# Basic Principles of an Effective and Efficient Qualification*)

Suggestions for practice – Part 3: Here we go – the implementation

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*This article is part of a 4-part series. Part 1 deals with basic principles, part 2 with planning, part 3 with implementation and part 4 with comparison with the rules and regulations.*

**Basic terms are defined, the concept for how to proceed is fixed, the scope of qualification is identified by means of risk analyses and listed in master documents. Roles and responsibilities are aligned on the part of the pharmaceutical manufacturer, GMP-relevant requirements for the technical systems are clearly described. So, nothing stands in the way of implementing the project – or does it? At this point at the latest, many other parties – manufacturers, suppliers, construction companies, in short: the project partners – come into play. In the so-called EPC phase (Engineering – Procurement – Construction) the project gains up speed and the full dynamics and complexity appears. Now it proves how good a developed qualification concept is, how easy or difficult it is to integrate suppliers and their input. Now GEP meets GMP and the topic of "integrated qualification", the combination of normal engineering activities and activities of qualification, would come to full fruition and could increase the efficiency of the project if the process were sufficiently established, which unfortunately is not yet the case consistently.**

**The following article deals with the topic of selection and involvement of the parties involved in the project, with the necessary quality systems and agreements, with the targeted use of tests carried out by the supplier in the factory (FAT) and on the construction site (SAT). The typical qualification activities related to Design Qualification (DQ), Installation Qualification (IQ), Operational Qualification (OQ) and Performance Qualification (PQ) are discussed and at the end it is briefly explained why there are no (or very few) real fast-track projects. In this article, too, the activities, not the documents and not the terms, should be in the focus.**

## With the Best to Success/ Supplier Qualification

Everyone would like to have them, and everyone would like to work with them, "only" with them – the

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started his professional career in 1987 at BASF AG, Ludwigshafen, after his university study as a chemical engineer at the Technical University (TU) Karlsruhe. For around 10 years he acted as an internal Good Manufacturing Practice (GMP) consultant. Besides establishing an efficient and cost-oriented qualification system, he also was active in numerous technical committees and associations on this topic, among others for the German Institute for Standardization (DIN), the German Chemical Industry Association (VCI), and the Society for Chemical Engineering and Biotechnology (DECHEMA). He was early involved in the preparation and commentary of the "Pharmaceutical Inspection Co-operation Scheme" (PIC/S) document PI006 (validation) and the Q7-GMP guideline of the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH). After another professional interlude, he founded 2002 the gempex GmbH, an international GMP service providing company, which he still is managing today. In addition to numerous publications, lectures, and talks, he has summarized his accumulated knowledge among others in the book "GMP, Qualification, and Validation of Active Pharmaceutical Ingredient Facilities" published by Wiley-VCH.

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best suppliers, manufacturers, installation companies and/or service providers. And of course, even more so when it comes to particularly quality-critical technical systems and plants. The selection is easy – you look for well-known names, carry out a supplier audit "quickly", look at the typical references and if the price is right, the matter is done!? Far from it – the fact is that it's not only the companies and the products that matter, but also their experts. In a booming market with increasingly shorter delivery times and a lack of specialists, there can't be as many highly experienced experts as the market actually needs. Therefore, other aspects become important, like e.g., the standardization and in connection with it the manufacturing, test and quality assurance processes established in the enterprises. And these must be questioned very specifically and intensively, at the latest in the context of supplier audits. A simple questionnaire or a quick visit is not enough. Information such as company history, size, creditworthiness, established technologies, developments, certifications, and references are certainly important, but the following questions are even more important (starting e.g., from a system supplier):

- How is the incoming goods inspection carried out, especially in connection with pre-tested components and certified materials (metallic materials, elastomers)?
- How is certificate management carried out and how is it prevented that certified and non-certified materials (e.g. Elastomer seals) are mixed up in the further production process?
- How is it ensured that production is only carried out based on approved technical documents and how are resulting changes in the production process dealt with?
- How is document management regulated regarding technical documents, version controls, red master documents[1)] etc.?
- Which intermediate quality inspections are established and how are these and their results documented?
- What manufacturing controls are there for the final product and at what level of detail are they recorded?
- To what extent and how detailed are test specifications available, especially for the FAT and SAT phases?
- What is the condition of measuring and auxiliary instruments used in quality control (e.g., Calibration)?
- Which project management processes have been established, especially when it comes to companies that will later be involved in the construction of the plant on site at the customer?

