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# QUALITY BY DESIGN- AN OVERVIEW ON OBJECTIVES AND APPLICATIONS

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## ABSTRACT

**Background:** Quality by design (QbD) is an essential part of the modern approach to pharmaceutical quality. This paper gives an idea about Quality by Design is emerging to increase the promise of providing safe and effective medicines to customers and to improve the efficiency of product quality. **Parameters:** It is based on the ICH Guidelines Q8 for pharmaceutical development, Q9 for quality risk management, and Q10 for pharmaceutical quality systems. QbD defines the quality Target Product Profile (QTPP), Critical Quality Attributes (CQA), Risk assessment, Control Strategy, and life cycle management to design and develop the formulation and process. **Conclusion:** The purpose of this paper is to explain how QbD may be applied to guarantee the efficient production and high quality of pharmaceutical goods.

**Keywords: Quality by Design, ICH Guidelines, QTPP, CQA, Control Strategy**

## INTRODUCTION:

Originating from the Latin term "Qualitus," which denotes overall excellence or a unique characteristic, comes the English word "quality." The ability to function as intended is the most basic definition of quality. Quality refers to how well a drug substance or drug product fits the purpose for which it was designed. This word contains a few characteristics including individuality, sturdiness, and purity

Dr. Joseph M. Juran initially coined the term "quality by design," or QbD, and the

automobile industry adopted it. In the pharmaceutical sciences, the Food and Drug Administration (FDA) introduced the concept of quality by design (QbD). as well as the Harmonisation International Conference (ICH). The fundamental idea behind quality by design is that "quality should be built into the product, not tested into it" **[1]**. To improve strong production processes, facilitate product quality, and create items under "Six Sigma," the pharmaceutical sector established the idea of quality by design or QbD.

"Six Sigma" is a set of procedures designed to improve processes methodically and get rid of statistically significant flaws. Since its inception, Six Sigma has come to be a crucial component of several total quality management (TQM) projects **[2]**. **Figure 1** Shows the QbD model.


**Figure 1: QbD Model**

## OBJECTIVES OF QbD

The main objective of QbD is to achieve quality products. Other objectives are:

1 To achieve positive performance testing.

2 To ensure the combination of product and process knowledge gained during developments **[3]. Figure 2** shows an overview of QbD

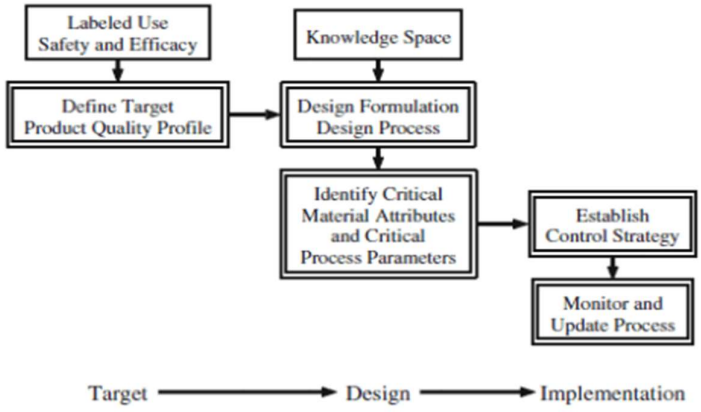


**Figure 2: Overview of QbD**

**BENEFITS of QbD**

1 Quality by Design is beneficial to businesses.
2 Get rid of batch failures.
3 Prevent issues with regulatory compliance.
4 Reduce alterations and expensive inquiries.
5 Encouraging technical personnel **[4]**.

**Table 1: Difference between the current approach and the QbD approach [5]**

| Current Approach | QbD Approach |
|---|---|
| Quality is assured by testing and inspection. | Quality is built into products and process by design and based on scientific understanding. |
| It includes only data-intensive submission which includes disjointed information without the "big picture". | It includes knowledge-rich submission which shows product knowledge and process understanding. |
| Here there is the "Frozen process", which always discourages changes. | Here there is a flexible process within the design space which allows continuous improvement. |
| Here, any specifications are based on batch history. | Here, any specifications based on product performance requirements |
| It focuses on reproducibility which often avoids or ignores variation. | It focuses on robustness which is understanding & control variation. |


**Figure: 3 ICH Activities**

**ICH ACTIVITIES**

ICH guidelines Q8 (on Pharmaceutical Development), Q9 (on Quality Risk Management), and Q10 (on Pharmaceutical Quality Systems) provide some assistance for manufacturers to implement Quality by Design into their operations (ICH Quality Guidelines), (CMC), (International Conference on Harmonisation). The ICH Steering Committee meets twice a year to discuss the progress of its efforts. This practical input should help ensure that quality risk management and knowledge management are used to make lifecycle adaptations that maintain process control and product quality **[6]**.

