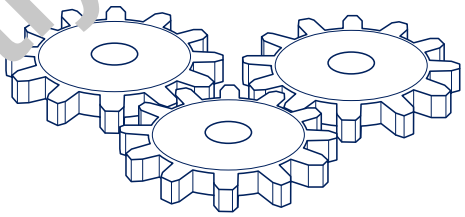
Technical Report No. 60

Process Validation:

A Lifecycle Approach

PCMO

Paradigm Change in
Manufacturing Operations℠



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PDA Task Force on Technical Report No. 60: Process Validation: A Lifecycle Approach

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

Process Validation: A Lifecycle Approach

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Paradigm Change in Manufacturing Operations (PCMO[SM])

PDA launched the project activities related to the PCMO[SM] 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.

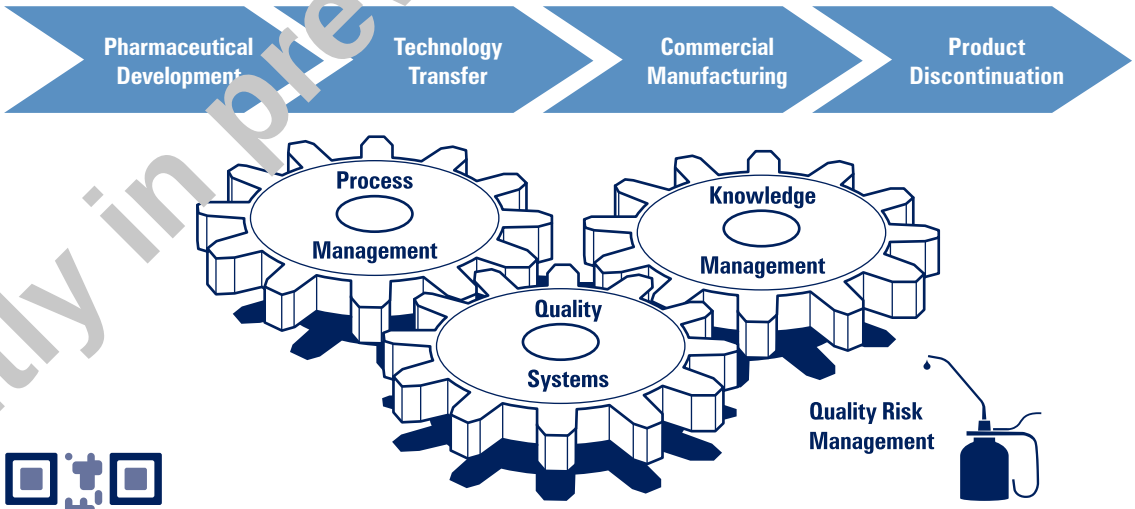
Using the Parenteral Drug Association's (PDA) membership expertise, the goal of the Paradigm Change in Manufacturing Operations Project is to drive the establishment of 'best practice' documents and /or training events in order to assist pharmaceutical manufacturers of Investigational Medicinal Products (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

The Product Lifecycle



For more information, including the PCMO[SM] Dossier, and to get involved, go to www.pda.org/pcmo

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1.0 Introduction

1.1 Purpose and Scope

This Technical Report (TR) is intended to provide practical guidance on the implementation of a lifecycle approach to pharmaceutical process validation (PV). It contains information that enables manufacturers to implement globally-compliant PV programs consistent with the principles of recent lifecycle-based PV guidance documents and current expectations for Pharmaceutical Quality Systems ***(1-4).*** In pharmaceutical manufacturing, "process validation" is the collection and evaluation of data -from the process design stage through commercial production that establishes scientific evidence that a process is capable of consistently delivering quality product ***(3).*** The U.S. FDA and EMA consider PV a requirement in both general and specific terms in current Good Manufacturing Practice (cGMP) guidelines and an essential element in the assurance of drug quality ***(2,3,5).***

The PV lifecycle concept links product and process development, the qualification of the commercial manufacturing processes, and maintenance of the commercial production process in a coordinated effort ***(3).*** When based on sound process understanding and used with quality risk management principles, the lifecycle approach allows manufacturers to use continuous process verification (enhanced approach) in addition to, or instead of, traditional PV ***(1,2,6).***

The information in this TR applies to the manufacturing processes for drug substances and drug products, including:

- Pharmaceuticals, sterile and non-sterile
- Biotechnological/biological products, including vaccines
- Active Pharmaceutical Ingredients (APIs)
- Radiopharmaceuticals
- Veterinary drugs
- Drug constituents of combination products (e.g., a combination drug and medical device)

This report is prepared for global use and applies to new and existing (i.e., legacy) commercial manufacturing processes. Its scope does not include manufacturing processes for:

- Medical devices
- Dietary supplements
- Medicated feed
- Human tissues

Although these product categories are outside the scope of this TR, its recommendations are based on modern quality concepts, ICH Quality Guidelines, and recent regulatory authority guidance documents. As such, it may be a useful reference in the development of PV lifecycle approaches for other product categories. The validation of ancillary supporting operations used in pharmaceutical manufacturing processes is not discussed in the report. Many PDA TRs already provide specific guidance for such procedures; for example, cleaning, aseptic process simulation, moist heat sterilization and dry heat sterilization ***(7-10).***

1.2 Background

The lifecycle concept includes all phases in the life of a product from initial development through commercial production and product discontinuation ***(4,11).*** The use of a lifecycle approach to pharmaceutical product quality is widely thought to facilitate innovation and continual improvement as well as strengthen the link between pharmaceutical development and manufacturing (ICH Q10). The lifecycle philosophy is fundamental in the ICH guidance documents for Pharmaceutical Develop-