These and more questions are to be directed specifically to the company being selected. It is not enough to receive the answer verbally or in a PowerPoint presentation. It is important to convince oneself on site of the existence of the processes and their active implementation – e.g., on the basis of already completed projects and their documentation.

This is not to assume that these companies only specify quality processes without having established them. But it is also true that the core competence and focus of manufacturers and suppliers in particular is more on the products, while the requirements for extensively documented quality assurance on the part of the customer are far more important and not insignificant for the end result (GMP compliance). And so, it is unfortunately not uncommon that there are often surprises and many discussions when working with suppliers, especially when it comes to documentation.

The supplier audit is certainly an important and established method to convince oneself of the quality of one's project partners. However, this is limited to the project critical suppliers who provide process and quality critical systems or services. Time and budget constraints usually do not allow – and it does not make sense – to subject each individual project partner to an intensive audit. There are additional tools, described below, to ensure the necessary quality.

## Rules of the Game on the Construction Site/Project and Quality Plan

Regardless of the quality assurance system of the respective project partner, it is important and always recommended, especially for complex projects, to regulate the cooperation and communication between the parties early and in detail for each individual trade. This ranges from the architect to the building contractor to the clean room builder, the installation companies and the equipment and system suppliers. The most important topics, which are to be regulated specifically for a project, include beside others:

- the project organization with roles and responsibilities
- communication in relation to contact persons, jour-fixe meetings to be arranged, e-mail communication, distribution lists and project notes
- the regular progress report including defect and deviation report
- document management, including labeling, version control, circulation, filing, archiving (this should also include setting deadlines for review and release, as well as handling copies intended purely for information purposes)
- the change management valid for the project phase with regulations for documentation and coordination

[1)] Master copy of a technical document (e.g., Design drawing) in which all changes are first entered manually in red until the next version is created.

- the definition of important breakpoints and decision points, including the persons responsible for the decision, and the way decisions are documented
- the definition of detailed planning and production processes with regard to interfaces to the client or to other trades, in particular interfaces to the quality unit of the client and subsequent plant operator
- escalation management to escalate critical problems that cannot be solved at certain levels, which then have to be solved at the next higher decision-making levels

Again, the list is not complete and may vary in scope and level of detail depending on the project. It has become established practice to record such regulations in a "Project and Quality Plan" (PQP), which is either prepared individually by the respective project partner or centrally by a project controller or a superior engineering unit. The centralized variant is to be preferred for highly complex projects with many project partners. A prime example can be found in the new guidelines for integrated qualification and validation published by the European Compliance Academy (ECA) [1].

Regardless of the name of the document, it is again essential that the contents – the work processes – are described in detail and specifically: *Who does what, how* and *where* is it documented. A copy & paste document with very general wording will not support the quality. An example of a detailed workflow in connection with technical documents was described in a previous publication [2].

The following important empirical values can be added to the above-mentioned regulations themselves:

- For e-mails e.g., we recommend setting up central project e-mail accounts. These accounts can be used for individual distribution lists, so that all communication is stored in a single e-mail archive.
- Basically, in project communication, e-mails should be regarded as verbal communication. Important information should rather be attached to the e-mail in a document, not in the e-mail itself. This simplifies filing and tracking.
- With notes it is recommended to arrange these as pure "result notes", i.e., only the results, definitions and To-dos of a meeting are documented, no prose.
- The most important control elements of a project are and will remain the project schedule and a continuous open points list, which is at best divided by trades, but is managed centrally. It is important to track *who* has to do *what* by *when*.
- A critical point are the interfaces to the quality unit of the future plant operator. Since this is generally associated with additional personnel resources and time expenditure, the integration should be reduced to what is necessary from a regulatory point of view and sensible for the later product quality. The integration of the quality unit in all technical details does not seem to make sense.
- Change management can also become a project obstacle if you try to handle all changes completely. Therefore, it should be tried to focus on the change of important quality-relevant facts that are normally defined in the user requirements specification (URS).
- Finally, the topic of "deviation management" should be mentioned once again. Here, too, it should be clearly defined in the PQP at an early stage e.g., what is a technical defect that still needs to be remedied, which is usually listed on a simple punch list, and what is a critical deviation, where the quality unit comes into play again, causes must be determined and evaluated. Here, too, the user requirements specification and the acceptance criteria derived from them can be used to define what constitutes a deviation from these specifications.

The list can be expanded as desired but would then belong more to the topic of good project management than to the topic of qualification.

