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Quality By Design Approach-To Analytical Method Validation

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Abstract

A pharmaceutical industry is highly regulated by a quality policy in its management. The principles of Quality by Design (QbD) must be applied to ensure the development of pragmatic and systematic methods while managing the risks associated with analytical methods. Quality by Design (QbD) is a scientific way to develop easy and robust analytical techniques for critical analysis. QbD is a significant part of the presentday approach to improving pharmaceutical quality. It can be described as a novel approach to development of any product which may increase efficiencies, offer regulatory relief and pliability, and also provide business advantages throughout the product lifecycle. In this regards, pharmaceutical industry is currently undergoing a significant transformation to streamline their research and development process, provide greater manufacturing flexibility and control, and to reduce regulatory burden. Using QbD, pharmaceutical quality is assured by understanding and controlling formulation and manufacturing variables. Some of the QbD elements include defining target product quality profile, designing product and manufacturing processes, identifying critical quality attributes, process parameters, and sources of variability and controlling manufacturing processes to produce consistent quality over time .The purpose of this article is to discuss the concept of pharmaceutical Quality by Design and describe how it can be help to ensure pharmaceutical quality and drug development.

Keywords: Quality by Design (QbD), Quality Target Product Profile (QTPP), Quality Risk Management (QRM).

Introduction

Drug development is approached holistically and modernly with QbD. Despite being novel to the pharmaceutical industry, this idea has already been thoroughly tested and used [1]. Quality in manufacturing is a measure of excellence or a condition in which there are no defects, deficiencies, or significant variations. This explanation concentrates on the QbD for generic medications. The ICH Q8 advice made reference to the idea of QbD when it stated that "quality cannot be tested into products." [2,3].The advantage of using Analytical Quality by Design (AqbD) is that method properties are understood. Enhanced information exchange, method development, and dynamic control strategies result in more effective regulatory oversight, operational elasticity, rational and scientific regulatory filing, shorter product time to market, less product rejection, and decreased change after approval. In

pharmaceutical quality systems, analytical techniques are a critical component of the control strategy (ICH Q10). It contains numerous parameters and characteristics relating to pharmaceutical products and substances, such as the way the instruments are used and the associated procedures. [4]

Components of QbD

A] Quality target product profile (QTPP)
B] Critical quality attributes (CQA)
C] Quality Risk assessment
D] Quality risk management (QRM)
E] Control strategy

A] Quality Target Product Profile (QTTP)

The FDA defines QTPP as the product's quality characteristics related to safety and effectiveness. It could cover the administration method, the dosage form, the delivery method, the dose strength(s), the container closing system, the pharmacokinetic consideration, and the standards for the quality of the drug product (e.g., sterility, purity, stability, and drug release). The QTTP is defined as "Prospective summary of the quality features of a drug product, taking into account safety and efficacy of the drug product, that will ideally be reached to ensure the required quality," by ICH Q8(R2). [4,5]

The FDA has released guidelines that outline the Target Product Profile (TPP), which places the consumer (patient) and the ideal product label at the focus. A variant of the TPP called the QTPP is more focused on the development's chemical, manufacturing, and controls (CMC) aspects..

It is important to recognize that the QTPP should only contain elements related to patient-relevant product performance. for example -Tablet density or hardness, for instance, might be specified for process monitoring but may not be included in the QTPP.[6]

B] Critical quality attributes (CQA)

The next step is to locate the relevant CQAs once the QTPP has been found. According to the definition of a CQA, there must be within the required limit, range, or distribution in order to maintain the desired quality of the product. [7,8]

The majority of the time, CQAs relate to the drug substance, excipients, intermediates (in-process materials), and drug product. Some have used CQA to define QTPP elements (such as dissolution), while others have used it to explain mechanistic elements that affect product performance (such as particle size and hardness). As a result, CQA is used to describe both aspects and determinants of product performance.

While developing biopharmaceuticals, identifying CQA qualities is a crucial first step as they may affect safety and efficacy and have the potential to be used as a quality attribute. The CQA assessment is based on the requirements of the product attributes required for the anticipated product performance as specified by the quality target product profile (QTPP) and takes other information sources into consideration for consideration in the following step. s. There is a different CQA for every analytical

method. HPLC (UV or RID) CQA is composed of the following methods: mobile phase buffer, pH, diluent, column selection, organic modifier, and elution method. The GC method's CQA variables include the gas flow, oven temperature, injection temperature, diluent sample, and concentration.[9,10]

C]Quality Risk Assessment

Risk assessment is a valuable analytical technique used in quality risk management (see ICH Q9) that can help identify material characteristics and process variables that could have an effect on the product CQAs. Risk assessment is frequently carried out early in the pharmaceutical development process and may be repeated if new information or knowledge becomes available.

