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# A Review on Quality by Design

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**ABSTRACT**

A key component of the contemporary advancement in pharmaceutical quality is quality by design, or QbD. Every regulatory agency has made quality a priority for pharmaceutical products. Customer satisfaction with regard to services, goods, and procedures is a measure of quality. The best way to improve the quality of any pharmaceutical product is through QbD. This article provides an overview of Pharmaceutical Quality by Design (QbD) and explains how it can be used to guarantee the caliber of pharmaceutical analysis. Throughout the product's design and development, it is crucial to determine the target product profile (TPP), quality target product profile (QTPP), and key quality attributes (CQA) for the desired product performance report. The goal of pharmaceutical development is to create high-quality products and manufacturing processes that reliably produce the desired results. Although quality cannot be tested into items, it should be incorporated into their design. Key components of Quality by Design, important quality criteria, and the Quality target product profile are all included. Additionally, it compares the quality of the product by Quality by Design with the quality by final product testing. The ICH Guidelines serve as the cornerstone of Quality by Design. Q8 for pharmaceutical development, Q9 for quality risk management, and Q10 for pharmaceutical quality systems are the ICH Guidelines that serve as its foundation. Additionally, it explains how Quality by Design can be used to pharmaceutical research and manufacture.

**Keywords :** introduction**,** definition **,** key elements, benefits, objective, application.

## Introduction :

The Latin term "Qualitus," which meaning "general excellence" or "distinctive feature," is where the word "quality" first appeared. "Fitness for intended use" is the most basic definition of quality. The appropriateness of a drug substance or medication product for its intended use is known as quality. Qualities like individuality, strength, and purity are included in this word. A drug product is considered high quality if it is free from contaminants and flaws and provides the therapeutic, pharmacokinetic, and reproducible benefits that are listed on the label. Quality has three dimensions: performance, dependability, and durability. [1]. Producing consistently high-quality products is essential in the pharmaceutical sector because only these might provide the intended therapeutic effects. The increasing quantity of research studies based on the QbD concept has further encouraged the regulatory agencies' to choose this product development process. [2].A better scientific understanding of critical process and product qualities, designing controls and tests based on the scientific boundaries of understanding during the development phase, and using the knowledge gained throughout the product's life-cycle to work on a constant improvement environment are all components of the "Quality by Design" (QbD) concept. In order to maintain the required level of product quality, QbD refers to a pharmaceutical development method that includes formulation design, development, and manufacturing procedures. To guarantee the establishment and application of the subject's knowledge in an autonomous and cohesive manner, guidelines and mathematical models are employed. [3].

**Definition [ICH Q 8(R1)]** : Based on sound research and high-quality risk management, this methodical approach to development starts with predetermined goals and places an emphasis on understanding the product and process as well as process control. [4].

**Definition [FDA PAT Guidelines, Sept. 2004] :** With the aim of guaranteeing the safety of the finished product, a system for planning, evaluating, and managing manufacturing through prompt measurements (i.e., during processing) of crucial quality and performance attributes of new and in-process materials and processes. [5, 6].

***Benefits of QBD : [7,8,9,10 ,12].***

- QbD is good Business
- Eliminate batch failures

- Minimize deviations and costly investigations
- Avoid regulatory compliance problems
- Organizational learning is an investment in the future
- QbD is good Science
- Better development decisions
- Empowerment of technical staff.
- 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.

## Objectives of QbD : [11]

The primary aim of Quality by Design (QbD) is to ensure the production of high-quality products. Additional goals include:

- Attaining favorable outcomes in performance testing.

- Integrating the knowledge of both product and process acquired throughout the development phase.

- Enhancing process capability while minimizing product variability and defects.

- Establishing significant product quality specifications that are informed by clinical performance.

- Improving process capability and reducing variability and defects through better product and process design, comprehension, and control.

- Boosting efficiencies in product development and manufacturing.

- Strengthening root cause analysis and the management of changes post-approval.

Essential components of Quality by Design (QbD) include:

1. Establishing the Quality Target Product Profile

2. Recognizing the Quality Attributes

3. Conducting a Risk Assessment Analysis

4. Identifying the Critical Quality Attributes and Critical Process Parameters

5. Defining the Design Space

6. Formulating a Control Strategy..

1. **Quality Target Product Profile : "**The "Prospective Summary of the quality characteristics of a drug product that ideally will be achieved to ensure the desired quality, taking into account safety and efficacy of the drug product" is defined by ICH Q8(R2) as the Quality Target Product Profile (QTPP). This framework serves as a vital instrument for formulating the drug development strategy. In recent years, the QTPP has been extensively utilized in development planning, clinical and business decision-making, interactions with regulatory agencies, and risk management. It outlines the essential quality attributes that a pharmaceutical product must possess to reliably deliver the therapeutic benefits as stated on its label.