## The Expert is Needed/Design Review

The EPC phase begins with the detail engineering, in which specialist engineers and design engineers translate the requirements specified in the user and system requirements into detailed implementation documents. It must be ensured that all requirements are completely and correctly implemented and that general GMP criteria not explicitly mentioned in the user requirements have also been taken into account. The general design-relevant GMP criteria include (depending on products and processes) beside others:

- easy and good cleanability (e.g., smooth surfaces)
- dead space free (avoidance of cross-contamination and germs)
- resistance (suitable metallic and non-metallic materials)
- drainability (avoidance of cross-contamination and germ nests)
- good accessibility for maintenance and calibration etc.

In principle, all "general GMP design criteria" are derived from the requirement that nothing may contribute to any kind of contamination of the product later manufactured in the plant. This, in turn, is essentially directed towards a design that allows good cleanability, in some cases good sterilizability, and also avoids contamination by unsuitable materials. Common standards of ASME, ASTM, EHEDG, 3-A, ISO[2)] and others offer a variety of technical solutions under the titles "Hygiene Design" and "Aseptic Design".

Ensuring the complete and correct implementation of require-

[2)] ASME, ASTM, EHEDG and 3-A are American and European industry associations that have published various standards on the subject of hygiene or sterile design.

ments is mainly done by means of document reviews, the "design reviews". This is a typical engineering task and not exclusively a qualification task. Such a document review is carried out e.g., also with regard to safety aspects. For this purpose, a specialist colleague (four-eyes principle) systematically goes through the created technical document, checks essentially on the basis of his expertise and marks critical points in the technical document. The document is then corrected and revised.

In the case of a GMP-regulated plant, nothing else is required in principle, except that the process must be systematically and thoroughly documented. Ideally, this is controlled by means of a checklist, a review plan that also contains the record protocol. This first defines the technical system with system boundaries, whose execution documents are to be checked. You define the persons responsible for the review and the process, how the review is carried out and how the results are documented (e.g., directly on the technical document). You ask whether all prerequisites for the review are met, e.g.:

- that the user requirements specification for the system are available.
- that these were intensively checked and answered by the system supplier.
- that the requirements were questioned with the help of a risk analysis.
- that the GMP regulations to be observed have been agreed.
- that changes from the original version of the user requirements specifications are documented and taken into account.

Finally, you define those documents that are to be subjected to an intensive review and list them in the log with the most recent revision number. Typically, these include Piping and Instrumentation flow diagrams (P&I flow diagrams), construction plans, layout plans, function plans, ductwork diagrams, specification lists, electrical plans, isometrics, and much more.

For the review itself, the easiest way is to directly mark the technical document with a stamp as a "test document", have the review carried out by a technical expert as described above, and have findings noted directly on the document. The user requirements specification should serve as a checklist and each requirement point should be checked off as "checked" directly or via a traceability matrix. This ensures that no requirement point is forgotten. The checked document must be marked as "checked", dated, and signed at the end.

Non-implemented or incorrectly implemented requirements or drawing errors must be corrected. Deviations from requirements that cannot be implemented as planned must be documented as deviations and discussed with the operator and the quality unit. Processing and filling out the review protocol then leads to the final design review report.

Basically, this is an engineering task, which is why we will first speak of the Design Review Protocol and Report. It can be included as an important and essential part of the design qualification, if the activities have been previously discussed with and approved by the operator's quality unit. However, the review itself should be the responsibility of the technical expert, who must of course be a different person than the planner or designer. The design qualification can then include further test points such as early comparison of the user requirements specification with the supplier specification.

## Technical Tests/FAT, SAT, Pre-Commissioning

It goes without saying that system suppliers in particular – regardless of GMP requirements – test their products at different times and according to their own specifications. This applies in particular after completion at the manufacturing plant as part of the final manufacturing inspection. This usually takes place without the customer and with its own internal documentation. Test points are e.g.:

- complete implementation according to plan
- correct specifications (materials and components)
- Dimensional accuracy and tolerances
- Manufacturing quality (connections, surfaces)
- Installation (arrangement of components, alignment, tightness)
- Basic functions (alarm, switching functions, controller functions)
- Performance parameters (depending on the system and if feasible in the factory)

If the customer is involved (often only a certain percentage of tests), this is now officially referred to as a Factory Acceptance Test (FAT) and is usually based on much more formal documentation, which is also agreed with the customer in advance and in many cases released by the customer. In these documents the tests are listed with implementation instructions and acceptance criteria and the results are entered as "actual values". A distinction is already made here between FAT protocol and FAT report. However, nothing has changed with regard to the test points, they are almost the same as those listed above.

