Quality by Design (QbD) in Pharmaceutical Industry

Dr. Shashi Kiran Misra
School of Pharmaceutical Sciences

INTRODUCTION

Pharmaceutical industry is constantly searching the ways to ensure and enhance product safety, quality and efficacy. However, drug recalls, manufacturing failure cost, scale up issues and regulatory burden in recent past produce huge challenge for industry. In traditional, the product quality and performance are predominantly ensured by end product testing, with limited understanding of the process and critical process parameters. Regulatory bodies are therefore focusing on implementing quality by design (QbD), a science based approach that improves process understanding by reducing process variation and the enabling process-control strategies.

QbD describes a pharmaceutical development approach referring to formulation design and development and manufacturing processes to maintain the prescribed product quality. Guidelines and mathematical models are used to ensure the establishment and use of the knowledge on the subject in an independent and integrated way. In order to initiate a successful QbD program, the first step is to identify those process parameters that are essential to product quality and develop well – validated analytical methodologies to monitor those parameters. The objective of this review article is therefore to provide a comprehensive understanding on various aspects of QbD, along with addressing the concerns related to its implementation.

KEY CHARACTERISTICS OF QBD

- A tool for focused & efficient drug development
- Dynamic and systematic process
- Relies on the concept that Quality can be built in as a continuum
- It is applicable to Drug Product and Drug Substance development (chemicals / biologics)
- It is applicable to analytical methods
- Can implemented partially or totally
- Can be used at any time in the life cycle of the Drug
- Always encouraged by Regulators.

BENEFITS OF QBD

- Eliminate batch failures
- Minimize deviations and costly investigations
- Avoid regulatory compliance problems
- Empowerment of technical staff
- Efficient, agile, flexible system
- Increase manufacturing efficiency, reduce costs and project rejections and waste
- Build scientific knowledge base for all products
- Better interact with industry on science issues Ensure consistent information
- Incorporate risk management
- Reduce end-product testing
- Speed-up release decision

KEY ELEMENTS OF QbD

ICH Q8: Pharmaceutical Development discusses the various elements of quality by design. These in combination with the enablers form the fundamental basis for the QbD approach to development.