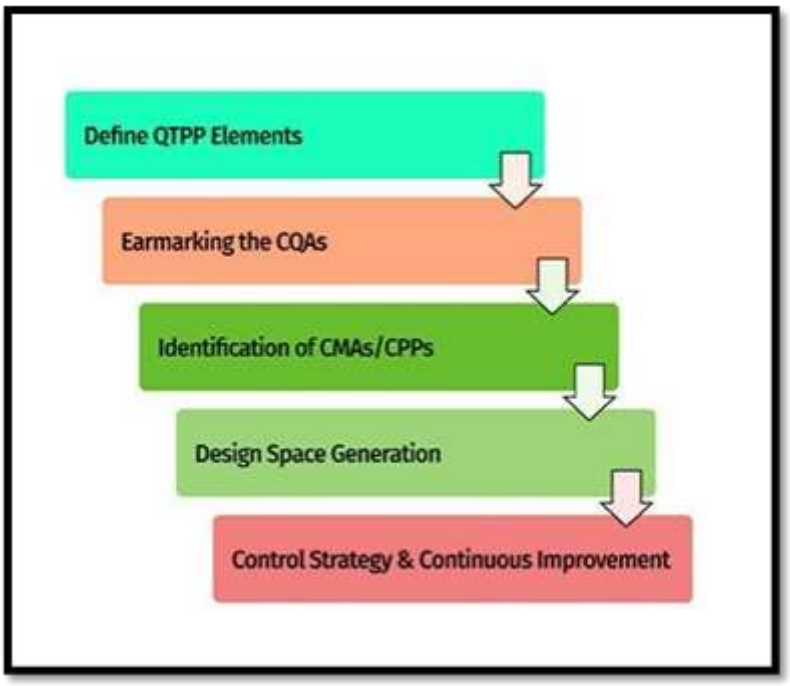


**Fig.no.1**

The QTPP aids formulation scientists in devising formulation strategies while ensuring the efficiency and focus of their work. Key aspects such as identity, assay, dosage form, purity, and label stability are integral to the QTPP. For instance, a standard QTPP for an immediate-release solid oral dosage form would encompass...

- Tablet Characteristics
- Identity
- Assay and Uniformity
- Purity/Impurity
- Stability, and
- Dissolution

2. Critical Quality Attribute: The identification of relevant Critical Quality Attributes (CQAs) follows the establishment of the Quality Target Product Profile (QTPP). A CQA is defined as "a physical, chemical, biological, or microbiological property or characteristic that must remain within specified limits, ranges, or distributions" to ensure the desired quality of the product. CQAs are generally associated with drug products, intermediates (in-process materials), and source materials (active ingredients and excipients). These attributes are essential for the performance of drug products, specifically regarding their intended efficacy, safety, and overall quality. This indicates that CQAs are specific components of the QTPP that may be adjusted in response to changes in formulation or process variables. For example, while the QTPP may encompass additional quality factors such as dosage form and strength—attributes that remain constant throughout the drug development process—CQAs will include attributes like assay, content uniformity, dissolution, and permeation flux, which are subject to modification based on formulation or process changes.Quality Risk Management :

3. **Design Space :** As defined by ICH Q8(R2), the design space encompasses a multidimensional array of interactions among process parameters and input variables, such as material characteristics, that ensure quality assurance. Operating within the design space is not classified as a modification. However, exiting the design space is deemed a change, which typically initiates the regulatory process for post-approval modifications. The design space is proposed by the applicant and requires approval from the regulatory authority. It is influenced by laboratory conditions and may differ based on the equipment and scale utilized. The processes at a commercial scale may remain unaffected by variations in scale. Therefore, validating the design space is essential until it is confirmed that it is independent of scale, making the commercial scale a critical factor [17].

