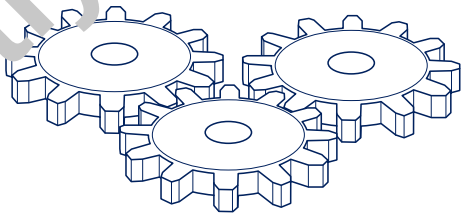
Technical Report No. 59

Utilization of Statistical Methods for Production Monitoring

PCMO

Paradigm Change in Manufacturing Operations℠



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This technical report was developed as a part of PDA's Paradigm Change in Manufacturing Operation (PCMO) project. The content and views expressed in this Technical Report are the result of a consensus achieved by the authorizing Task Force and are not necessarily views of the organizations they represent.

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Paradigm Change in Manufacturing Operations (PCMO[SM])

PDA launched the project activities related to the PCMO program in December 2008 to help implement the scientific application of the ICH Q8, Q9 and Q10 series. The PDA Board of Directors approved this program in cooperation with the Regulatory Affairs and Quality Advisory Board, and the Biotechnology Advisory Board and Science Advisory Board of PDA.

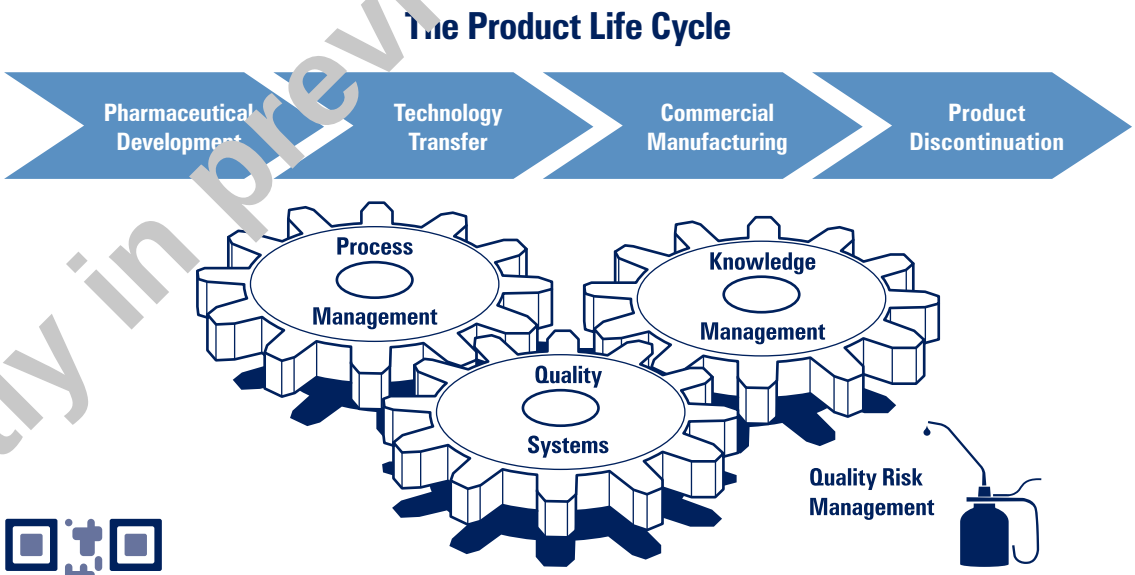
Although there are a number of acceptable pathways to address this concept, the PCMO program follows and covers the drug product lifecycle, employing the strategic theme of process robustness within the framework of the manufacturing operations. This project focuses on Pharmaceutical Quality Systems as an enabler of Quality Risk Management and Knowledge Management.

Using the Parenteral Drug Association's (PDA) membership expertise, the goal of the Paradigm Change in Manufacturing Operations Project is to drive the establishment of 'best practice' documents and /or training events in order to assist pharmaceutical manufacturers of Investigational Medicinal Products (IMPs) and commercial products in implementing the ICH guidelines on Pharmaceutical Development (ICH Q8, Q11), Quality Risk Management (ICH Q9) and Pharmaceutical Quality Systems (ICH Q10).

The PCMO program facilitates communication among the experts from industry, university and regulators as well as experts from the respective ICH Expert Working Groups and Implementation Working Group. PCMO task force members also contribute to PDA conferences and workshops on the subject.

PCMO follows the product lifecycle concept and has the following strategic intent:

- Enable an innovative environment for continual improvement of products and systems
- Integrate science and technology into manufacturing practice
- Enhance manufacturing process robustness, risk based decision making and knowledge management
- Foster communication among industry and regulatory authorities



For more information, including the PCMO Dossi.e., and to get involved, go to www.pda.org/pcmo

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1.0 Introduction

As manufacturers seek to improve the quality of their goods, statistical methods have been rediscovered as vital tools for successful development and manufacturing. Industries like automotive, electronics, and consumer products grow and change partly as a result of adopting statistical methods.

The pharmaceutical and biopharmaceutical industry increasingly recognizes the importance of statistical methods to consistently create products that conform to predetermined quality characteristics. Statistical methods provide objective evidence in meeting this goal and are fundamental for understanding the process, which enables further improvement and development.

Industry and regulatory bodies are working together to provide guidance and frameworks on the use of statistical methods. The International Conference on Harmonisation, International Standards Organization and European Union have provided guidance on the use of statistical methods.

In light of the increased focus on this topic, this PDA Task Force recognized the need to provide guidance to help companies identify and use statistical methods. The primary objective of this Task Force was to convey the appropriate use of statistical methods at a level most can understand.

1.1 Purpose and Scope

The purpose of this document is to present relevant and easy-to-use statistical process control (SPC) methods that are applicable to the pharmaceutical/biopharmaceutical industry. Advanced statistical methods, such as multivariate models and Design of Experiment (DoE) will not be considered. An overview of acceptance sampling is also included in **Section 4.0**.

1.2 Implementation to Support Decision Making

Statistical methods are intended to improve the quality of decision-making. They are simply a means to a result. If the manufacturer does not first understand *why* it is utilizing a statistical method, problems such as failing to detect important signals or over-detecting unimportant normal variation can occur. Caution should be exercised to first establish the question to be answered and then the statistical method to aid in answering the question.

The statistical methods may be used in an ongoing program to analyze collected data. Timely evaluation of data allows the prompt detection of undesired process variation, which facilitates process understanding and may support responses to control variability.

To best aid the end-user, each statistical method is described in the following format:

- Description
- Typical Applications
- Pros and Cons
- Technical Details and Examples (see appendices)

The guidance contained in this document is not intended to establish mandatory standards for using statistical methods across a product's lifecycle.