Michael Hiob, Thomas Peither, Ulrike Reuter

GMP Focus

Principles of Equipment Qualification

A Guide for Drug and Device Manufacturers

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Principles of Equipment Qualification

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Introduction

An equipment qualification provides needed evidence that equipment is fit for its intended purpose and is functioning appropriately. In the manufacturing world, the head of manufacturing or quality is usually responsible for ensuring equipment is qualified.

If third parties are contracted to perform equipment qualifications, those responsibilities should be regulated in a contract. Qualifications should be documented in the form of qualification plans and reports and should be reviewed annually as part of the product qualification report. External consultants and equipment suppliers are often involved in the qualification process.

An equipment qualification is handled in different phases of the equipment lifecycle, starting with design qualification, installation qualification, and then operational qualification and performance qualification.

Every step in the equipment qualification formally comprises a plan, the execution and a report. In general, the execution of a qualification step can only be started when the previous step has been completed.

The selected procedure is described and justified in the overall strategy of the validation and qualification master plan. This underlying strategy is set for all qualifications.

Factory acceptance tests or site acceptance tests can be used as part of the equipment qualification. In each phase the work to be performed must be described in detail in a qualification plan and the execution is to be documented in a qualification report.

An important component of any qualification activity is the risk analysis. It serves to determine potential risks and their root causes as well as the definition of appropriate measures to minimize the risks. The extent and depth of the qualification can be defined based on the risk analysis.

This report walks pharmaceutical manufacturers through the process of how to perform an equipment qualification. Maintaining the qualification status occurs via continuous equipment monitoring as well as appropriate change control management.

About the Authors

Thomas Peither has been a GMP consultant for 18 years and an expert in the European GMPs. He cofounded the GMP publishing company Maas & Peither (Germany, USA) and the midsize pharma consulting company Halfmann Goetsch Peither (Switzerland, Germany, Singapore), which advises numerous pharmaceutical companies.

Michael Hiob is Ministerial Pharmaceutical Director for the Ministry of Social Affairs, Schleswig-Holstein, Kiel. He has worked as a laboratory manager and GMP inspector in the area of pharmacovigilance. He is currently responsible for supervising GMP inspections. He was head of the Qualification/Validation expert group for more than ten years.

Ulrike Reuter is a mechanical engineer with Sanofi-Aventis Deutschland GmbH in Frankfurt. As an engineer in a pharmaceutical company, she strives to reconcile technical and GMP requirements. She is currently working on implementing the new Annex 15, Annex 11 and other technical GMP issues as part of operational support and project management.

Official Requirements and Agency Expectations

An equipment qualification serves to prove that equipment is fit for its purpose. In this context, "fit for purpose" means that it can be demonstrated that the equipment meets the purpose for which it was intended. "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 life cycle 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 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 International Society for Pharmaceutical Engineering (ISPE) 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, which limit values and establish 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 to document proper functioning of the equipment.

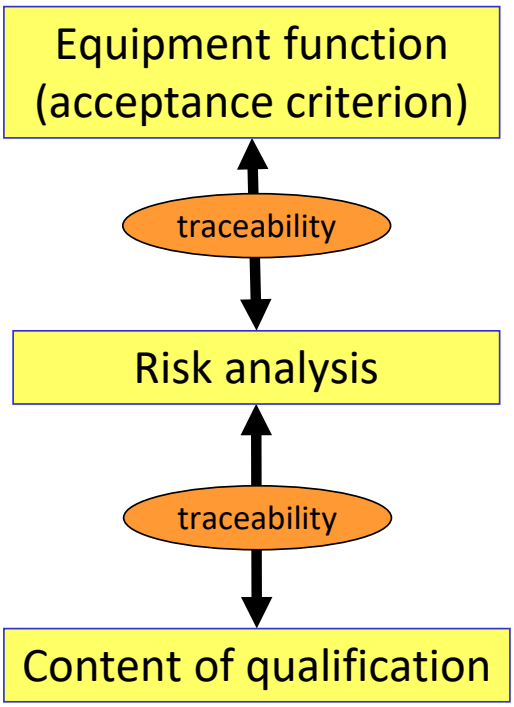
Critical equipment functions dictate the establishment of the risk analysis, and the risk analysis dictates the breadth of the qualification work. These relationships should be made clear in the documentation. Figure 1 (see page 6) provides a schematic of the relationship between these elements.

The robustness of the equipment functionality influences the reproducibility of manufacturing processes and thus the critical quality attributes. To recognize and assess these interdependencies, manufacturing staff need to have both the 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.

And, as more outsourcing takes place for various manufacturing processes, more checks are needed to maintain a well-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.

Figure 1: Traceability of qualification exercises



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

Obviously, experience in operations with similar or the same equipment should be reflected in the risk analysis and qualification. However, a compilation of multiple equipment units together into a group of which a single unit is taken as representative of the whole group and is qualified, 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 involved in the qualification should be adequately qualified for the task. Only approved procedures should be employed, and all tasks and documents should be monitored. The quality system should also define who the qualification personnel report to.

It should be noted that qualification exceptions for existing equipment are no longer allowed. In the past, it was possible to perform retrospective qualifications based on reviews of past experience. Regulators expect that existing equipment be qualified according to Annex 15, which

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Any questions? Please contact us:

Phone +49 7622 66686-74 (Ms. Annette Crawford)
E-Mail annette.crawford@gmp-publishing.com