PDA
Parenteral Drug Association

Technical Report No. 54-5

Quality Risk Management for the Design, Qualification, and Operation of Manufacturing Systems

PDA Quality Risk Management for the Design, Qualification, and Operation of Manufacturing Systems Technical Report Team

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Technical Report No. 54-5

ISBN: 978-0-939459-96-4

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1.0 Introduction

Identifying and managing risk in the pharmaceutical and biopharmaceutical industry is vital to establishing and enhancing understanding of medicinal products, processes, and production and supporting manufacturing systems to minimize potential negative impacts on patients. The industry and health authorities share the common goal of protecting the quality of the product and public health through the reliable supply of safe and effective medicines. Yet, the processes and systems involved in drug product manufacturing inherently entail some degree of risk. Left unmanaged, this could jeopardize the ability to achieve the goal of manufacturing quality and safe drug products. The application of Quality Risk Management (QRM) principles and practices can be used to ensure that high-quality medicines are available to the patient when needed.

Although ICH Guideline Q9, *Quality Risk Management* ***(1),*** presents general principles of risk management, examples of various risk management tools and potential areas where risk management may be applied, it does not provide details on how to use QRM principles or tools to manage risks throughout the design, qualification, and operation of manufacturing systems (see PDA *Technical Report 54*, *Implementation of Quality Risk Management for Pharmaceutical and Biotechnology Manufacturing Operations* ***(2)***). In applying QRM to the design, it is possible to determine the potential causes of process failure and identify control elements to manage the failure modes/hazards to an acceptable level of risk.

1.1 Purpose

This technical report provides a practical guide on how to manage quality risks throughout the manufacturing system lifecycle and illustrates concepts through two case studies, thereby bridging the gap.

1.2 Scope

The information in this technical report is applicable to both new and existing manufacturing systems for clinical and commercial drug substances and products, packaging, warehousing, and critical utility systems. It focuses on manufacturing systems determined to have an impact on product quality. The inherent assumption is that each firm will adapt this content according to its specific needs. QRM deliverables should be based on risk to product/patient, novelty, complexity, and design input (level of customization).

This technical report does not represent or replace regulatory requirements or guidances, nor does it establish legally enforceable guidelines.

1.3 Overview

ICHQ9 provides a standard approach for the application of risk management activities to the manufacturing system lifecycle:

The risk management process should be initiated prior to design of the system. Quality Risk Management can be used to focus the design and specification development effort. Process and product knowledge evolve over the course of the pharmaceutical development program. Early planning facilitates appropriate data gathering from Stage 1, Process Design, in which a quality risk assessment is performed subsequent to initially identifying the critical quality attributes and defining the manufacturing process and associated critical process parameters ***(3).***

Due to the pace of change that may occur early in the manufacturing system lifecycle, risk assessments and identified controls may require frequent updates. Manufacturing system definition and design documents should be updated when controls/critical aspects are identified to reduce residual risk to an acceptable level.

Controls/CAs should be incorporated during the design process, verified at design review/design qualification, and verified during the installation and operational test phases of the qualification lifecycle.