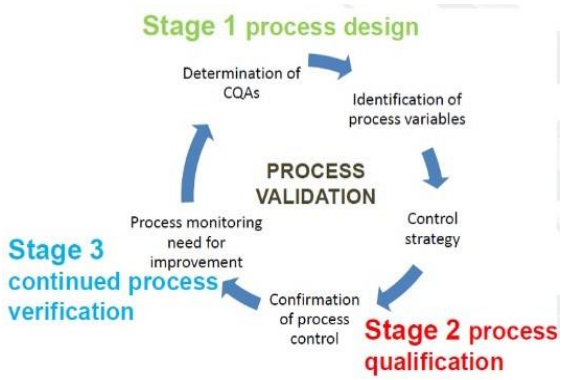
PROCESS PERFORMANCE QUALIFICATION (PPQ) FACTSHEET

What for…?

The pharmaceutical industry is one of the most intensely regulated industries. One regulatory requirement is to validate the process to ensure that the process consistently deliver quality products. Since 2011 the FDA recommends a lifecycle approach to process validation, including three stages: Stage 1-Process Design, Stage 2-Process Performance Qualification (PPQ), and Stage 3-Continued Process Verification over the lifecycle of the process and product.



In Stage 2, the manufacturing process is upscaled from pilot/clinical trial scale to commercial scale. The produced PPQ batches/conformance lots are evaluated to determine whether the products have the required quality, safety, and efficacy and are comparable with the clinical trial material.

Facing the challenge…!

The performance of Process Performance Qualification is certainly not a “copy-paste” exercise and derives from the information of the drug and process development phase.
It requires knowledge of product, process and analytical development phase and knowledge of laws, regulations, guidelines, progressive regulatory expectations from national and international authorities.

Typical Process Validation Inspection Observation items:

- ✓ Lack of or inadequate process validation
- ✓ Lack of validation of a filtration time and of a filter replacement
- ✓ Lack of validation of holding times for intermediates
- ✓ Process validation activities/results have not been adequately documented/approved
- ✓ Procedures to validate and approve processes that cannot be fully verified by inspection and tests were not established
- ✓ Process validation reports for API did not have criteria for acceptable reduction of the specified impurities. Batch record review (20 consecutive batches) found that post-validation batches showed typical levels of impurities were much higher than in the validation batches

How can we support you with respect to PPQ activities?

Progress-PME employees are very experienced along the three validation stages in a lifecycle of a drug as defined by the FDA. They can support you with:

- ✓ Validation management / lead to support your organization to set up a validation program and validate the processes
- ✓ Help to define validation strategy (e.g. justification of number of PPQ runs) and criteria (e.g. Critical Quality Attributes and Critical Process parameters acceptance criteria (part of QbD))
- ✓ Writing Regulatory submission documentation, e.g. overall summary reports, PPQ reports, product characterization/impurities reports
- ✓ Performing a Quickscan/GAP analysis to determine the status of deliverables required at each stage of the project
- ✓ Knowledge management which comprises the available analytical/product/process information from early development phase through validation phase

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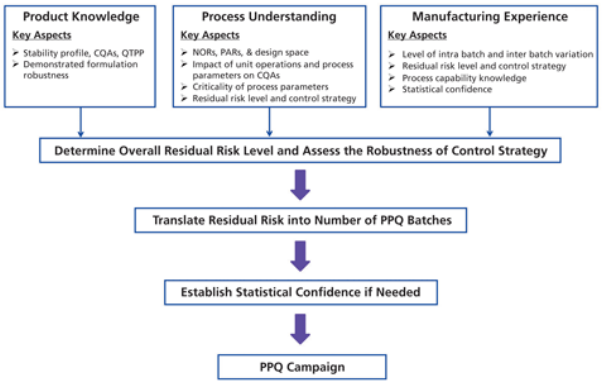
Lifecycle approach process validation

In 2011 the FDA published a guidance on process validation that promotes the "lifecycle" approach to process validation including scientifically sound process design practices, robust process qualification, and continued process verification. In Stage 2 of the process validation lifecycle the activities should be justified based on product and process understanding as well as an adequate demonstration of manufacturing control during small scale/pilot scale production.



However, this FDA guidance does not explicitly indicate their expectation for the number of process qualification batches. Their expectation is that a rational decision regarding the number of PPQ batches based on product knowledge and process understanding is made by the manufacturers. Based on the gained product knowledge, process understanding, and small (pilot) scale/clinical manufacturing experience, the overall residual risk level associated with the manufacturing should be determined. The residual risk should subsequently translated into the number of required PPQ batches.

Track record and facts

This is a selection of our main Stage 2 / PPQ experience:

- ✓ We have provided program managers to lead multiple project teams and project managers to lead CMC/validation (sub) teams; this in several cases in collaboration with CMO organizations
- ✓ We have provided validation project SME's, such as process experts, qualification, scale-up, tech transfer, PPQ, cleaning validation, QA project support, etc.
- ✓ We have supported organizations to prepare CMC submission documentations, e.g. process development life cycle documentation, qualification and PPQ (summary) reports, cleaning validation reports, etc.
- ✓ Additionally we supported clients to prepare for pre-approval inspections, to respond to audit observations made by FDA and European authorities and to answer questions from regulatory agencies related to validation aspects as part of IMPD/IND submissions and submitted variations

Who are we….?

Progress-PME is an independent Project Management and Consultancy Company with customers in life science, (bio)pharmaceutical, medical device and healthcare industries.

The company was founded in 1999, operates internationally and provides support throughout the entire range of process development to commercial production.

Progress-PME provide services in the field of project and interim management and Consultancy.

Fields of expertise: CMC, Quality (cGxP), Validation, Engineering, LEAN Six Sigma.