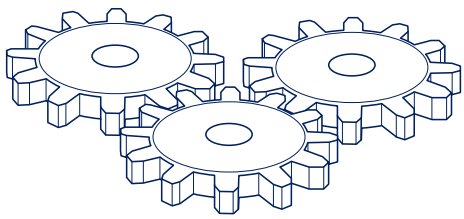
Technical Report No. 54-3

Implementation of Quality Risk Management for Pharmaceutical and Biotechnology Manufacturing Operations

Annex 2: Case Studies in the Manufacturing of Pharmaceutical Drug Products

PCMO℠
Paradigm Change in Manufacturing Operations℠



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Annex 2: Case Studies in the Manufacturing of Pharmaceutical Drug Products

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DISCLAIMER: 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 Technical Report Team 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.

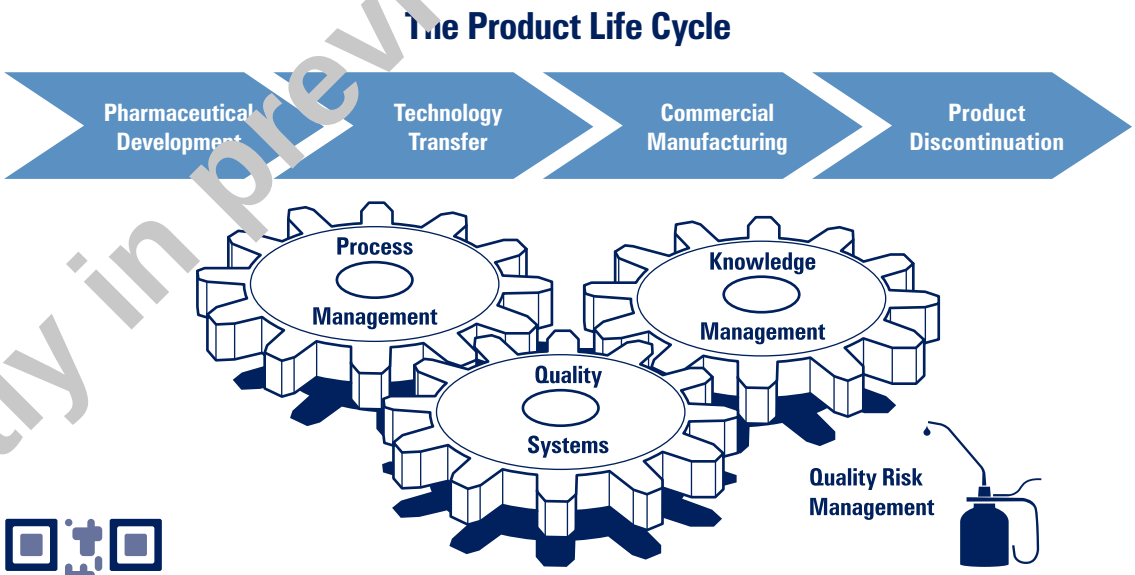
Although there are a number of acceptable pathways to address this concept, the PCMO program follows and covers the drug product life cycle, employing the strategic theme of process robustness within the framework of the manufacturing operations. This project focuses on Pharmaceutical Quality Systems 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 life-cycle 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 Dossier, and to get involved, go to www.pda.org/pcmo

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1.0 Introduction

Identification and management of risk in the pharmaceutical industry are vital to understanding pharmaceutical products and processes to minimize potential negative impacts on patients.

In the highly regulated pharmaceutical industry, it is important that significant risks be formally identified, reduced, controlled, and effectively communicated throughout the supply chain and the product lifecycle. Both industry leaders and regulatory authorities understand that some degree of risk is inherent in the manufacturing and use of drug products, but they share the common goal of protecting the patient. Formal risk-management tools can be used to effectively document and communicate this control.

ICH Quality Guideline Q9: Quality Risk Management presents general principles of risk management and examples of various risk management tools ***(1).*** However, Q9 does not provide details on how to use these tools in real-world pharmaceutical situations. This document is provided to bridge the gap using case studies from industry to illustrate how various risk management tools are applied.

Risk management is most effective when used prospectively during product development or conceptual design, when design and control systems are easily modified to reduce risk and improve product quality. Building quality into drug products up front is better than testing these products for defects later. Nonetheless, risk management can also be effectively used for an actual defect in or incident involving a commercialized product to identify the root cause and prevent recurrences. Examples of prospective and reactive risk management approaches are included in these case studies.

These case studies were selected to represent some areas that are of current concern to our industry: particulates in liquid products, viral clearance in a combination product, lyophilization, and supply chain contamination. Use of several risk management tools is illustrated in these examples. The steps in the case studies are presented according to the QRM model from Q9 (risk assessment, risk control, risk communication, and risk review).

The benefits of QRM include providing a proactive means to identify, control, and communicate quality issues; improve decision making; reduce regulatory compliance risk; and reduce patient risk. Every manufacturer's product and process is unique, and risk tolerance varies among manufacturers. Therefore, it is not possible to provide case studies and examples that fit every circumstance in pharmaceutical manufacturing. These case studies present the use of QRM in real-world situations but are only illustrative and represent just one way to manage risk.

1.1 Purpose and Scope

This document is a supplemental annex to PDA Technical Report No. 54, *Implementation of Quality Risk Management for Pharmaceutical and Biotechnology Manufacturing Operations* ***(2).*** It provides specific case study examples of how to apply quality risk management (QRM) to the manufacturing of pharmaceutical drug products. This document is one in a series of similar documents that provide additional examples of how to apply risk management tools across the product supply chain, from the starting materials (active pharmaceutical ingredients [APIs] and excipients) through manufacturing to stoppering and capping.

NOTE: There is no one way to apply QRM. The technical report team chose these four case studies to illustrate the adaptability of QRM tools to help solve various problems, implement corrective actions, and keep processes in a state of control.