QUALIFICATION OF A PACKAGING LINE FOR CYLINDRICAL CONTAINERS AND BLISTER PACKS

A. Bödeker\(^1\), H. Bensmann\(^2\), G. Kutz\(^1\)
\(^1\)Pharmaceutical Engineering, FH Lippe und Höxter, University of Applied Sciences, Detmold, Germany
\(^2\)Haupt Pharma Münster GmbH, Münster, Germany

1. Introduction

The manufacturing process is a complex as well as a problematic topic for every pharmaceutical company. That is why all parts of equipment should be qualified ensuring a manufacturing process taking place within the fixed specifications.

In order to reach this goal, clear and precise background information about the equipment to be qualified, their way of operation, controlling functions, the manufacturing process and the pharmaceutical product itself including its components are of outstanding significance.

In this case the packaging line to be qualified can be characterized by the following aspects:
- merger of new parts of equipment as well as of equipment being already in use
- ability to process cylindrical containers as well as blister packs
- very flexible concerning containers’ and packaging materials’ dimensions.

2. Aims and Objectives

The outstanding aims of this qualification have been to carry out a risk analysis taking all parts of equipment into consideration and to put up plans on DQ, IQ, OQ and PQ considering the packaging line as a whole as well as all products which are going to be produced on this special packaging line. Therefore, PQ has been carried out for the packaging line as a whole. In order to reduce the extent of qualification, bracketing and matrixing has been used. The risk analysis should mention all aspects of the whole including the machines being already used. In addition, the influence of the identified risk on the product and its quality has been evaluated. This way, the extent of qualification could be decreased.

3. Structure and Procedures

Although all new parts of equipment had been ordered including qualification documents (risk analysis, plans on Design Qualification (DQ), Installation Qualification (IQ) and Operational Qualification (OQ)), an additional risk analysis was needed taking the facilities being already used as well as the transitions between the single facilities into consideration. As IQ as well OQ for the new facilities have been carried out separately, those parts of qualification for the facilities being already in use have been carried out that way, too. As PQ has to consider the whole packaging line during routine packaging process, a quite complex structure for qualification results.

3.1 Risk analysis

A risk based approach is claimed for qualification and validation in the Annex 15 of the EC-GMP guide [2]. Failure Mode and Effect Analysis (FMEA) is the most common technique used to identify and counter weak points of products and processes [1]. Whenever a risk influences products’ quality/ safety or the continuity of the ongoing process checking the packing line’s “reaction” has to take place by performing challenge tests. This method is a more practical way which is accepted by legal authority. All identified risks influencing products’ quality and / or safety are part of the regular extent of in-process-controls (IPC}s). Resulting from this, fulfilling IPC’s specifications have been taken as “acceptance criteria” for PQ.

3.2 Performance Qualification

Tests belonging to PQ for the packaging line are divided up into two groups:
1. tests on safety devices (emergency-off switches, backup limit switches)
2. tests on the routine packaging process.
Another aim of the PQ was to prove that the filling machine is able to count up to 100% correctly, which has been proved by performing extended IPCs within all batches produced until the packaging line has finally been released for routine production. The additional testing of the safety devices became necessary, because all emergency-off switches of all facilities belonging to the packaging line have been connected with each other so that pushing any emergency-off switch of any facility forces a complete stoppage of the whole packaging line. The second group is again divided up into placebo batches, representative products and remaining products.

The representative products have been defined by reducing the whole variety of products processed on the packaging line on those products representing the whole variety. Within this framework, “bracketing and matrixing” has been used. An detailed overview on the structure of PQ is given in the following graph:

![Graph 1: structure of PQ](image1.png)

All batches produced during qualification have to fulfill all acceptance criteria from the IPCs already known from routine packaging process. Differing from routine packaging process, the extent of IPCs is intensified and packaging line’s performance is evaluated as well.

### 3.3 Bracketing and Matrixing

The variety of products produced on the packaging line is characterised by the following aspects:
- used caps: screw cap or stopper
- filling amounts: 10 to 1,000
- containers’ dimensions:
  - diameter: 20 – 55mm (machines’ specifications: 20 – 90mm)
  - height: 35 – 110mm (machines’ specifications: 35 – 200mm)

In order to reduce qualification’s extent bracketing and matrixing has been used to identify the representative products, from which two batches each fulfilling all acceptance criteria are needed for qualification. The way carried out to reach the goal is shown in graph 2:

![Products filled into containers](image2.png)

Graph 2: definition of the representative products

As the representative products cover all products, one batch each of the remaining products will be sufficient. Another advantage, in addition to the reduced extent of qualification work, is that in the case of new products, they could be treated as “remaining products” and qualification’s extent decreases.

### 4. Results and conclusions

By carrying out an a risk analysis combined with bracketing and matrixing, the extent of qualification e.g. for a packaging line can be reduced. But it becomes obvious, that a clear procedure has to be carried out taking all aspects of the process, the products and the facilities into consideration.

### References