Risk analysis contributes to method or process quality improvement. Additionally, it determines how an input variable will affect a method or process. One can identify key characteristics that will affect the product's final quality through risk assessment.

Risk assessment is a systematic approach to evaluating, controlling, communicating, and analyzing quality risks throughout the product life cycle, according to the ICH Q9 criteria. Risk evaluation relies heavily on prior product knowledge, including accumulated laboratory, non-clinical, and clinical experience with specific product quality qualities.[13,14].

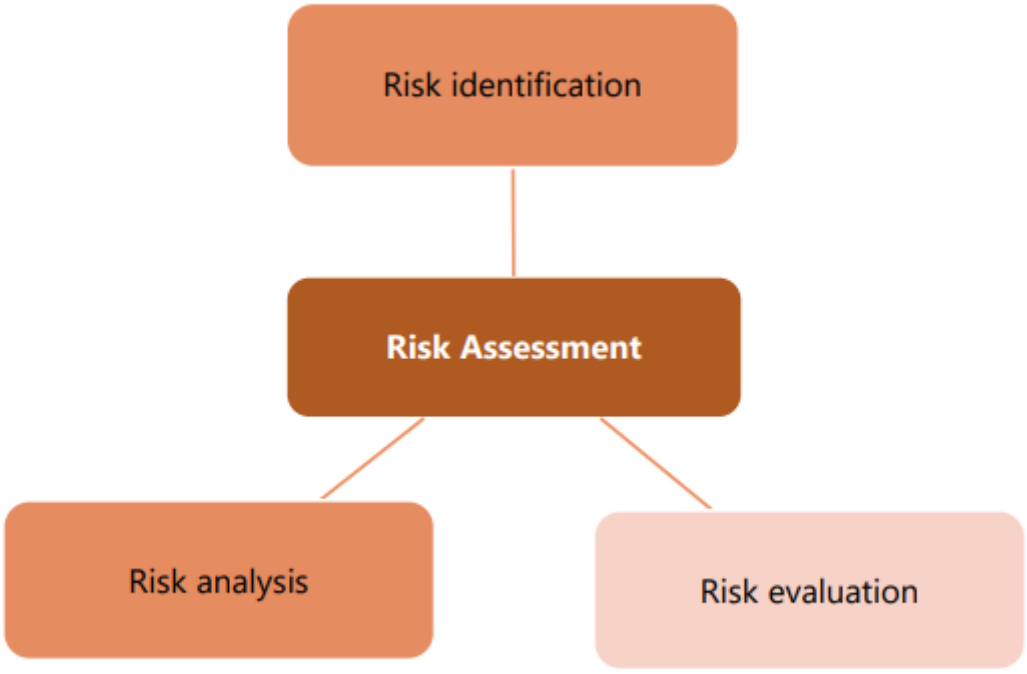


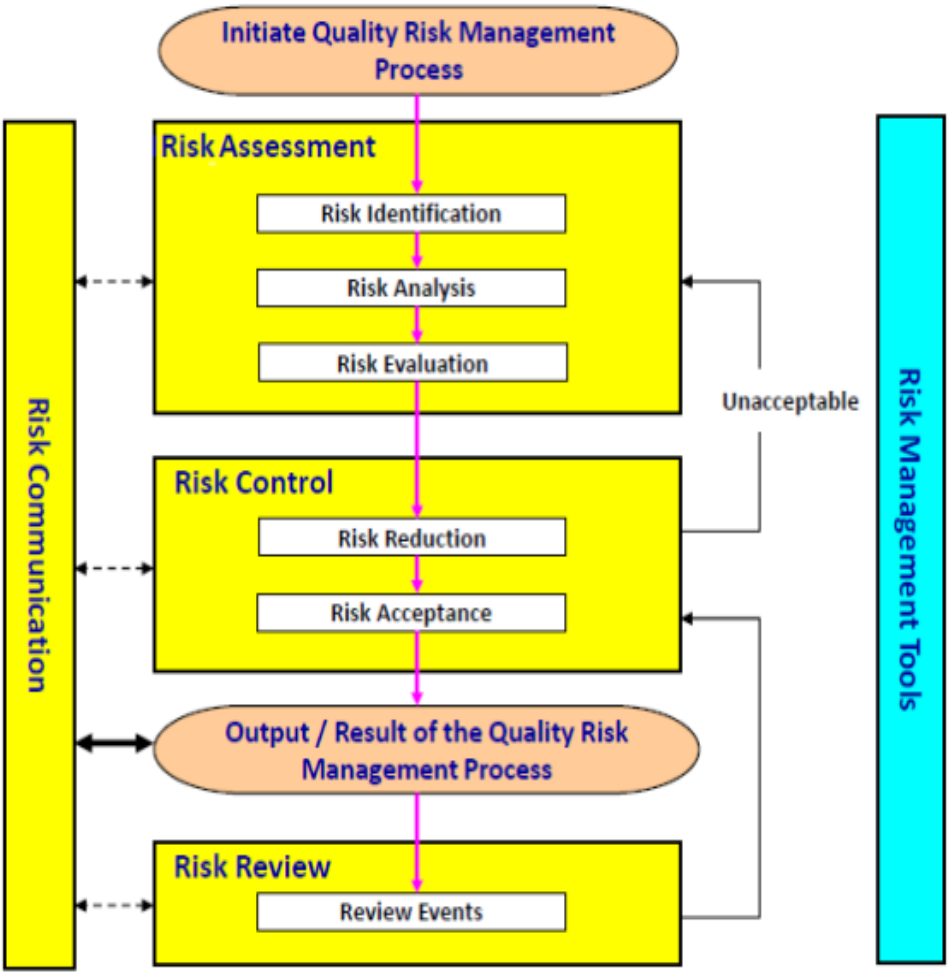
Figure 2. Steps in the risk assessment

d] Quality risk management (QRM)

According to the FDA, quality risk management (QRM) is a systematic method for the evaluation, control, communication, and review of risks to the drug product's quality throughout the product

lifetime. In order to detect risks in a process or event, analyze their significance, and take the necessary steps to minimize those risks if they are deemed unacceptable is the purpose of quality risk management (QRM). [11,12]

The Quality Risk Management ICH Q9 guideline provides a framework for starting and maintaining a risk management process. The following are some relevant tools for QRM:



E] Control Strategy

The control strategy is a tool used in control design. Controls may comprise metrics and characteristics relating to drug substances, ingredients, and component parts, operating conditions for facilities and equipment, in-process controls, finished product requirements, and techniques and frequencies relating to monitoring and control. [15].According to the definition given by ICH Q10, a control strategy is "a planned set of controls derived from current product and process understanding that assures process performance and product quality."