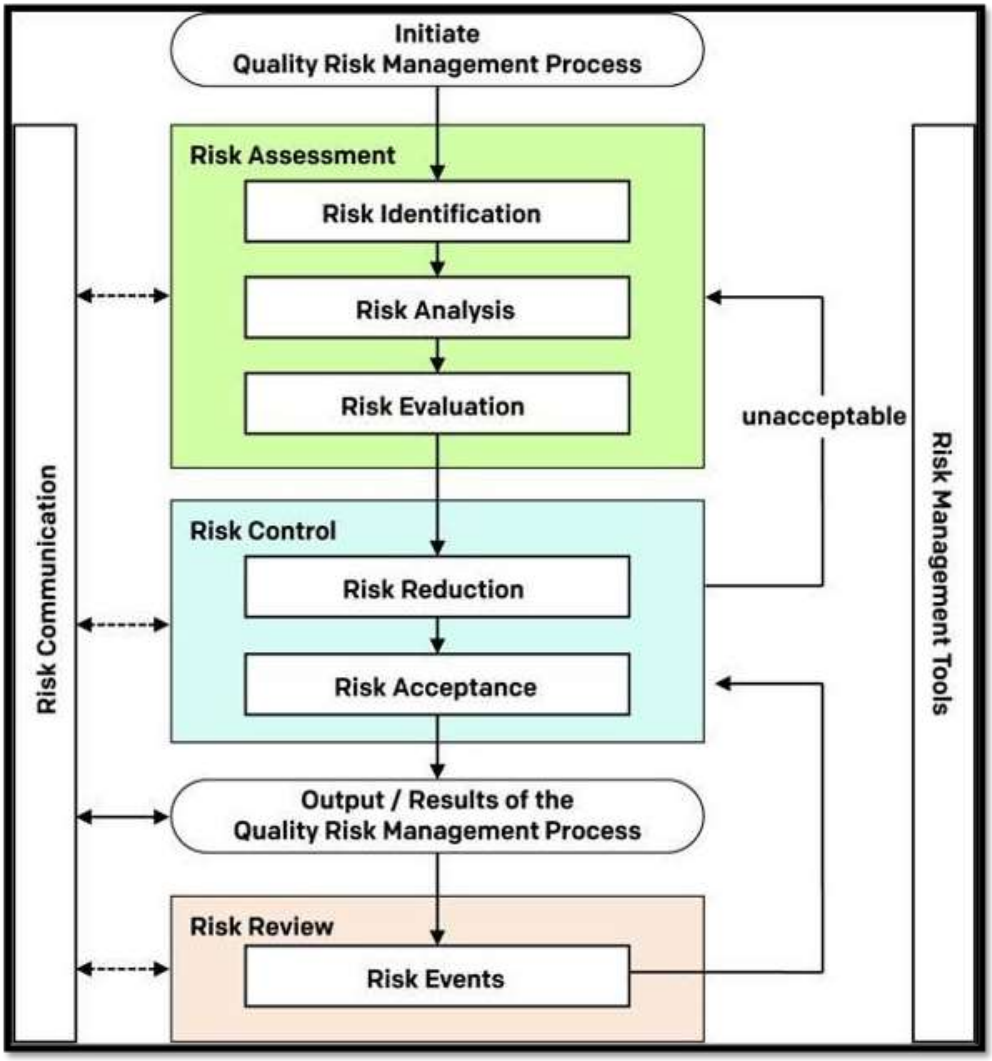


**Fig.no.2**

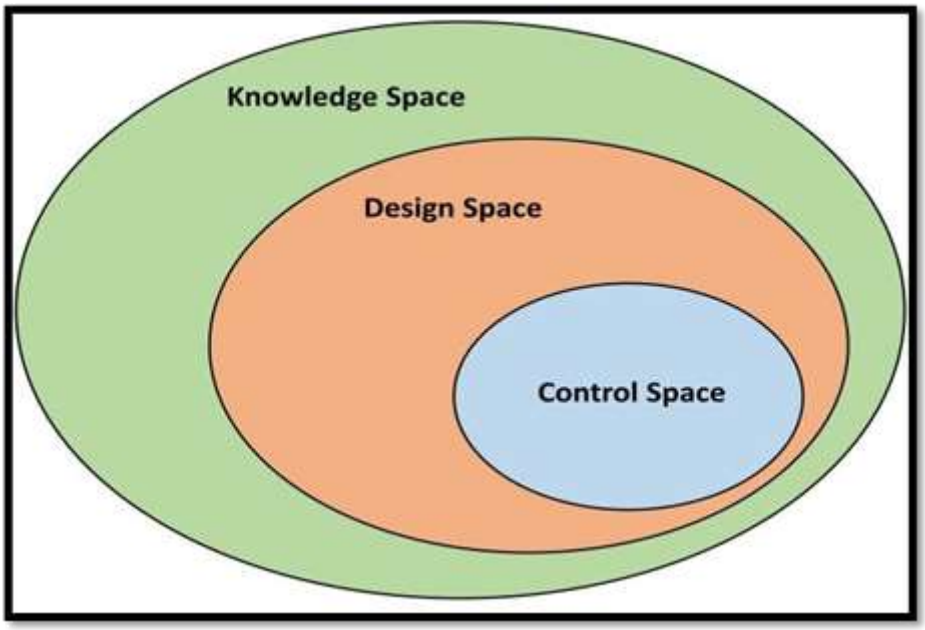


**Fig.no.3**

Control Strategy: The term "control strategy" refers to a systematic arrangement of controls that is based on the current understanding of products and processes, ensuring both process performance and product quality. Within the Quality by Design (QbD) framework, the control strategy is shaped by a risk assessment that evaluates process capability alongside the criticality of the Critical Quality Attributes (CQA). The control strategy may encompass various elements, including lot release testing, process monitoring, characterization testing, comparability testing, stability testing, procedural controls, and in-process controls. The specific components of the control strategy may include:

