Principles of Qualification

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6 min. reading time

by Michael Hiob, PhD

A qualification serves to prove that equipment is fit for purpose. In this context "fit for purpose" means that it can be demonstrated that the equipment meets the proscribed requirements. "Fit for purpose" also means that the equipment meets the requirements in a reproducible manner – that is with a high level of statistical probability. Qualification activities are always associated with statistical investigations.

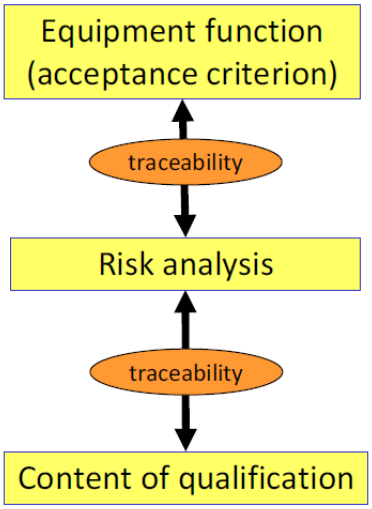
Qualification is oriented along the lifecycle of the equipment. Every phase from design up until decommissioning of the equipment is to be assessed in a risk-based manner.

A fundamental requirement for a successful equipment qualification is the good design of the equipment. Good design ensures the desired functionality, effective controls as well as effective cleaning and maintenance of the equipment. The responsibility for the equipment design lies generally with the equipment supplier. Good Engineering Practice (GEP) as defined by the ISPE (International Society for Pharmaceutical Engineering) is "*Established engineering methods and standards that are applied throughout a project's life cycle to deliver appropriate, cost-effective solutions.*" GEP Standards are established in norms such as ISO/DIN, the Society of German Engineers (VDI) and in the baselines of the ISPE.

Core elements of all qualification work are the acceptance criteria, such as limit values or specifications. Thus, it is necessary to set the acceptance criteria before performing the qualification. When determining the acceptance criteria requirements references can be made to the drug product manufacturing instructions, registration documents, industry norms or risk analyses.

The breadth and intensity of the required qualification work should be identified via risk analysis. This should reflect the complexity of the equipment design and the variability associated with it. The greater the complexity and variability of the equipment the higher the requirements will be on the control functions which can document the proper functioning of the equipment.

Critical equipment functions dictate the establishment of the risk analysis, and the risk analysis dictates the breadth of the qualification work. These relationships should be made clear in the documentation. Figure 1 provides a schematic of the relationship between these elements.



Sub-function No. 2 „drying“ 2.1 Parameter		
Acceptance criterion No.	Risk analysis No.	Qualification test No.
2.1.1 Temperature	R 2.1.1	Q 2.1.1
2.1.2 Inlet air	R 2.1.2	Q. 2.1.2
2.1.3 Exhaust air	R 2.1.3	–
2.1.4 Duration	R 2.1.4	Q 2.1.4

Figure 1 Traceability of qualification exercises

The robustness of the equipment functionality influences the reproducibility of manufacturing processes and thus the critical quality attributes. To recognize and assess these interdependencies it is necessary to have knowledge and experience in the operation of the equipment as well as relevant processes. This knowledge base is not always present at the manufacturing site. The greater the separation of labor is (catchword: outsourcing), the more necessary it is to maintain a functioning Information and Communication Management System among the involved parties. This includes the internal equipment installation and the customer in the pharma-production company as well as the equipment supplier and operator. A properly functioning exchange of information is an essential prerequisite for successful risk management and qualification.

It is a matter of course that experience in operations with similar or the same equipment should be reflected in the risk analysis and qualification. A compilation of multiple equipment units together to a group of which a single unit is taken as representative of the whole group and is qualified, however, is not acceptable. In contrast to process and cleaning validations, the bracketing approach is not possible for equipment qualifications. Most notably the installation and operation qualifications cannot be transferred from one equipment unit to another of the same type. A qualification evaluates and tests a specific piece of equipment individually.

All qualification tests should be performed under *near-operational conditions*. This includes, for example, environmental conditions, equipment parameters and their upper and lower limits, the run time per shift as well as equipment stops and interventions.

Qualification teams should be made up of representatives of multiple disciplines. This may include representatives from Engineering, Production, Quality Assurance and Quality Control.

Personnel which are involved in the qualification should be adequately qualified for the conferred task. Only approved procedures should be employed. All tasks and documents should be monitored. The QS system should define who the qualification personnel reports to.

An exceptional procedure for existing equipment is no longer intended. In the past it was possible to perform retrospective qualifications based on reviews of past experience. It is now expected that existing equipment be qualified according to Annex 15, which went in effect in 2001 for the first time. All the special exceptions were removed with the revision of Annex 15 in 2015. Qualified equipment is imperative for manufacturing and it is not permitted to operate existing equipment with the intention of performing a retrospective qualification at a later time.

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