

What for...?

Continued Process Verification (CPV) is the third validation stage in a lifecycle of a drug as defined by the FDA. The CPV program starts after a successful Process Performance Qualification (PPQ) and continues during the commercial phase of the drug.

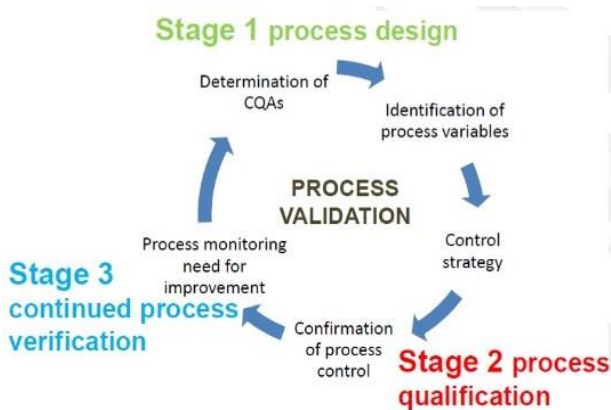


Figure 1. Process Validation Lifecycle

An important part of the CPV program is the monitoring of the commercial production process. By performing statistical process control (SPC) it is possible to determine whether the commercial production process remains in a state of control (validated status). Thus, integrating a CPV program into the Quality System is an essential tool of the Quality Risk Management by providing information to:

- ✓ Determine the robustness of the process
- ✓ Determine the impact of process deviations on product quality
- ✓ Determine the efficacy of implemented CAPA's (Corrective Action Preventive Action) and changes
- ✓ Support technology transfer of the process and analytical methods
- ✓ Support implementation of process optimization

Facing the challenge...!

Implementation of an effective CPV program is a complex and certainly not a “copy-paste” exercise and comprises the information of the whole lifecycle of a drug.

It requires knowledge of laws, regulations, guidelines, progressive regulatory expectations from national and international authorities, knowledge of product, process and analytical development phase and knowledge of trending/SPC.

How can we support you with your CPV program? Progress-PME has a broad CPV expertise and can support you on management and tactical levels by performing:

- ✓ Assessment of the current state of the CPV program in your company
- ✓ Development of a sound and “fit for company” CPV policy that reflects regulatory expectations and proper tie-ins with other Quality Management Systems
- ✓ Development of a sound SPC policy to perform the daily data analysis according to the CPV policy and regulatory standards.
- ✓ Support and/or perform of SPC analysis on a daily basis including interpretation of the results and the use of statistical tools
- ✓ Support, perform, and lead “Out of Trend” Root Cause investigations in a multidisciplinary team
- ✓ Write and review (annual) data trending reports as part of the APR/PQR
- ✓ Answer questions from the regulatory agencies and respond to audit observations related to CPV/trending

Track record and facts

This is a brief summary of our CPV legacy:

- ✓ We provided interim managers to lead CPV/SPC teams
- ✓ We successfully developed and implemented a “fit for company” CPV and SPC policy
- ✓ We supported several clients to perform CPV activities such as SPC/trending analysis on a daily basis and Out of Trend investigations
- ✓ We supported several clients to write and report trending data as part of the APR/PQR
- ✓ Additionally we supported clients to respond to audit observations made by FDA and European authorities and to answer questions from regulatory agencies related to CPV/trending

Typical CPV Inspection Observation Items:

- ✓ Lack of clear roles and responsibilities with respect to the CPV program
- ✓ Lack of written procedures for evaluations done at least annually including provisions for a review of manufacturing process data
- ✓ Missing Review of a representative number of batches
- ✓ Lack of a statistical process control procedure to monitor manufacturing process performance (validated status) including the follow up of the evaluation
- ✓ Actual yield and percentages of theoretical yield are not determined at the conclusion of each appropriate phase of manufacturing processing
- ✓ In-process specifications are not consistent with previous acceptable process averages and variabilities (determined by the application of suitable statistical procedures)

Process Control

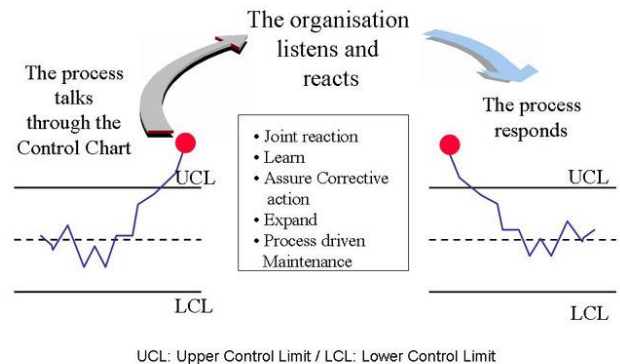


Figure 2. Feedback loop of Statistical Process Control

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.