After transport, installation, and connection of the system at its destination, some of the previously performed tests must be repeated – if the transport could have had a negative influence on the test result. In addition, tests must be carried out which were not previously possible in the manufacturer's factory (e.g., because corresponding power supplies were not available). These tests are known as Site Acceptance Tests (SAT) and are formally treated in the same way as the FAT. Here, too, the future operator and his quality unit already have a say.

■ **Figure 1**

| LOGO | CLIENT | | Report No. |
|---|---|---|---|
| | LOCATION | Lot No. | Sub-lot No. |
| | PROJECT | System Description | |

**Mechanical Check List : Drum**

| Item No. | Service | DWG/DOC. No. | Manufacturer | No. of Sheet |
|---|---|---|---|---|
| | | | | |

Inspection

| No. | Check List | Result Yes | Result No |
|---|---|---|---|
| 1 | Check that nameplate details are correct and complete. | ☐ | ☐ |
| 2 | Check location, elevation, orientation and level of vessel. | ☐ | ☐ |
| 3 | Check that baseplate is grouted and the anchor bolts are fully tightened. | ☐ | ☐ |
| 4 | Check for any installation damage. | ☐ | ☐ |
| 5 | Check that vessel and internals are installed in accordance with approved drawings. | ☐ | ☐ |
| 6 | Check cleanliness of vessel and internal. | ☐ | ☐ |
| 7 | Check that pipe flanges correctly align with nozzle flanges when pipe is disconnected. | ☐ | ☐ |
| 8 | Check that all internal bolts are tightened. | ☐ | ☐ |
| 9 | Check all platforms and ladders are in accordance with approved drawings and manways are accessible and suitale for operation. | ☐ | ☐ |
| # | Check painting , insulation, internal lining for damage. | ☐ | ☐ |
| # | Check that manhole covers are ready for closing. | ☐ | ☐ |

