Macedonian Pharmaceutical Bulletin, 72 (Suppl 1) 87 - 88 (2026)
Online ISSN: 1857-8969
DOI: 10.33320/maced.pharm.bull.2026.72.03.041
Short communication

Statistical tools for ongoing process verification

Ana Sudjukovikj*, Andrijana Markoska, Olivera Budjakoska, Katerina Aleksievska Beldedovska, Ana Ivcheska, Verica Marinova, Elizabeta Karadzinska, Olivera Paneva

Alkaloid AD Skopje, Blvd. Aleksandar Makedonski 12, 1000 Skopje, North Macedonia

Introduction

Ongoing Process Verification (also known as continued process verification) is documented evidence that the process remains in a state of control during commercial manufacture (European Commission, 2015b).

The term "continued process verification" is used in US and the term "ongoing process verification" is used in EU. The terms are considered to be equal.

The purpose is to identify the occurrence and cause of process variability, monitor the degree of variability, determine its impact on the processes, as well as to control it, thereby improving the stability and capability of the processes (European Commission, 2015b).

The data collected (quality attribute and critical quality attribute) should be evaluated with appropriate statistical tools, where applicable, to evaluate process performance and to verify that the quality attributes and critical quality attributes are adequately controlled during production (European Commission, 2015a; European Commission, 2015b).

The objective of this targeted narrative review was to summarize the principal statistical tools applicable to ongoing process verification and to propose a practical framework for their selection and interpretation according to data type.

Statistical tools in Ongoing Process Verification (OPV)

A practice-informed targeted review of EU GMP, EMA, FDA and ISPE guidance (European Commission, 2015a; European Commission, 2015b; EMA, 2014; FDA, 2011; ISPE, n.d.) and established statistical literature was performed. Statistical tools were compared according to data type and structure, temporal dependence, source of variability, specification limits, distribution, sample size and monitoring objective. The findings were combined with practical OPV experience to develop a concise tool-selection framework.

Statistical tools used in ongoing process verification (OPV) are: descriptive statistics, time series plot, control charts and process capability analysis. These tools are applied to continuously monitor and evaluate process performance, enabling the identification of variability, assessment of process stability, and assurance of consistent product quality throughout the lifecycle of the process.

Descriptive statistics – summarize, organize, and describe the main features of the data using numerical measures.

Time Series plot – graph displaying data points in chronological data order over uniform intervals. It is used to examine the relationship between the results and when establishing of control limits is not adequate because of the parameter type and narrow specification limits.

*asudjukovikj@alkaloid.com.mk

Control charts - used to monitor process performance by distinguishing common cause variation inherent to the process and special cause variation arising from external influences. Control charts provide real time monitoring and are essential tools for quality control, process improvement and trend analysis (trend is a pattern observed in a dataset over a certain period, used to describe whether the data show an accidental or unexplained movement in part or all of the dataset, indicating a lack of consistency and stability).

A control chart consists of: data points (plotted in observation); center/mean line (X) (represents the process mean); upper control limit (UCL) – upper boundary of expected variation; lower control limit (LCL) – lower boundary of expected variation; and the upper specification limit (USL) and lower specification limit (LSL) that are prescribed for each parameter.

I – MR Chart (Individuals – Moving Range Charts) – used to monitor process stability and variation when data consists of single, individual observations rather than subgroups. The MR chart helps detect sudden increases of variation, process instability and measurement inconsistency.

Process capability analysis – used throughout the product lifecycle to analyze and reduce process variability and ensures that products meet required specifications. Process capability focuses on the uniformity of a process, where variability in critical quality characteristics determines the consistency of output. Variability can be considered in two ways: the natural or inherent variation at a specific moment and the variation observed over time. The estimate of process capability may be in the form of a probability distribution having a specified shape, center (mean), and spread (standard deviation).

Process capability indices are Cp and Cpk. Most commonly used are Cp and Cpk which takes in account common cause variability.

Cp measures the process's potential capability to meet the two-sided specifications. It does not account for the process average.

Cpk takes process centering into account and is one-sided process control ratio for the specification limit nearest to the process average.

Recommended Minimum Values of the Process Capability Indices are between 1.00 – 1.33. If the Capability Indices are less than 1.00, the process is not capable of producing a product within the specification limit. If the Capability Indices are above 2.00, the process is highly capable of producing a product within the specification limit (Montgomery, 2009).

Conclusion

Statistics as a discipline and the statistical tools are essential in OPV process because they provide scientific basis for decisions whether the processes are under control, capable, stable and predictable. Techniques such as descriptive statistics, time series plots, control charts and process capability analysis help identify variability, ensure process stability and maintain product quality within specified limits. Control charts enable real-time monitoring and detection of process deviations, while capability indices such as Cp and Cpk evaluate whether the process consistently meets required specifications. By enabling real-time monitoring and early detection of variability, these tools play a vital role in maintaining product quality, reducing risks, and supporting continuous improvement. Their implementation strengthens operational efficiency and ensures consistent compliance with quality and regulatory standards.

References

European Commission, 2015a - The rules governing Medicinal Products in the European Union, Volume 4: Good Manufacturing Practice, Medicinal Products for human and veterinary use, Ch. 1 Pharmaceutical Quality System. European Commission Health and Consumers Directorate-General.

European Commission, 2015b - The rules governing Medicinal Products in the European Union, Volume 4: Good Manufacturing Practice, Medicinal Products for human and veterinary use, Annex 15 Qualification and Validation.

EMA, 2014 - Guideline on process validation for finished products - information and data to be provided in regulatory submissions, EMA/CHMP/QWP/BWP/70278/2012-Rev1.

FDA, 2011 - Guidance for Industry: Process Validation: General Principles and Practices, CGMP, Revision 1.

ISPE,n.d.- Good Practice Guide: Practical Implementation of the Lifecycle Approach to Process Validation.

Montgomery, D. C., 2009 - Introduction to Statistical Quality Control, 6th Edition.