Procedure: Statistical Process Control

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# Purpose

The purpose of this procedure is to describe the requirements for statistical process control (SPC) to manage process variation and achieve quality requirements at [Company].

# Scope

The scope of this procedure includes the use of statistical process control to manage a process’s critical process parameters (CPPs) to thereby ensure the final product has its required critical quality attributes (CQAs). This procedure identifies statistical techniques required for establishing, controlling, and verifying the acceptability of process capability and product characteristics. This procedure also defines statistical rationale for establishing sampling plans.

# Responsibilities

The following roles and responsibilities are associated with this procedure.

|  |  |
| --- | --- |
| Role | Responsibility |
|  | List key responsibilities for each role mentioned within the procedure. |
| Quality Manager |  |
|  |  |
|  |  |

# Procedure

## General

Product CQAs are determined during the development phase of a product. For legacy products, CQAs are generally well understood due to the years of manufacturing experience and process understanding.

The Critical Process Parameters (CPPs) are the process parameters that must be controlled within an allowable range to ensure the product produced meets the CQA requirements (refer to Procedure *QP718: Validation of process and software*).

SPC is a method of quality control which uses statistical methods to monitor and control the variation of a process. SPC can be applied to any process where the output can be measured. Applying SPC to control CPP set points of a stable process should result in the parameters meeting specification requirements.

Causes of variation:

* Common cause variations are sources of variation inherent to a process – SPC is an option for managing these variations
* Special cause variation are unpredictable and intermittent causes of variation e.g. breakdowns, operator adjustments, natural disasters, etc.

## Understanding the process and specification limits

Outputs from process validation activities include process specifications and the controls/precautions to be implemented to reduce special cause variations to a manageable level (refer to Procedure *QP718: Validation of process and software*).

Process specifications set the acceptable operational range of parameters that will produce acceptable outputs and the limits beyond which out-of-specification results will be produced.

In a typical process, the specification outlines key parameter:

* set-points
* acceptable operating ranges
* the range in which adjustments should be made
* out of specification limits

**Note**: Specifications can be used to develop ‘Control Charts’ as per Section 4.3.

While a process is running, measureable (quantifiable) in-process parameters can be monitored and (based on the results) the set point can be adjusted to keep the process running acceptably using SPC techniques. This defines the control strategy. This process prevents the process from going outside of the validated parameter range due to common cause variations.

Process validation should verify the adequacy of the control strategy

SPC may also be used to produce statistical evidence to justify quality decisions relating to purchased product, qualification of installations, complaints, and service performance.

## Control charts

Control charts, refer to figure 1, are used to measure and monitor outputs of in-process checks or test results. The bands are usually set based on experience and/or on a statistical basis.

Regularly during in-process checks, data is plotted on the control chart and when results fall outside of the target zone, or there is an adverse trend, adjustments are made to get the process back in control. Where results fall ‘out of specifications’, deviations are raised to correct the problem (refer to Procedure *QP805: Control of non-conforming product*).

Figure 1: Control chart

|  |  |
| --- | --- |
| Out of specification (Above) |  |
| Upper Control Limit |  |
| Minor upper adjustment zone | X X |
| Target zone | X X X X |
| Minor lower adjustment zone | X |
| Lower control limit | X |
| Out of specification (Below) |  |

Specification limits may relate to processing speeds, material characteristics, chemical characteristics, temperature, pH, colour, etc.

## Acceptance Sampling Plans

Acceptance sampling plans will be used in manufacturing to decide whether to accept (release) or to reject (hold) lots of product.

Acceptance Sampling Plans are a Statistical Quality Control technique, where random samples are taken from a lot, and upon the results of appraising the samples, the lot will either be rejected or accepted. This sampling allows disposition without doing 100% inspection.

Sampling methods will be determined by Military Standard (MIL-STD-105E)/ISO2859 in conjunction with Device Risk Management (refer to Procedure QP812: Device Risk Management)

Acceptance sampling will be used for the following:

* Starting material acceptance (discrete units)
* Process validation
* Investigations

### How to implement Acceptance Sampling

Criteria will be determined for the *acceptability* level of incoming or outgoing materials. Acceptability level is termed “Acceptable Quality Level” – the minimum level at which a lot is accepted. AQL is not a measure of quality.

There are 2 different categories of inspection:

* + By Attributes (pass/fail) – (pass/fail) by far most common in GMP.
  + By Variables (measurement dependent) – rare in GMP.

Different inspection levels:

Standards provide different sampling requirements for different types of tests – e.g. reduced, normal, tightened.

## Process Capability

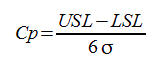
Certain outputs lend themselves to capability analysis which is the most common tool for GMP applications.

In equipment qualification, Cp is primarily used for filling lines and other dosing equipment and is useful in specialist applications.

Wall thickness, opening torque, etc.

Process capability, Cp, is used to assess the ability of a process to produce results within its specified limits.

Cp is simply a ratio of the specification range to 6 standard deviations of the data set.



Cp will quantitatively output how tightly the process operates within the specification range.

## Automated SPC systems

Systems can be used to automatically monitor and make adjustments to parameters controlling a process to keep the process outputs in specification. Such systems must be validated, routinely retested and maintained in a validated, calibrated and operational state (refer to Procedure *QP718: Validation of process and software).*

## Using SPC results

SPC results may be used as statistical evidence to justify quality decisions relating to in-process checks, purchased products, system qualifications, complaints, service performance, investigations and product release.

Appendices

Amend as required or delete.

Definitions

Amend as required or delete.

| Term | Definition |
| --- | --- |
|  | Insert terms/abbreviations and definitions for those used within the procedure. Do not include any terms or abbreviations not used within the procedure. |
| CPP | Critical Process Parameter |
| CQA | Critical Quality Attribute |
| AQL | Acceptable Quality Level |
|  |  |

Document Information

| Revision History | | | |
| --- | --- | --- | --- |
| Revision | Modified by | Change Control No. | Description of Change |
| 01 |  |  |  |
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Complete the above fields for each revision of this document. Ensure that there is sufficient description of changes so that the change history of this document can be followed. Additional columns can be added to include document/change tracking numbers generated by your company’s systems if required (eg. change control).

| Associated forms and procedures | |
| --- | --- |
| Doc. No. | Document Title |
| QP718 | Validation of process and software |
| QP805 | Control of non-conforming product |
| QP812 | Device Risk Management |

List all controlled procedural documents referenced in this document (for example, policies, procedures, forms, lists, work/operator instructions)

| Associated records | |
| --- | --- |
| Doc. No. | Document Title |
|  |  |

List all other referenced records in this document. For example, regulatory documents, in-house controlled documents (such as batch record forms, reports, methods, protocols), compliance standards etc.

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