

Robustness is the ability of a process to consistently produce the same product while remaining unaffected by small variations in the process. It is possible to have a repeatable process and not have a robust process, but it is unlikely to have a robust process that is not repeatable.

One approach to evaluating robustness of a process is to evaluate challenge conditions during a separate PQ study. In this approach, challenging the validity of the Normal Operating Range limits is considered Performance Qualification (PQ). This type of PQ is considered 'worst-case' or 'most appropriate challenge' of the parameter limits.

The number of PQ batches may vary depending on the number and range of critical parameters to be qualified.

Another (more common) approach is to obtain information on challenge conditions during process development. The PQ or process development studies are then followed by Process Validation (PV). In the PV, all process parameters are set to target and typically 3 consecutive batches are produced to satisfy the requirement for reproducibility.

The ranges of the critical process parameters must be defined. They may be defined either during performance qualification or during process development.

Example 1 (PQ for a process)

It has been demonstrated in the pilot plant that lubricant blending for 7 minutes leads to acceptable product. Seven minutes is chosen as the target lubricant blend time for the regulatory filing. The production blender with an automated timer is qualified for +/-15 seconds (0.25 minute) and 7 minutes is target blend time. In the PQ, blend time should be qualified at times above and below the target (e.g. 5 and 9 minutes). Then, in PV, the three validation lots would be manufactured at target (NOR range would be 6.75 -7.25 minutes).

The PQ has confirmed the limits and the PV have been performed in triplicate at target. Therefore, data has been obtained demonstrating the robustness of the NOR/regulatory range and reproducibility of the process.

Example 2 (PQ for a system)

A reactor is controlled by an automated DCS (distributed control system) that is a direct impact system as defined in the project plan. During OQ portions of the DCS and the reactor are tested individually. The Performance Qualification (PQ) portion of the system qualification is defined to execute critical functional testing to demonstrate that the systems perform reproducibly in the normal manufacturing environment. This would typically include using water and/or solvent runs in the reactor while evaluating the SOPs (Standard Operating Procedures). The PV of product processes in the reactor will follow the successful reactor PQ.