**MATERIALS AND METHODS**

**ELEMENTS OF QbD**

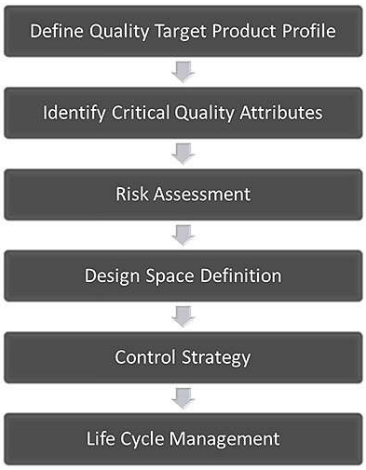


**Figure:4 Elements of QbD**

This are the elements of QbD in the **Figure 4**.

**QUALITY TARGET PRODUCT PROFILE [QTPP]**

The QTPP serves as an overview of the drug development program, which is essential to the entire process of finding and developing new drugs. Quality, safety, and efficacy are related to "considering and planning with the end in mind," which includes things like dose form, route of administration, bioavailability, strength, and stability **[7].**

**CRITICAL QUALITY ATTRIBUTES [CQA]**

Identifying the correct CQAs is the next step after determining QTPP. According to definitions, a CQA is "A physical, chemical, biological, or microbiological. A quality or attribute that must be within a certain range, limit, or distribution to guarantee the intended level of product quality **[8]**. **Figure 5** shows the decision tree of CQAs.

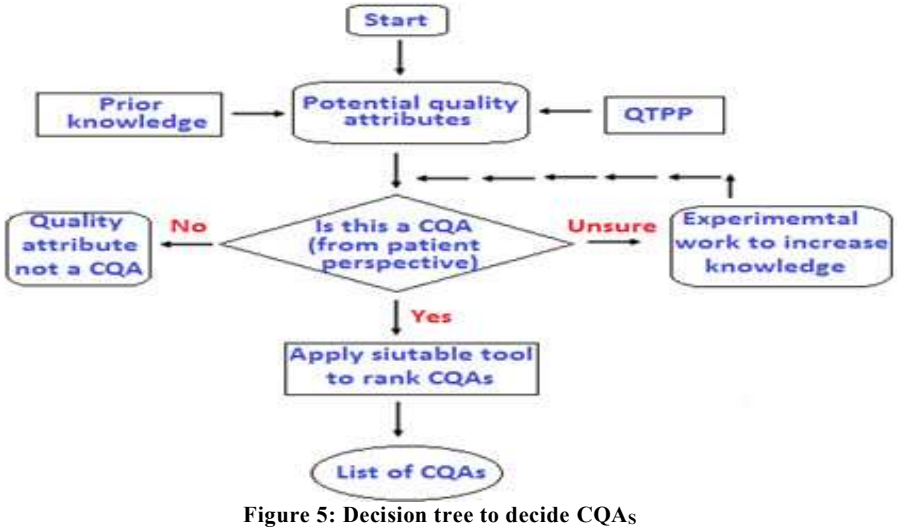


**Figure 5: Decision tree to decide CQAs**

**RISK ASSESSMENT**

QRM is a systematic method for the assessment, control, communication, and review of risks to the drug product's quality, according to the FDA throughout the lifespan of the product. Therefore, the purpose of QRM is to detect risks in a process or event, evaluate their relevance, and, if necessary, take appropriate action to minimize such risks. **Figure 6** Shows the Quality Risk Assessment Process **[9]**.