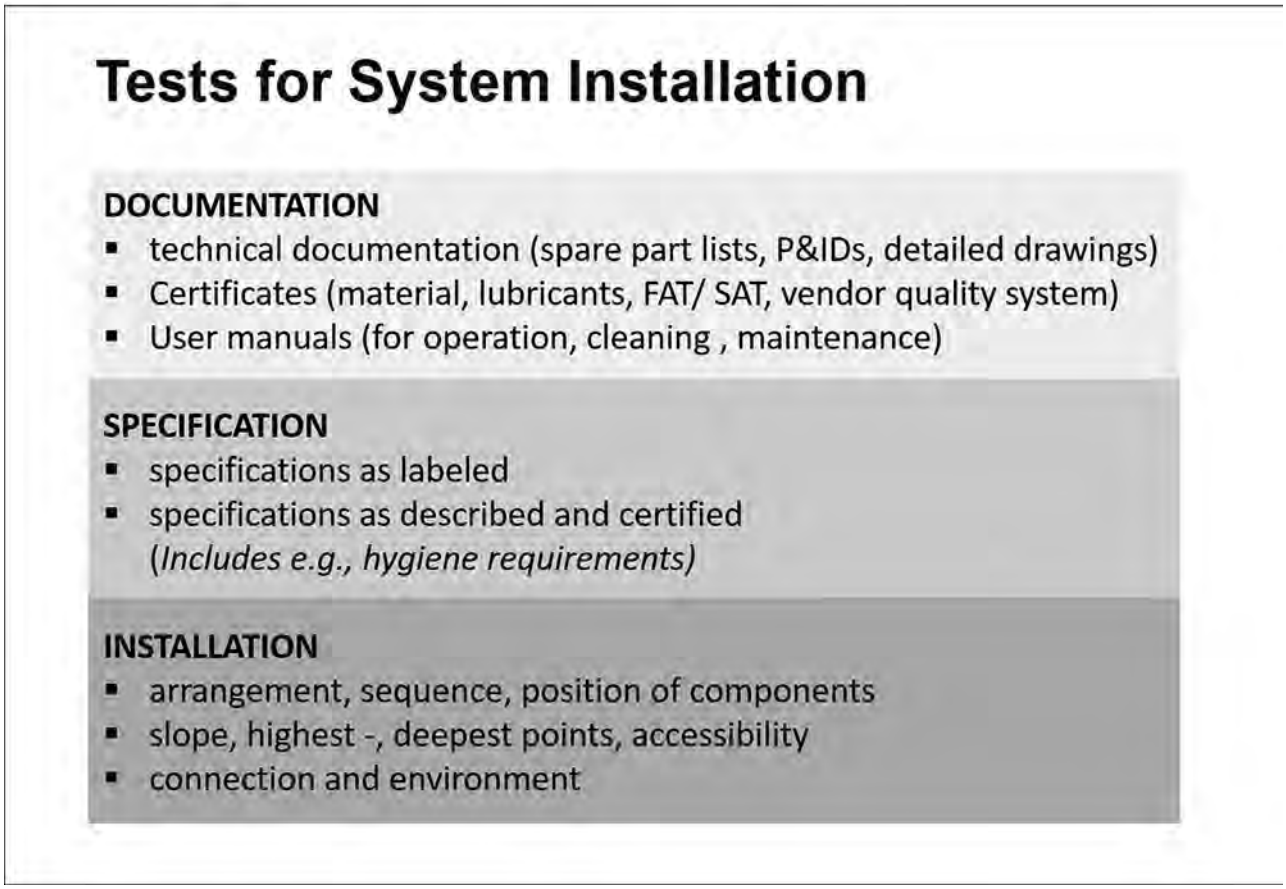
Comments _____

| Inspection Result | |
|---|---|
| Accept | Reject |
| | |

| Prepared by : | Verificado por : | Performed by : | Accepted by : |
|---|---|---|---|
| | | | |
| Date : | Date : | Date : | Date : |

***Example pre-commissioning checklist (source of all figures: the author).***

**Figure 2**




***Typical test points construction and installation.***

The FAT and SAT are the system suppliers' own tests. If the systems are interconnected and connected to form a complete system, further technical tests are required to prove their smooth interaction. This is especially true for multi-component systems, as are common in the field of active ingredient production or biotech plants.

These tests fall under the term "pre-commissioning" and are also carried out according to detailed checklists and often also based on technical documentation. A very well-known example is the P&I walk-down, i.e., the engineer in charge systematically runs the plant on the basis of the P&I drawing and notes down all abnormalities and deviations on this document. Typical supplementary tests are here:

- connection to the correct supply and disposal facilities
- correct interconnection of the systems
- function and control sequences, interlocks, function of safety devices and automation
- leak tightness of the connecting lines
- general integrity and accessibility, etc.

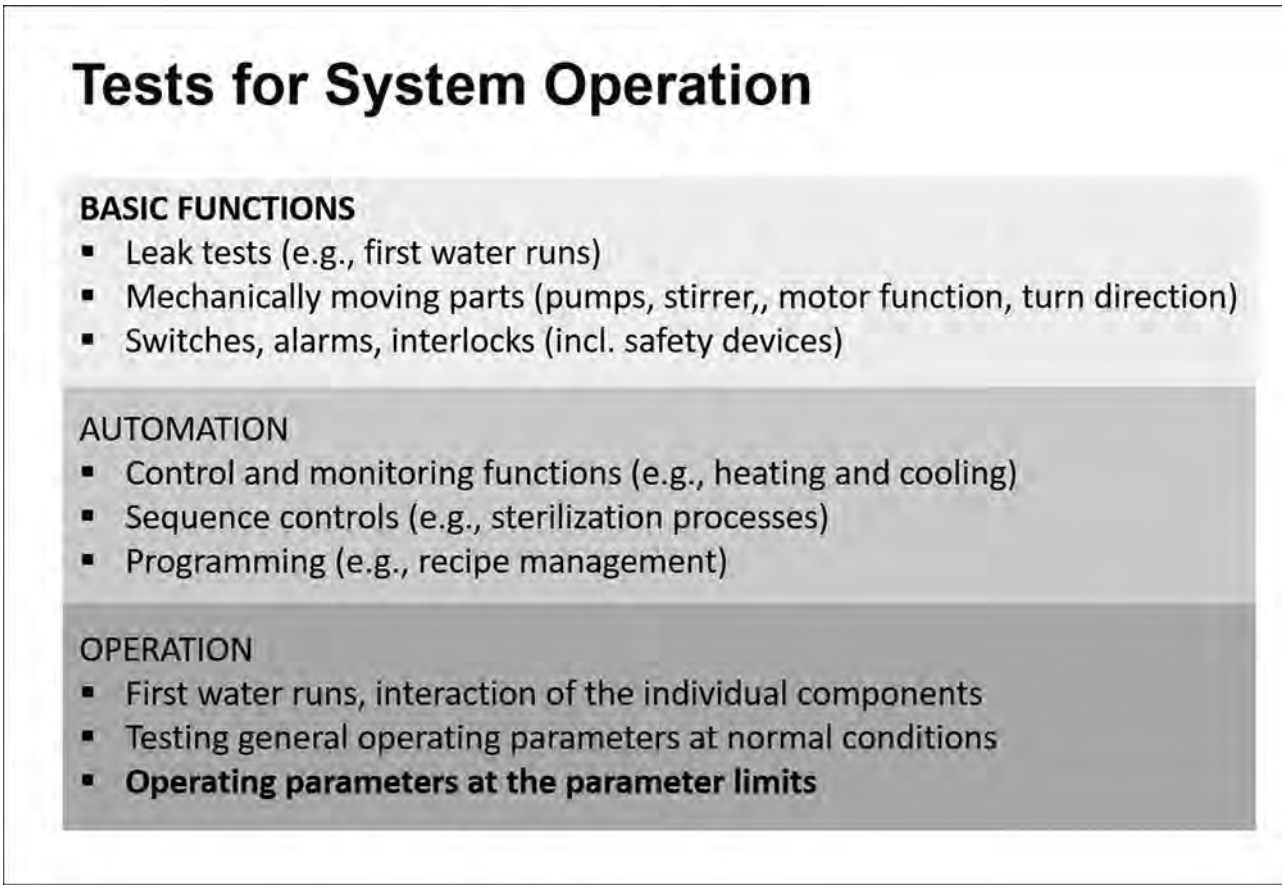
Interestingly, these tests in particular – although of enormous importance – are not initially viewed as critically as the FAT and SAT. The way and the level of detail of the documentation is often left to the engineers and there the standards range from almost non-existent records to highly professional checklists and inspection documents depending on the history and origin of the engineering company. Companies that come from the petrochemical industry, e.g., can often offer highly precise document and checklist systems due to the high safety standards of such plants (fig. 1).

