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Know How - Design Pharmaceutical Qualification Processes Efficiently

An interview with GMP expert Ralf Gengenbach, gempex GmbH

**The question of whether pharmacists implement GMP compliant qualification of production facilities or the validation of associated processes no longer arises today.
Today, the question is how the effort can be kept as low as possible in order to ensure GMP compliant product quality, whilst maintaining productivity at the same time.
Read our interview with GMP expert Ralf Gengenbach, Managing Director of gempex GmbH, who discusses where there is room for optimization in qualification.**

Mr. Gengenbach, what does the concept of qualification according to the GMP guidelines mean?
Qualification is a sub-topic of Good Manufacturing Practice (GMP) and is mainly used for pharmaceutical quality assurance. This is documented evidence that a technical system meets all of its requirements and provides the required performance. The technical system, respectively the plant, should be correctly specified, installed and reliable. According to this definition, the qualification has been in existence for years.

If you say that the qualification already exists according to the definition, are there still difficulties in understanding the implementation of the qualification?
Absolutely and unfortunately again and again. The problem is that the subject of qualification is often confused with the checking and testing of a technical

Ralf Gengenbach

After completing his university education as a chemical engineer at the Technical University (TU) Karlsruhe, Ralf Gengenbach started his professional career in 1987 at BASF AG, Ludwigshafen.

For more than 10 years he acted as an internal GMP consultant, where in addition to establishing an efficient and cost-oriented qualification system in numerous specialist committees on this and similar topics, he also contributed at the German Institute for Standardization (DIN), the Association of the Chemical Industry (VCI) and the Society for Chemical Engineering and Biotechnology (DECHEMA). Early on he was involved in the drafting and commenting of the "Pharmaceutical Inspection Co-operation Scheme" (PIC / S) document PI006 (validation) and the Q7 GMP guidelines of the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH).

After a further professional stopover, in 2002 he founded gempex GmbH, an international GMP service company.
In addition to numerous publications and lectures, he has summarized his accumulated knowledge in the book "GMP, Qualification and Validation of Active Substance Plants" published by Verlag Wiley-VCH.

system. A qualification is documented evidence of a desired condition and is not a test of a system, device or software. This means that ideally, the qualification only begins after successful testing and when all errors in the engineering area have been fixed. A nice example is a typical vacuum cleaner salesman: He demonstrates the suction power of his device at the trade fair without first testing it on site. If he were to document the suction power, we would speak of a qualification.

A nice illustrative example. An interim question: How does the pharmaceutical manufacturer ensure that the equipment of the supplier/service provider works perfectly within the framework of its qualification?

The pharmaceutical manufacturer can delegate the task of qualification to its suppliers, but ultimately the pharmacist remains responsible for providing evidence of correct performance. As a customer, the pharmaceutical manufacturer must therefore check and formally approve all documents that serve the purpose of qualification and therefore has the corresponding responsibility to provide evidence.

GMP is increasingly allowing the pharmaceutical manufacturer to refer to the technical test documents of the system suppliers or the engineering department - provided that they ensure beforehand that the technical tests are carried out and documented according to the relevant specifications. Previously the pharmaceutical company more or less created checklists and sometimes repeated tests as far as it could. Today, the authorities and regulations allow a reference to the technical documentation of the device manufacturer if it is mutually agreed as to how the supplier carries out the tests and the documentation.

That means the documentation of the qualification does not have to be as extensive as it is often assumed?

Exactly. The more good and solid technical documents such as standardized design drawings or function plans available (these should be used as a proof basis), the fewer documents have to be prepared in the qualification. This makes the qualification process leaner and many times more efficient.

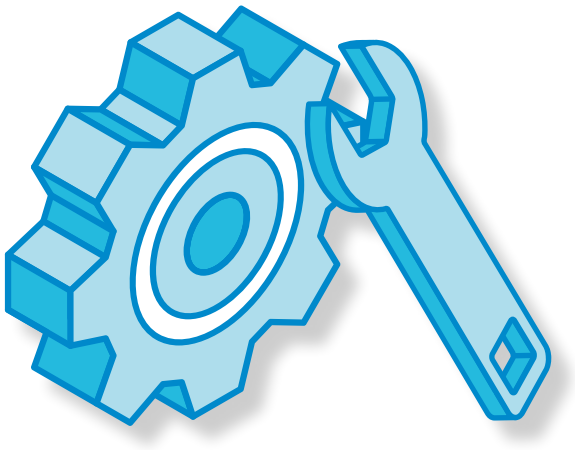
Why is there room for interpreting the specifications and implementing them?