It involves the following key elements during pharmaceutical development

1. Define the Quality Target Product Profile

2. Identify the Quality Attributes

3. Perform a Risk (Assessment) Analysis

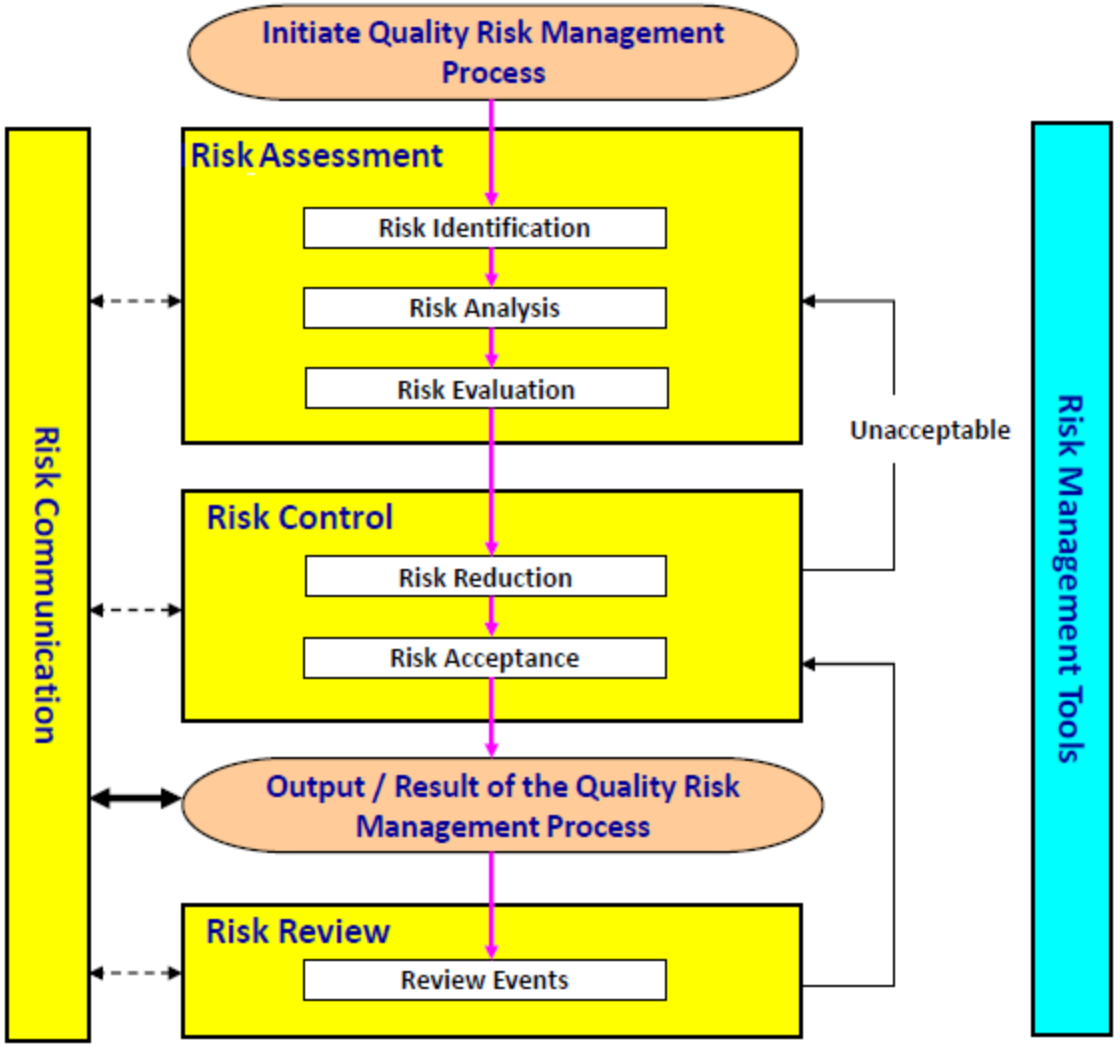
4. Determine the Critical Quality Attributes and Critical Process Parameters

5. Determine the Design Space

6. Identify a Control Strategy

QUALITY RISK MANAGEMENT (QRM)

The FDA defines a Risk Management as, a strategic safety program designed to decrease product risk by using one or more interventions or tools. It is systematic process for the assessment, control, communication and review of risks to the quality of the drug product across the product lifecycle



CHALLENGES

Though Quality by design is an essential part of the modern approach to pharmaceutical quality, but Lack of understanding regarding the pharmaceutical process is the cause and also the major limitation for QbD implementation. Pharmaceutical companies are traditionally tuned to care more about the end product, with little emphasis on the science-based understanding of the process involved. The majority of pharmaceutical companies feel that there is a need for a more easy guidance on how to actually implement QbD.

The challenges occur within companies

1. Internal misalignment (Disconnect between cross functional areas,
 e.g., R&D and manufacturing or quality and regulatory)
2. Lack of belief in business case i.e. there is a lot of uncertainty over timing of and investment requirements for QbD implementation.
3. Lack of technology to execute (e.g., Difficulty managing data, limited understanding of Critical Quality Attribute (CQA) implications)
4. Alignment with third parties (i.e., How to implement QbD with increasing reliance on suppliers and contract manufacturers.

Challenges, directly related to the regulatory authority

1. Inconsistency of treatment of QbD across regulatory authority
Lack of tangible guidance for industry
2. Regulators not prepared to handle QbD applications
3. The way promised regulatory benefits are currently being shared does not inspire confidence
4. Misalignment of international regulatory bodies
5. Current interaction with companies is not conducive to QbD
6. It is accepted that the challenges and concerns associated with the implementation of QbD can only be resolved if there is efficient communication between the industry and the regulatory bodies.