In the field of finished medicinal products, pre-commissioning only plays a role in cleanroom technology and technical building equipment, since most process plants are self-contained systems that are not linked further (e.g., coater, tablet press). The technical inspection of the process equipment is adequately covered here by the FAT and SAT.

## Trust is Good .../the Qualification

The tests described above are all to be assigned to the technical tests,

■ **Figure 3**




***Typical test points function.***

which should always be carried out independently of the GMP requirements within the framework of good engineering practice. If tests are carried out against clearly defined acceptance criteria, they are generally referred to as verification, i.e., confirmation that a desired result has been achieved. In the GMP-regulated environment, however, even more is expected: the unambiguous confirmation with formal proof that the technical system is "fit for intended use" – capable for the intended use – whereby the verification must be carried out under the supervision of the quality unit of the plant operator. It is important that the scope of testing, the depth of testing and the acceptance criteria that are used for the verification are previously agreed with the quality unit and formally released for implementation – e.g., with the help of the qualification plans.

The scope of testing itself ranges from ensuring the complete scope of delivery and integrity, to correct specification, setup, and installation, to ensuring that all functions are guaranteed and error-free. Figure 2 and 3 show a list of test points that must be covered at least within the scope of a qualification.

On closer inspection, one finds that these reviews hardly differ from those carried out within the framework of good engineering practice. This is exactly what was expressed long ago in the guidelines published by PIC/S on the subject of validation. There it says:

*"The concept of equipment qualification is not a new one. Many suppliers have always performed equipment checks to confirm functionality of their equipment to defined specifications, both prior to and after installation."* And further: *"However, documented records of qualification and validation work in general have sometimes not been given sufficient consideration by either equipment supplier or pharmaceutical companies in the past."* [3]

In other words: the testing activities are almost identical, the essential difference to a qualification is probably the documentation and the integration of the quality unit.

Even if these statements are still true today – at least for most of the tests listed in fig. 2 and 3 – there are still further criteria that constitute a qualification and must be observed. The operator, e.g., is required not only to test systems at their intended operating point, but also to prove their functionality at the oper-

ating parameter limits (fig. 3). In addition, the operator is required to demonstrate and ensure the performance of the system in relation to the intended process and the intended products. Can desired throughputs and yields be achieved constantly, can homogeneity be achieved in the mixing vessel after a given time or can the exact specified dosage be achieved in a filling process? Can parameters that are decisive for product quality be kept within the accuracy? Or are the sterilization processes so reliable in terms of temperature distribution and time maintenance that there is no risk for the product? All these questions must be verified by means of appropriate test procedures, with the quality unit taking care of everything.