Good Manufacturing Practice provides general guidelines and not detailed standards as to what to look out for in an individual system. The field of devices, systems and technologies that are used in the pharmaceutical industry is so broad that there cannot be a standard for every technical system. In fact, I myself only know one ISO standard for a technical device in relation to the subject of qualification, which also makes suggestions for documentation. Due to this variety of systems, it will not be realistic or possible to write a standard for carrying out the qualification for each system, e.g. a dosage, a scale, a filling, etc. The guidelines are therefore kept general and consequently the task of testing should be left to the engineers and thus often to the system manufacturers; the qualification should then refer to it.

What do you see as the greatest challenge in terms of qualification - especially when errors occur?
If the qualification is purely an obligation to provide evidence, then the prerequisite for this is a high-quality, technical product. If errors from Good Engineering Practice (GEP) creep in during qualification, the qualification process becomes very complex and many times more expensive than if the errors were discovered and eliminated as part of the GEP. Why? If the engineers or technicians in the factory have completed a system and discover an error while performing the functionality test, then this error is corrected or, if necessary, repaired. The responsible technician can tick the checklist that is often used. This is the usual troubleshooting in the technical field.

However, if the error were to appear in the course of qualification, it is a deviation in the sense of GMP and no longer a "simple" error. This means that an extensive root cause research and an extensive error interpretation must be carried out, which can easily result in five to six pages of documentation. It is then important to edit these pages, fill them in and let them circulate in the various specialist departments, including the manufacturer and the quality unit.
The bottom line: The worse the engineering process is, i.e. there is no Good Engineering Practice (GEP), the more complex the qualification process becomes.

Is the elimination of errors within the qualification more of an isolated case?
Unfortunately errors in qualification are not uncommon, especially when it comes to larger projects. This is mostly due to the issue of time pressure. In order to act quickly and to be able to deliver products quickly, final tests or inspections are consciously or unconsciously pushed into the qualification.



From our many years of experience, we can say that postponing the tests has the opposite effect: the costs and the planned project duration are many times higher or longer. An example: We supervised a project to qualify an autoclave that is used for sterilization. Such a qualification usually takes four to six weeks. Due to the many technical errors that emerged in the qualification, the project ultimately lasted six months, which actually led to production losses. Unfortunately, we have seen projects fail for this reason.

The key to efficient qualification is therefore good engineering.

The risk analysis is the central tool of qualification. What do you need to consider?
The authorities expect pharmaceutical manufacturers to focus on the critical elements during qualification. Aim is to ensure that the pharmaceutical manufacturer understands its process absolutely and does not create documents just like that, but has a targeted overview of the risks of the individual systems and their effects on the entire process or the end product. The pharmaceutical industry today speaks of the so-called CQAs and CPPs. CQAs are "Critical Quality Attributes" - critical properties of a product or intermediate product at a specific process point. The CPPs, the critical process parameters, are derived from these properties. These parameters are the requirements for a system, e.g. temperature or pressure. As an example: By means of a risk analysis, the critical points in the interaction between the scales, dosing unit and a pump are considered and then the focus is on these parameters during the qualification. The risk analysis therefore helps to concentrate on these critical points and thus reduces the qualification effort to the essentials.

Many project partners come into play when implementing a validation and qualification project: How can suppliers and pharmaceutical manufacturers work together successfully in order to meet the high requirements efficiently?
There are intensive efforts to harmonize the interaction between suppliers, engineering and pharmaceutical manufacturers. This starts early with the planning and becomes particularly important in the so-called EPC (Engineering, Procurement and Construction) and commissioning phase. There is also a guideline that gives recommendations on communication channels, project schedules and the distribution of tasks between the partners involved, particularly with regard to qualification. There are many points to consider that go far beyond the topic of qualification, so that the cooperation between all parties involved goes hand in hand over the long term or on a project basis.

What risks do pharmacists take when qualification concepts are made leaner?
Actually none! I would put it another way: Often the required GMP and qualification activities are clearly exaggerated in order to be on the safe side. This is usually not in the interest of the inspecting authority, because it is not clear at a glance whether the pharmaceutical manufacturer has recognized its critical control points in the process. In my opinion, the good and close cooperation with suppliers, designers and engineers offers the greatest safety.

Thank you for this interesting interview.

Would you like to find out more?

Are you interested in the topic of qualification? On https://www.gempex.de/gmp-knowledge/ you will find a number of articles that deal with qualification.

The GMP experts at gempex will be happy to answer any further questions you may have:
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