1. Management of raw material characteristics (such as active pharmaceutical ingredients, excipients, and primary packaging materials) informed by their influence on processability and product quality.
2. Definition of product specifications.
3. Implementation of procedural controls.
4. Oversight of facility controls, including utilities, environmental systems, and operational conditions.
5. Regulation of unit operations that affect downstream processing or the quality of the final product, such as the effects of drying on degradation and the influence of granulate particle size distribution on dissolution.
6. Verification of input material characteristics (including active pharmaceutical ingredients, excipients, and both primary and secondary packaging materials) based on their impact on processability and product quality.
7. Establishment of product release and shelf-life specifications.
8. Development of standard test procedures for finished products.
9. Maintenance of facility controls, such as utilities, environmental systems, and operational conditions (including temperature and relative humidity).
10. Creation of standard operating procedures (SOPs) or guidelines to monitor Out of Specification (OOS) results, Out of Trend (OOT) occurrences, deviations, and similar issues.

## Application of QbD : [19]

1. **Pharmaceutical development:**

Nowadays, QbD is widely employed in all stages of pharmaceutical product development and has many applications. Analytical techniques, drug compounds, formulation, dissolution tests, bioequivalence studies, clinical trials, and manufacturing are all developed with its help.to create a high- quality product and a production procedure that reliably produces the product's desired performance.

**2. Office of New Drug Quality Assessment (ONDQA):**

1. Science-based assessment
2. Restructured organization and reorganized staff –premarket staff and post market
3. CMC Pilot
4. A number of applications submitted
5. Lessons learned
6. Evaluation of information 7.Implementation of PMP.

**3. Office of Generic Drugs (OGD):**

1. QbD contains the important scientific and regulatory review questions
2. Evaluate whether a product is of high qualityDetermine the level of risk associated with the manufacture and design of this product
3. 416 applications received using QbD by June 2007
4. Successful in ensuring that questions address issues regarding QbD.

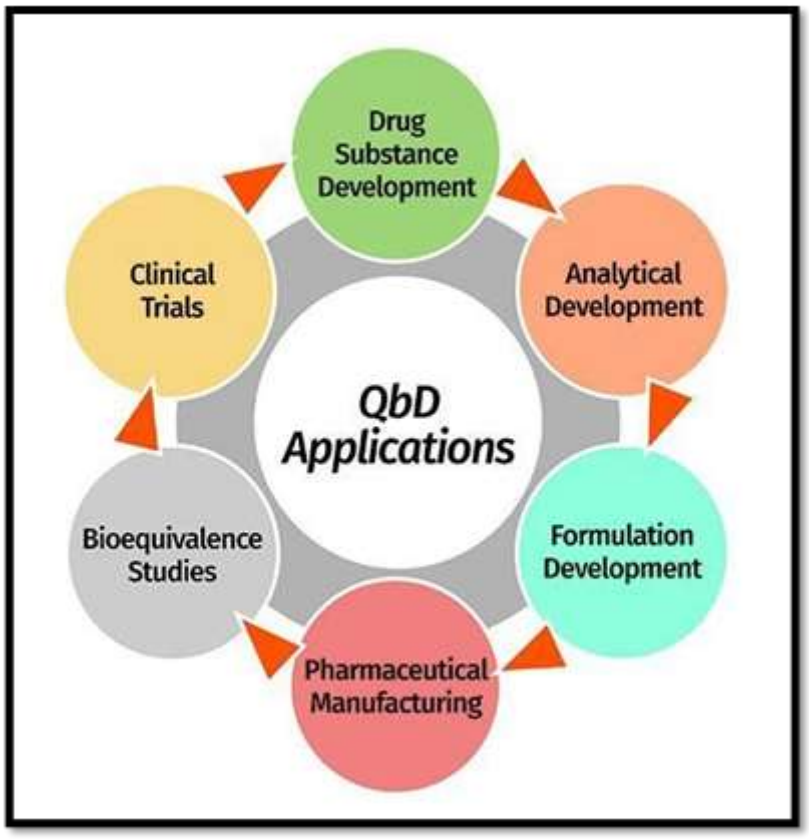


**Fig.no.4**

## Conclusion:

Based on current guidelines and reference materials, quality by design, or QbD, is a concept that is suggested to enhance process understanding. QbD is a quality system that establishes future regulatory requirements while building on the past. Pharmaceutical processes such as drug development, formulations, analytical techniques, and biopharmaceuticals are where QbD becomes significant. The regulatory requirements are the primary driver of QbD adoption. For the pharmaceutical sector to officially promote its products, regulatory compliance is necessary.

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