will find answers to the following questions:
- What questions are typically asked during inspections based on current rules and regulations?
- Which reference documents (e.g. CFR, EU GMP Guideline, IPEC) comprise the GMP-requirement in question?

Supplier audits as well as inspections by the authorities are, in many regards, stressful situations for the auditee. There is generally a great deal hanging on the result of the inspection, whether it is an order from an important customer or approval for a new product. This means that all the members of staff involved in the inspection are under intense psychological pressure, which can make it difficult to present normally self-evident processes to the inspector in a comprehensible way and to answer questions fully and correctly.

Common concerns include the following:
- Will we be able to provide the correct answers or explanations to the questions posed in spite of general nervousness?
- Can we prove everything with documented evidence?
- Can we explain that (and how) our GMP or QA system works?
- Is our GMP status adequate?
- Will the staff make oversights because they feel watched or because they are scared to fail?
- Will the inspectors set "traps"?
- Will someone be caught out by their own reasoning because they want to make a particularly good impression?
- How will we stand internally after the inspection, e.g. with regard to other departments?

Only preparation can help to relieve these uncertainties and **self-inspection** can play an important element of this (Kapitel D.7). The advantage of a self-inspection is that you can play with an open hand and any deficiencies that are recognized can be corrected immediately. The disadvantage is that an internal auditor is generally too familiar with the individual processes (even to the extent of wearing professional blinders) and only uses the internal terminology.

This only reflects the reality of an inspection by the authorities or a customer to a limited degree: here, the auditee may find himself confronted with terms or questions that he had not considered in the same way. The generality of a question is often a worry: what is the meaning of "adequate water systems"? What is the inspector driving at when he asks about "suitable equipment" or "qualified personnel"? Even the terms used in the GMP rules and regulations do not always correspond to the expressions used in the company and can cause uncertainty: for example, if the "test procedures" are queried, does this mean the control procedures, the testing instructions, the testing plan, the analysis procedure, the IPC instructions, the calibration procedure or the stability plan? What does "process instruction" mean in a particular instance? The manufacturing formula in accordance with EU GMP, the processing instructions in accordance with EU GMP, the manufacturing description in accordance with CFR, the master production record in accordance with CFR, the batch production record in accordance with CRP or even an SOP?

Suppliers, in particular, who have generally structured their quality management system according to ISO 9000 or recently ISO 9001, use very different terms than the GMP inspector of a customer, for example. How do "quality planning", "quality control", "quality assurance" and "quality improvement" translate into GMP terms? Is "OOS" concerned with quality fault management or remedial actions? Can SPC and the concept of validation be made consistent?

For suppliers, an aggravating factor is that they are often confronted with GMP requirements that the pharmaceutical customer has been only too eager to pass on to the supplier. However, on closer inspection, many of these customer requirements cannot be traced back to legal requirements because they only relate to pharmaceutical products and not to the active pharmaceutical ingredient, excipient, packaging material or item of equipment.

To prepare for such general questions, an external consultant can be appointed to carry out a **mock inspection**. On the one hand, this allows the "real situation" to be tested and, on the other hand, it allows any weaknesses to be identified, which would not be obvious internally.

Alternatively or in addition to this, it is worth using checklists to deal with the questions that a GMP inspection may typically bring up. These can be considered carefully beforehand, e.g. which internal documents need to be kept at hand for a certain question – this will save some moments of panic during the inspection. Some US inspectors, in particular, like to use checklists, such as those in the Compliance Policy Guides or Compliance Policy Manual, to prepare themselves for the inspection. These sorts of checklists can also be used by the auditee as a useful preparatory aid.

However, when using **checklists** to prepare for an **inspection**, it must be taken into consideration, that:
- Simply filling in these lists can at best provide an initial overview. However, it does not replace the intensive challenge of the individual Quality System in place.
- Checklists can never be as comprehensive, exhaustive or specific enough to do justice to the situation at every (pharmaceutical, supplier, packaging, etc.) company with all the various product ranges, different equipment pools and organizational differences.
- On the other hand, it will also include many questions that may not be applicable to the particular (pharmaceutical, supplier, packaging, etc.) company. However, it is still useful to be prepared for these questions so that you are not irritated during the actual inspection and can point out that a certain requirement only applies to pharmaceutical products, for example and not to active pharmaceutical ingredients, etc.
- Specific national legal requirements may have to be considered in addition.

