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# REVIEW ARTICLE: QUALITY BY DESIGN (QbD)

**Mimansha Patel**
*Department of Quality Assurance, India.*

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**ABSTRACT**

There is massive competition worldwide and growing impact of Information technology, the pharmaceutical industry needs to improve its performance. Newer technologies need to be implemented that can effectively reduce cost of production and at the same time improves product quality and regulatory compliance. Quality by Design is an approach that has been offered by the United States Food and Drug Administration (USFDA) which if implemented properly can save significant amount of time and cost and at the same time can improve final product quality and regulatory compliance which can increase the speed of product to reach in to the market for the patient safety. This article discusses the background of quality by design concept, basis of Quality by Design, and its approach across the product life span and benefits that it offers.

***Corresponding author***
**Mimansha Patel**
Department of Quality Assurance,
India.
patelmimansha3@gmail.com

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## INTRODUCTION

In 2002, the U.S. Food and Drug Administration (FDA) published a guidance document for pharmaceutical companies on cGMP for the 21st century. This guidance document expressed a strong desire that companies should build quality, safety and efficacy in to their product. This concept is now known as Quality by Design (QbD)[1].

Quality by design (QbD) is the concept first developed by the famous quality expert named Joseph M. Juran in his 1992 book called "The New Steps for Planning Quality in to Goods and Services". He believed that quality could be planned in the very first stage of the production rather than final testing. The concept was first used in automobile industry. There is one article published in June 2007 titled "Elucidation: Lessons from the Auto Industry" says that Toyota Automobiles was the first company who implemented many Quality by Design concept to improve their automobiles in 1970s. That is why we can say that Quality by Design concept is new only for FDA regulated industries and not for other industries like technology, aeronautics, telecommunications etc. In other words, we can say that the computer we use, the phone we answer, the airplane we ride, the car we drive and the camera we use are all products of Quality by Design but we cannot say that whatever tablet we ingest and whatever biologics we use are the products of Quality by Design.

In 1990s, many of the medical device manufacturing company has implemented Quality by Design aspect which resulted in reduced risk and manufacturing cost and at the same time increased patient safety and product efficacy. From the success of QbD aspect in medical device manufacturing, the FDA officials felt that this concept has to be applied to drugs and biologics also. So, the internal discussion in FDA started in late 1990s and finally they published a concept paper in 2002 on cGMP in 21st century. With the huge help of some pharmaceutical companies, pilot programs were started to share the Quality by Design application and process understanding with the other companies.

**"The FDA publication defined Quality by Design as:**

- Developing a product to meet predefined product quality, safety and efficacy; and
- Designing a manufacturing process to meet predefined product quality, safety and efficacy."[1]

**Definition**

Quality by Design is a systematic approach to development that begins with predefined objectives and emphasizes product and process understanding and process control, based on sound science and quality risk management.[3]

A system for designing, analyzing and controlling manufacturing through timely measurements (i.e. during processing) of critical quality and performance attributes of new and in-process materials and processes, with the goal of ensuring final product safety.[3,4].

**Traditional approach & Enhanced QbD approach[2].**

| Aspects | Current | QbD |
|---|---|---|
| Pharmaceutical Development | Empirical, Random, Focus on optimization | Systematic, Multivariate experiments, Focus on control strategy and robustness |
| Manufacturing Process | Fixed | Adjustable within design space, managed by company's quality systems |
| Process Control | Some in-process testing | PAT utilized, Process operations tracked and trended |
| Product Specification | Primary means of quality control, based on batch data | Part of the overall quality control strategy, based on desired product performance |
| Control Strategy | By testing and inspection | Risk-based control strategy, real-time release possible |

**Benefits of QbD**[5,6]

- 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

**Benefits to Industry6**

- Ensures better design of products with less problems in manufacturing
- Reduces number of manufacturing supplements required for post market changes –rely on process and risk understanding and risk mitigation
- Allows for implementation of new technology to improve manufacturing without regulatory scrutiny.
- Allows for possible reduction in overall costs of manufacturing –less waste.
- Ensures less hassle during review –reduced deficiencies –quicker approvals.
- Improves interaction with FDA –deal on a science level instead of on a process level.
- Allows for continuous improvements in products and manufacturing process.

**Primary QbD Documents**[7]

**Risk Assessment Report(s)**

- Performed throughout QbD Process
- Particularly important to process development

**Quality Target Product Profile (QTPP)**

Defines the desired product characteristics and sets development goals.

**Control Strategy Summary**

Defines the process, its inputs and outputs, and how it is controlled.

**PPQ Report(s)**

Formal verification that the process Control Strategy has been defined appropriately and repeatedly produces the desired results.

**Continued Process Verification (CPV) Reports**

Assuring that during routine commercial production, the process remains in a state of control (FDA); involves feedback loops into the QbD "process" where intentional process changes and/or observed variability is assessed for risk, characterized, re-validated, etc.

**Quality Target Product Profile (QTPP)**[7]

**Necessary Elements**

- Quality characteristics: sterility, purity etc. (including specific safety-related impurities where necessary)
- Pharmacokinetic characteristics: dissolution etc.
- Therapeutic effect
- Target patient population: neonate, adult etc., clinical diagnosis
- Shelf life: temperature, light conditions etc.

**Desired Elements •**

- Dosage form: liquid for injection, solid tablet etc.
- Route of administration: oral, IV, IM, SC
- Clinical setting: self or clinic administration
- Primary/secondary packaging: glass or plastic vial/syringe; blister packaging etc

**Other Elements as Appropriate**

It is important to acknowledge that QTPP should only include patient relevant product performance elements. For example, tablet density or hardness may be included as a specification for process monitoring but may not be included in QTPP. Also, if particle size is critical to the dissolution of a solid oral product, then the QTPP should include dissolution but not particle size.

**CONCLUSION**

- QbD helps to identify and justify target product profiles, product and process understanding.
- Continuous improvement can be ensured through QbD.
- Robust manufacturing method can be developed.
- QbD is a quality system that builds on past and sets future regulatory expectations.

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