In other words: While all basic tests regarding specification-compliant manufacture and installation, including ensuring basic functionality, are more or less covered by good engineering, the responsibility for demonstrating performance remains with the operator. He must know the critical quality attributes of his products and the correlating critical process parameters by means of development and risk analysis. He must develop suitable tests to demonstrate performance. He must challenge these tests together with technical experts and the quality unit and coordinate them to guarantee the correct procedure.

## What Does a Porsche Have to Do With Qualification?/Forms

In the previous section it was pointed out that documentation plays a major role in a qualification. The aim is not only to enforce a certain systematic approach, but also to ensure that acceptance criteria and procedures for tests are coordinated with regard to the verification objective, ideally in a team of experts. Furthermore, good documentation offers the possibility that a quality unit can fulfil its supervisory duty.

Accordingly, the necessary qualification protocols and reports have developed over the years. The minimum requirement is that the goal, procedures, responsibilities, acceptance criteria and documentation specifications must be described. There are no specifications for the form and structure and thus an infinite number of variants have been developed. Despite this multitude, however, 2 models can be distinguished in principle:

1. A model widely used in the pharmaceutical industry, which is mainly based on checklists. In this model, all specification requirements from technical documents are transferred into checklists, acceptance criteria are formulated more or less concretely, and the requirements are checked against the real situation – if feasible – during the implementation (sample in fig. 4). Checklists are often found that try to go deep into the details of the technical requirement without ever having the chance to reach the level of detail of a technical document.
2. A more established model in the chemical industry, where qualification documents increasingly refer to test procedures and test documents of engineering technology. Acceptance criteria here are oriented more to the successfully performed technical test. Test basis are increasingly the technical documents (sample in fig. 5).
   This difference –also with regard to industry – is due not least to the fact that in the chemical environment, engineering with its test documents is much more pronounced than in the pharmaceutical environment, where more finished machines and equipment are purchased, which undergo their technical tests as part of the FAT and SAT.

If one reflects now the remarks of the preceding section, then it is actually obvious to divide tests for the proof of the "fit for intended use" into 2 groups – such tests, which can be classified actually as "Basics" and assigned to the engineering technology, and such tests, which require a deep product and process understanding and which can be arranged in a target-oriented manner exclusively by the later operator of the plant. For the former, it would make sense to fulfill the qualification by proving that manufacturers and engineers have done their homework and that corresponding technical test documents (FAT, SAT, walk-down protocols, etc.) are available. The focus within the scope of the qualification should be on ensuring that the scope and depth of the technical tests and the level of detail of the documentation are properly coordinated, otherwise it will not be possible to make a reference from within the qualification. In the second group of tests, the operator is not spared the need to think about this and develop suitable test scenarios.

A comparison with a process from our everyday life may be permitted here. The purchase of a Porsche will certainly be primarily characterized by wishes regarding the appearance, the equipment with a view to comfort requirements and the engine performance, which is expressed in acceleration and speed. Since price and safety requirements will certainly play a not unimportant role here, it can be assumed that a conscious buyer will also carry out appropriate checks when receiving the vehicle. It is difficult to imagine that he will now generate checklists on the basis of which he will check tolerances of piston rings, cylinder dimensions or even the correct design of the engine. Instead, he will rely on the quality of the manufacturer, at most accepting the certificate of factory acceptance as documented evidence. What he will focus

■ Figure 4

**Plant Installation**

Execution:

The system is checked to see whether all the information available matches the information given on the system. It is also checked whether the systems have been set up as described in the installation plans/P&I diagrams.

| System Identification and Specification | | | as specified | | Punch-free | | Att. |
|---|---|---|---|---|---|---|---|
| | | | yes | no | yes | no | |
| Extruder | Manufacturer | | | | | | |
| | System ID | | | | | | |
| | Model/Type | | | | | | |
| | Realization | Synchronized | | | | | |
| | Installation | Acc. P&I-Diagram PI-XXX | | | | | |
| | | Acc. Layout L-XXX | | | | | |
| | | Acc. Layout „Cylinder arrangement“ | | | | | |
| | | Acc. Layout „screw geometry“ | | | | | |
| | Environmental Conditions | Humidity max. 95 % | | | | | |
| | | Temperature. max. 40 °C | | | | | |
| | Drive Type | DC motor | | | | | |
| | Drive Power | 2,2 kW | | | | | |
| | Rotation max. | 2.800 rpm | | | | | |
| | Screw Speed | 500 rpm | | | | | |

| Tests executed by | Date | Signature |
|---|---|---|
| | | |
| Checked for compliance | Date | Signature |
| | | |

***Sample qualification checklist.***

on, however, are his “user requirements” – comfort, acceleration, the maximum speed he can reach on the highway, the equipment, appearance and possibly some safety features.