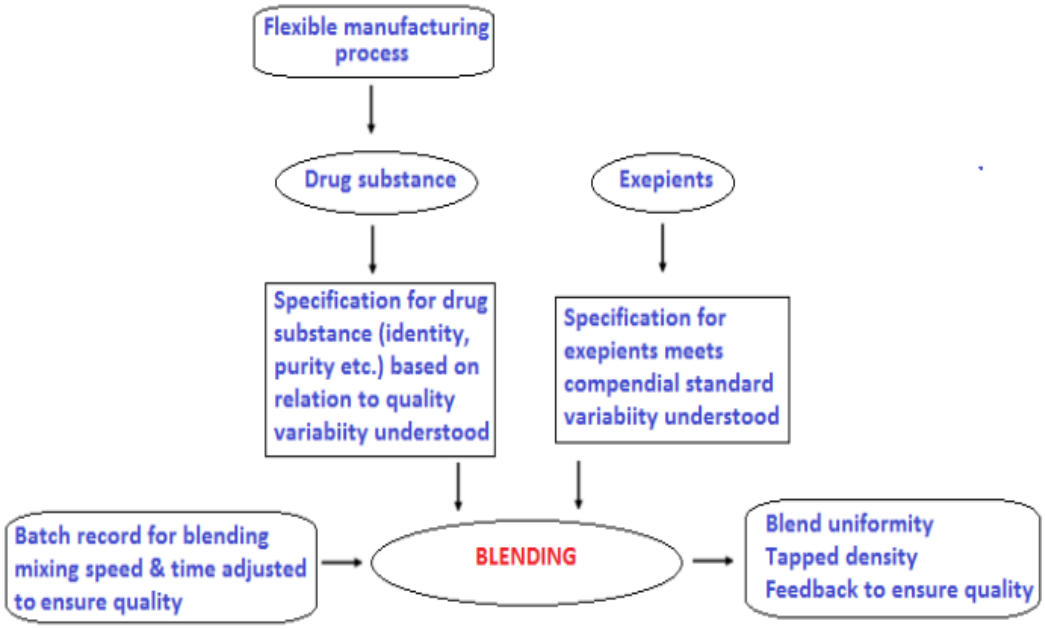


Fig. 4. Example of control strategy for QbD process.

Specifically, the control strategy may include [26]:

1Control of input material qualities (such as drug ingredient, excipients, and major packaging materials) based on knowledge of their effect on the capacity to process or the quality of the final product.

2. Specifications for the product

3. Procedural controls

4. utilities, environmental systems, and operational conditions are examples of facility controls.

5. Controls for unit operations that influence downstream processing or the quality of the final product (example- the impact of drying on degradation, particle size distribution of the granulate on dissolution)

6. A monitoring programme for verifying multivariate prediction models, such as full product testing at regular intervals.

Benefits of QBD [16,17,18,19]

- QbD promotes business.
- Avoid batch failures
- reduce costly deviations and investigations
- Restrictive compliance issues should be avoided.
- Learning within organisations is an investment in the future.
- QbD is excellent science.
- better choices for development
- technical staff empowerment

Advantages

- Patient safety and product effectiveness are important.
- The pharmaceutical process and methods are understood scientifically.
- It involves developing products and procedures.
- Risk assessment is done using science.
- Criticalquality attributes are recognised, and their impact on product quality is analyzed.
- It provides a reliable method or procedure.
- Business benefits are another motivating factor for adopting QbD.

Challenges

•Lack of confidence in the business case, or the uncertainty surrounding the timing and financial commitments necessary for implementing QbD.

•Lack of technology to carry out (example- difficulties maintaining data, poor understanding of significance of Critical Quality Attributes (CQA)

•Agreement with outside parties (i.e., How to implement QbD with increasing dependency on suppliers and contract manufacturers?)

•The regulatory authority is directly involved with the following six challenges

•Treatment of QbD across regulatory authorities is inconsistent.

•A lack of concrete recommendations for industry

•Regulators are not equipped to deal with applications for QbD

•The current distribution of the projected regulatory benefits does not give rise to trust.

•Misalignment of global regulatory organisations

•Existing business interactions are not QbD-friendly

•It is accepted that effective communication between the industry and the regulatory bodies is necessary to address the difficulties and problems related to the implementation of QbD.

Applications

1. For chromatographic technique
1.1. In determination of impurity
1.2. In screening of column used for chromatography
1.3. In development of HPLC method for drug products/ substances
1.4. In capillary electrophoresis
1.5. In stability studies
1.6. In UHPLC
2. For hyphenated technique
2.1. In LC–MS method development
3. In bioanalytical method development

4. In dissolution studies
5. For spectroscopic measurements
5.1. In handling complex spectroscopic data
5.2. In mass spectroscopy
5.3. In near infrared
6. Other applications of QbD or elements of QbD
6.1. Pharmaceuticals
6.1.1 In modified release products
6.1.2. In sterile manufacturing
6.1.3. In solid oral dosage form
6.1.4. Contribution of (SEM/EDX) to QbD by investigation of pharmaceutical materials
6.1.5. In gel manufacturing
6.1.6. QbD for ANDAs
7 Clinical.

CONCLUSION

QbD is a vital instrument that promotes process understanding, which is essential for assuring the performance and quality of products. It includes a variety of tasks like technology transfer, control inspections, deviation reduction, and the creation and advancement of analytical methods. Analytical method development and evaluation can be done using QbD.

QbD is a vital instrument for promoting process knowledge, which is necessary for guaranteeing the effectiveness and quality of products. It involves a range of activities, including the development and improvement of analytical techniques, technology transfer, control inspections, and deviation reduction. QbD can be used for both the development and evaluation of analytical methods

In order to implement QbD and AQbD, terminology and concepts must be harmonised. Human resources for industry and regulatory organisations must also be trained and educated, and there is a need for guidelines on how to record information acquired throughout the development of pharmaceutical methods.

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