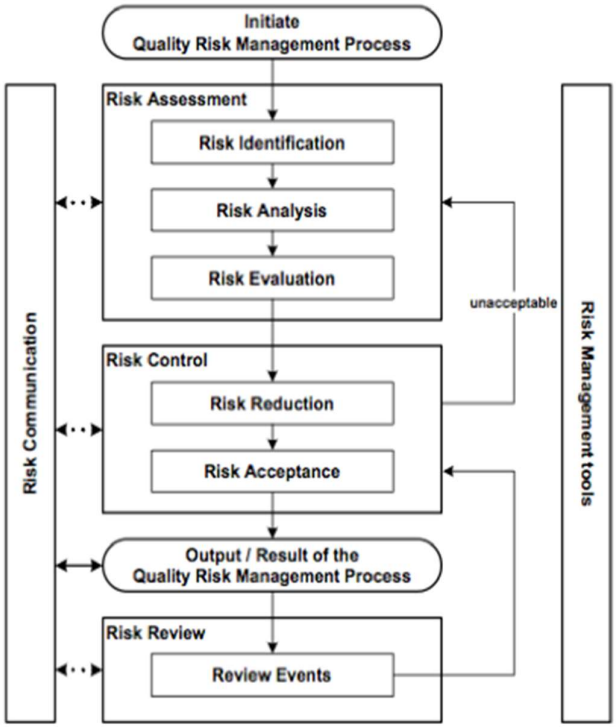


**Figure 6: Overview of typical quality risk assessment process**

In quality risk management (see ICH Q9), risk assessment is a useful analytical tool that may be used to find material properties and process factors that may have an impact on the product CQAs. Early in the pharmaceutical development process, risk assessment is often conducted and may be repeated if new data or understanding becomes available **[10].**

**DESIGN SPACE**

The defined range of process parameters that have been shown to offer quality assurance is known as the design space. There are situations when formulation features can also be applied to design space. It is commonly accepted that operating inside the design area does not mean departing from the permitted ranges for formulation properties and process parameters. Leaving the design space is seen as a change, and doing so would typically start the regulatory post-approval change procedure. **Figure 6** shows the Design Space.

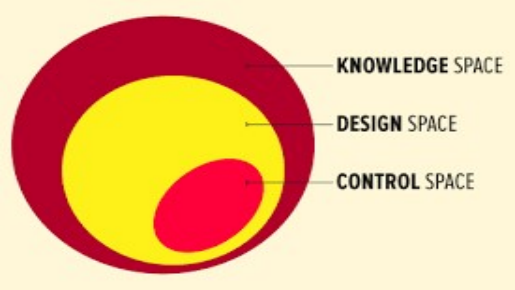


**Figure 6: Design Space**

**DESIGN OF EXPERIMENT**

The efficient method of designing trials is called the design of experiments (DOE), which enables the data to be analyzed to provide reliable and objective results. The phrase "design of experiment" refers to a methodical, planned approach for establishing the connection between variables influencing a process and its outcome**.**

**Types of Design of Experiments Commonly Used**

1.Screening Design (S.D)

2. Response Screening Design

3.Fractional Factorial Design

4. Placket-Burmam Design

5. Box-Behnken Design **[11].**

**CONTROL STRATEGY**

"A planned set of controls derived from current product and process understanding that assures process performance and product quality" is how ICH Q10 describes a control strategy. A control strategy makes sure the process stays inside the parameters that the design space specifies.

Specifically, the control strategy may include:

1. Control of input material attributes (e.g., drug substance, excipients, primary packaging materials) based on an understanding of their impact on process-ability or product quality.

2. Product specifications

3. Procedural controls

4. Facility controls, such as utilities, environmental systems, and operating conditions **[12].**

**LIFE CYCLE MANAGEMENT**

To make sure the process is operating as expected to provide the desired product, process performance can also be tracked. Quality characteristics are in line with what the design space projected. As more experience is obtained via routine [monitoring], this might involve trend analysis of the production process **[13].**

**APPLICATIONS OF QbD [14].**

1. For Chromatographic technique

- In stability studies
- In capillary electrophoresis

2. In dissolution studies

3. For spectroscopic measurement
4. In Biopharmaceuticals
5. In analysis of API and Excipients **[7, 8, 10, 14, 22-29]**.

Quality by design (QbD)– a comprehensive systematic approach to pharmaceutical development and manufacturing Advancement in the pharmaceutical development and manufacturing by Qbd can be explained against traditional approach.

**PHARMACEUTICAL ASPECTS: TRADITIONAL vs.QbD APPROACH [15].**

Advancements in pharmaceutical development and manufacturing by QbD can be explained against the traditional approaches as below **(Table 2):**

**Table 2: Pharmaceutical Aspects: Traditional vs. QbD approach. Aspects Traditional QbD**

| Aspects | Traditional | QbD |
|---|---|---|
| Pharmaceutical development | Empirical | Systemic, Focus on control strategy and robustness |
| Lifecycle management | Post-approval changes needed | Continual improvement enables design space |
| Manufacturing process | Fixed | Adjustable within the design space |
| Control strategy | Mainly by intermediate product and end product testing | Risk-based, Controlled shifted upstream, Real-time release |
| Product specification | Based on batch data | Based on the desired product performance |
| Process control | Offline analysis wide or slow response | PAT is utilized for feedback and provides real-time |

## CONCLUSION

Quality by Design is intended to enhance process knowledge and is based on existing guidance and reference documents. QbD becomes important in the area of pharmaceutical processes like drug development, formulations, analytical methods, and biopharmaceuticals. The application of the QbD principle can change the chemistry, manufacturing, and control regulatory process into a science and risk-based assessment.

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