It is advisable to keep this example in mind, knowing that everything stands or falls with good engineering. A bad engineering cannot be made good by any qualification in this world.

## The Dream of the Fast Track Project/Summary

In an increasingly global and competitive world, the time factor, the topic “product to market” is evident. It is therefore not surprising that projects are under ever increasing time pressure, turning fast track projects into ultra-fast track projects, which in the end seldom meet this requirement and rather fulfil the low track project criterion. The reasons for this are manifold and

**Figure 5**

Check for completeness and correct labeling of all components

The check for completeness and correct labeling of machines and apparatus, pipelines, fittings, PCT devices and units is carried out when checking the associated P&I diagrams. Here, in particular, the identification that is important for operation (e.g. numbering of quality-relevant operating elements, sampling devices) must be clarified beforehand in the validation team, and the representation in the P&I diagram provided for the test must be ensured. The diagrams receive a red test stamp with a date and signature field in preparation for the test and are enclosed with the present test plan.

During the check, the positive result is marked by a red tick on each piece of checked information in the P&I diagram. This is a 100% check. If components are missing, unintended components are installed or components are incorrectly labeled, the defect is given a number in the P&I diagram and listed in the associated list of defects. After the first complete check, the P&I diagram and the list of defects must be dated and signed by the inspector. The rectification of the defect is indicated by a red tick both in the list of defects and in the P&I diagram. Each entry made after the initial test must be dated and signed by the tester.

| | |
|---|---|
| Implementation: | Preparation of the P&I diagrams and implementation of the 100% inspection is carried out by the assembly engineer. |
| Acceptance criteria: | All components must correspond to the representation in the P&I diagram be present and properly marked. |
| Raw test documents: | P&I diagram |

***Sample qualification with reference to R&I walk-down.***

the questions, why the Chinese or even an Elon Musk deliver projects in a much shorter time, become more and more agonizing. In addition to a lack of standardization, too many discussions and too much elaborate formalism, the issue of qualification plays a not inconsiderable role in terms of time and cost factors, especially in pharmaceutical construction projects. Discussions and excessive formalism often drastically delay projects, especially in the final phase. The doomed to failure attempt to achieve more quality through more paper slows down projects in this phase. The GMP principle of producing quality and not testing it into the product does not only apply to the pharmaceutical final product. It also applies to the plant itself. Poorly designed and built plants do not become better through qualification.

Factors that can improve this situation have been discussed extensively in the 3 contributions to this series and can be summarized as follows:

- It is important to speak the same language and to clearly define what is "testing", what is "verifying" and what exactly means "qualifying" and when I do what. Qualifying comes after successful testing, after successful verification.
- Qualification requires the integration of the quality unit with necessary formalism and should therefore be reduced to the really critical aspects. Verification is the task of engineering technology and requires only good documentation practice.
- FAT, SAT and Pre-Commissioning are important and valuable activities of technology and can or should be used in the context of qualification by referencing. This requires prior consultation with the operator and his quality unit.
- The key is good engineering practice, which requires qualitatively reliable manufacturers and suppliers, ultimately experts in their

field. However, since there are not an unlimited number of experts, attention must be paid to established processes and project procedures must be clearly regulated in a PQP. The tool must be right.

- As in product development, quality is also generated in engineering at an early stage – in the planning phase. An important quality assurance instrument here is the design review, which requires technical experts who focus on the technical execution documents and not on checklists.
- The right quality can only be produced if the specifications derived from the product and processes are correct. It is therefore important that operator requirements focus on these aspects and do not degenerate into technical specifications.
- Risk analysis and risk management make sense if the tools are used sensibly. Not every step needs a failure mode and effect analysis (FMEA). Sometimes common sense, a profound discussion among experts is enough, which is then documented with results and without number games.
- As with all processes, a clear, simple and understandable concept and an early start with the involvement of the necessary experts is a key to success. This also applies to the entire qualification process. Quality cannot be set at the end of the project and reduced to a mere quality check.

Many of the theses presented here are neither new nor surprising. Unfortunately, even after more than 30 years of qualification, they are still difficult to implement. Documents, forms and formalistic procedures block the view of the essential. The 4th and last part of this series of articles will shed light on whether these suggestions and procedures are also in line with regulatory requirements.

The 4th part of this series will be published in one of the next issues of this journal.

## LITERATURE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