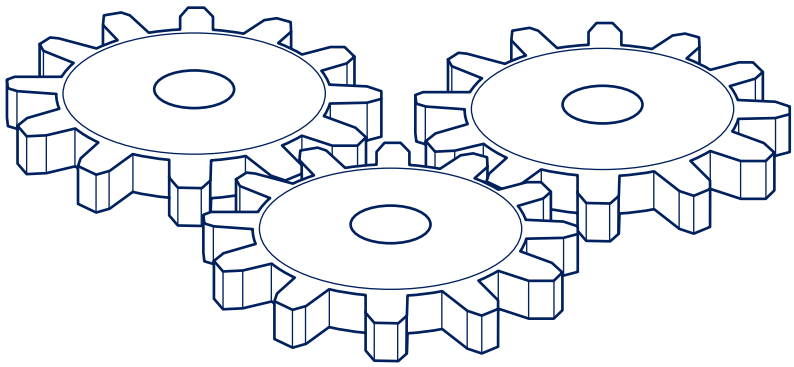
Technical Report No. 54

Implementation of Quality Risk Management For Pharmaceutical and Biotechnology Manufacturing Operations



PCMO[SM]

Paradigm Change in Manufacturing Operations[SM]

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PDA Technical Report 54: Implementation of Quality Risk Management for Commercial and Biotech Manufacturing Operations Task Force Members

Authors

Emabelle Ramnarine, Task Force Leader, Genentech

Jeffrey L. Hartman, Co-Leader, Merck

Thomas Genova, Ph.D., Johnson & Johnson

Laura Huffman, United States Food and Drug Administration

Kathy Lee, United States Food and Drug Administration

Michael A. Long, Ph.D., ConcordiaValSource

Kevin O'Donnell, Ph.D., Irish Medicines Board

Jayesh Patel, F. Hoffmann-La Roche Inc.

Siegfried Schmitt,* Ph.D., PAREXEL Consulting

Rebecca Spohn, Amgen Inc.

Edward C. Tidswell, Ph.D., Baxter Healthcare Corporation

Robert P. Tomaselli, Johnson & Johnson SPT

Anthony C. Warchut, PAREXEL Consulting

Other Contributors

James Agalloco, Agalloco & Associates, Inc.

James E. Akers, Akers, Kennedy and Associates

Kristen Anderson, United States Food and Drug Administration

Veronique D. Davoust, Ph.D., Pfizer

Lance D. Goodreau, New England BioLabs

Ghada Haddad, Genentech

William Harclerode, Forest Labs

Kristin Murray, Pfizer

Stephen Reich, Pfizer

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

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Paradigm Change in Manufacturing Operations (PCMO℠)

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.

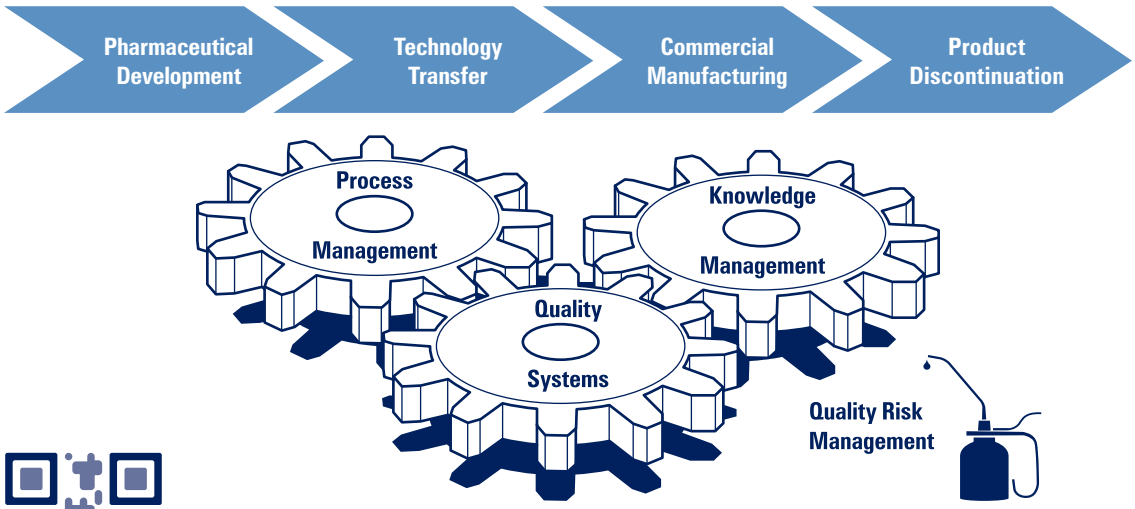
Using the Parenteral Drug Association's (PDA) membership expertise, the goal of the Paradigm Change in Manufacturing Operations Project is to drive the establishment of 'best practice' documents and /or training events in order to assist pharmaceutical manufacturers of Investigational Medicinal Products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

The Product Life Cycle



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

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1.0 Introduction

This technical report provides detailed guidance for the application and implementation of quality risk management (QRM) principles throughout the product lifecycle. The report emphasizes QRM application during commercial manufacturing and integrating QRM into the Pharmaceutical Quality System (PQS). Companion documents provide detailed examples of characteristic operations and how QRM principles and tools can be applied for biotechnology and sterile manufacturing of APIs, drug product (liquids and solids) manufacturing, packaging and labeling (e.g., *PDA Technical Report No. 44).*

QRM is integral to an effective Pharmaceutical Quality System. Per ICH Q10, *Pharmaceutical Quality System*, QRM is an "enabler" (along with knowledge management) that can provide a proactive (while also supporting a reactive) approach to identifying, scientifically evaluating, and controlling potential risks to product quality and patient safety. QRM facilitates continual improvement of process performance and product quality throughout the product lifecycle ***(1).***

Per ICH Q9, *Quality Risk Management*, "Risk management is the systematic application of quality management policies, procedures, and practices to the tasks of assessing, controlling, communicating, and reviewing risk."***(2)*** *It is important to understand that risk assessment is not synonymous with risk management.* To be effective, risk management should holistically encompass the entire product lifecycle. QRM is a living process and should be managed based on knowledge gained throughout the product lifecycle. ICH Q9 specifically provides guidance on the principles and tools of QRM ***(2)***.

Implementation of QRM offers many benefits to industry and regulators. When applied effectively, these tools and principles enable more effective and consistent risk-based decision-making (by regulators and industry) regarding the quality of drug substances and drug (medicinal) products across a product's lifecycle. When successfully integrated into a company's PQS, QRM may reduce the level of regulatory oversight that is applied to a company. This idea is further developed in ICH Q10, which discusses the potential opportunities to be gained from the use of QRM in terms of risk-based approaches. Effective risk management ensures better understanding of the product and process by identifying gaps in knowledge and can enable a company to prioritize and focus resources appropriately.

QRM has been well established in the device and other non-pharmaceutical industry sectors. Over the last few years, the pharmaceutical and biotechnology industries have begun to implement the principles and tools laid out in ICH Q9 in order to ensure that safe and efficacious drug products are consistently delivered to every patient**.**

Realization of QRM is an evolutionary process. It requires a paradigm shift in mindset, behaviors and in the way people work. **Figure 1-1** depicts an example of a maturity model for QRM.