A list of questions can also be useful for the auditor when preparing for the inspection to ensure that all the relevant aspects are discussed. Nevertheless, an inspection is not only about asking the right questions, but also assessing the corresponding answers. A checklist cannot take on this task. The checklist alone is often unsatisfactory for documenting the findings during the inspection (e.g. marking yes or no). More meaningful descriptions are very important in order to classify the deficiency (Kapitel D.7).

The following is a catalogue of typical general questions, which may be asked during an inspection. The questions are referenced to the corresponding GMP regulations. In cases of doubt, the relevant original text can be quickly found.

A table divided up as follows is recommended for documenting the answers during an inspection:

Question	yes or fulfilled	partially fulfilled/ acceptable	partially fulfilled/ not acceptable	no	Comment/examined document
1.					
2.					
etc.					

Typical audit questions		Assessment				CFR reference	EU GMP Guideline
		yes/met	partly met/ accepted	partly met/ not accepted	no		
4.10	Are measures taken to avoid cross-contamination?	☐	☐	☐	☐	211.42	3, 3.6, 3.8, 3.14, 3.15, 3.22, 5.9, 5.17–5.21 Part II: 4.13, 4.42
4.11	Ventilation						
4.11.1	Are the ventilation and air conditioning systems qualified, are they regularly maintained and checked?	☐	☐	☐	☐	211.46	3.3, 3.12 Part II: 4.21
	• Are there separated ventilation systems for highly active agents?	☐	☐	☐	☐	211.46	3.6
4.11.2	Are filters regularly changed and checked?	☐	☐	☐	☐		
4.11.3	Is a cross contamination in the ventilation and air conditioning system ruled out (circulating air, waste air, air flow)?	☐	☐	☐	☐		Part II: 4.21
4.12	Control of temperature and moisture						
4.12.1	Do constant conditions exist concerning temperature, moisture and, if applicable, particle and bacterial count?	☐	☐	☐	☐		
4.12.2	Are temperature and humidity constantly checked?	☐	☐	☐	☐		
4.12.2.1	Storage rooms?	☐	☐	☐	☐		3.19
4.12.2.2	Production rooms?	☐	☐	☐	☐		
4.12.2.3	Rooms with sensitive appliances?	☐	☐	☐	☐		
4.12.2.4	Are all measures taken in case of overrun or lower deviation?	☐	☐	☐	☐		1.4 ix
4.13	Is the lighting adequate?	☐	☐	☐	☐	211.44	3.3, 3.16 Part II: 4.5
4.14	Are the installed finishes for the walls, ceilings and floors capable of not emitting particles into the room?	☐	☐	☐	☐	211. 42c10i	3.9
4.15	Are the rooms easy to clean and, if necessary, to disinfect?	☐	☐	☐	☐	211.42 211.56	3.9, 3.14 Part II: 4.10
4.16	Is the access to GMP-areas restricted to authorized personnel?	☐	☐	☐	☐	211.28c	3.5, 5.16
4.17	Is it ensured that production areas are not used as a passage by staff members who do not work in these areas?	☐	☐	☐	☐		3.5
4.18	Do the personnel enter production areas solely via the changing rooms, or via the double door system (if applicable)?	☐	☐	☐	☐		
4.19	Is it ensured that street clothes are not taken into rooms with specific requirements?	☐	☐	☐	☐		Annex 1: 20, 42
4.20	Are Quality Control laboratories separated from production areas?	☐	☐	☐	☐		3.26–3.29 6.5 Part II: 4.16
4.21	Are the water systems adequate?	☐	☐	☐	☐	211.48	3.43 Part II: 4.30, 4.34
4.22	Are waste and sewage disposed of safely and hygienically?	☐	☐	☐	☐	211.50 211.56a	3.11 Part II: 4.24, 4.6

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