

Review on Quality By Design (QBD): A Concept for Development of Quality Pharmaceuticals”.

Bhalke Supriya Bhausahab, Proff . wakchaure Yogita , Dr.Megha Salve

Department Of Bachelor In Pharmacy
Shivajirao Pawar College Of Pharmacy, Pachegoan, Ahamadnagar-413725

Submitted: 20-11-2023

Accepted: 30-11-2023

ABSTRACT:

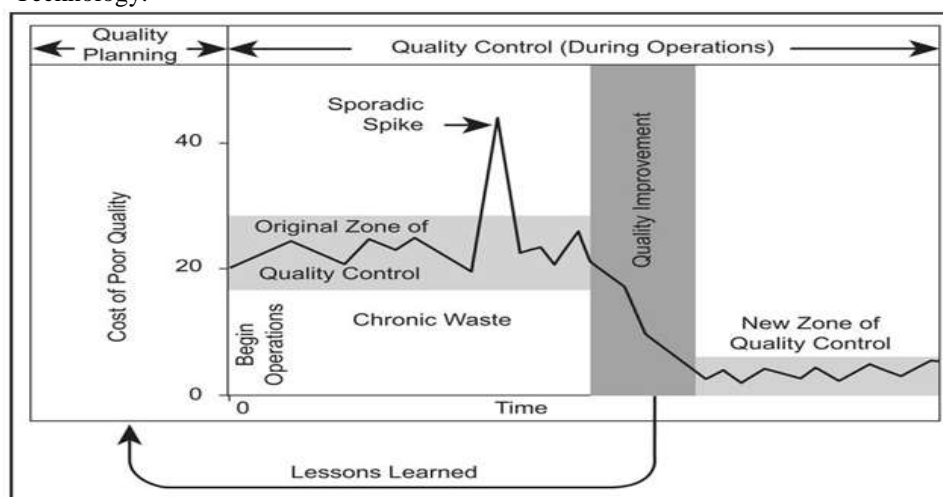
Quality by Design (QbD) is the best key to ensure the quality of all pharmaceutical products. QBD strengthens the promise of providing customers with safe and effective medicines and promises to improve the efficiency of product quality. According to this concept, which covers the entire product design and development process, it is important to identify the desired product performance ratio [target product profile “TPP,” target product quality profile “QTPP”] and the critical quality attributes (CQAs). . Recognize the influence of raw materials [critical material attributes (CMA)] and critical process parameters (CPP) on CQA and identify and control sources of variability. The pharmaceutical development plan is to develop high quality products, and the manufacturing process always ensures the future performance of the product. Quality by Design is based on the ICH guidelines Q8 for the pharmaceutical industry for development, Q9 for quality risk management and Q10 for pharmaceutical quality systems.

Keywords: Quality by Design(QbD), ICH guidelines, Quality Target Product Profile, Process Analytical Technology.

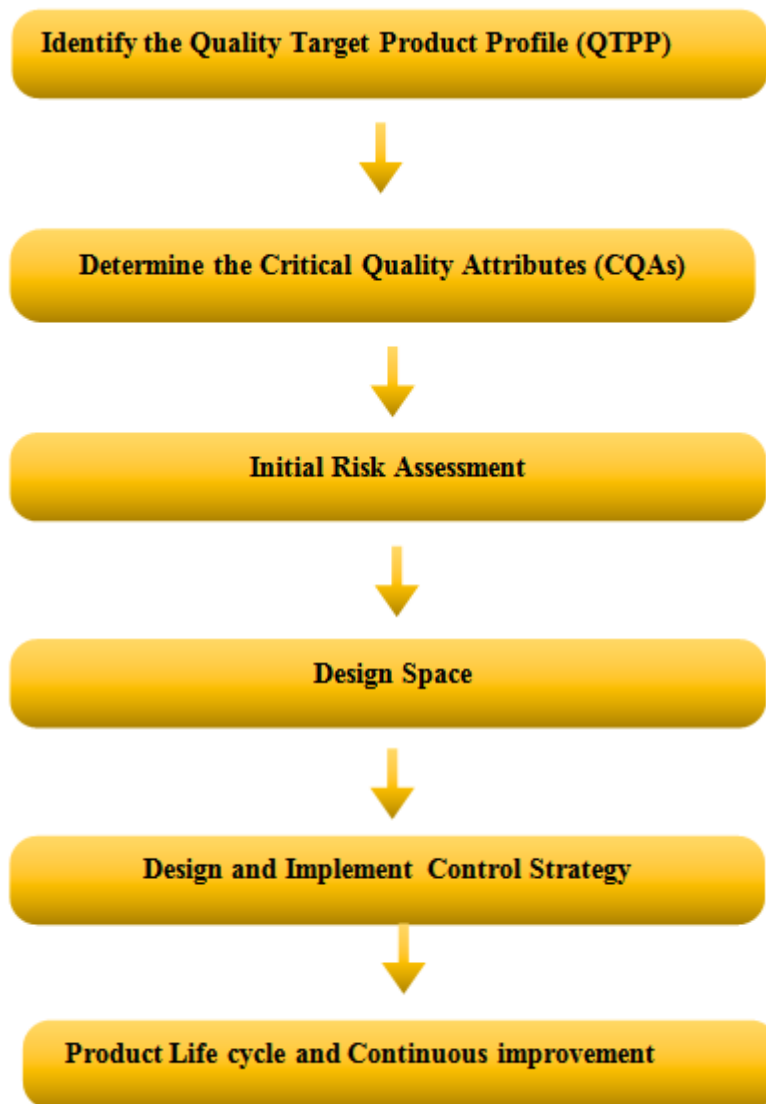
I. INTRODUCTION

Pharmaceutical Quality by Design (QBD) is a systematic development approach that starts with predefined goals and focuses on understanding and controlling manufacturing and processing processes, based on sound scientific principles and quality risk management. To describe quality through design, we must first define what we mean by quality. Quality is “the standard or expediency.” This term includes attributes such as identity, power and purity.

The term “Quality by Design” was first coined in 1985 by Dr. Joseph M. Juran introduced in his publication Juran on Quality by Design. The starting point was the assumption that quality cannot be tested on a product, but must be taken into account in the design phase. He suggests the Juran trilogy in which he describes the three pillars of quality. These three elements are quality planning (design phase), quality control (continuous inspections to ensure process control) and quality improvement (including proactive refinement of processes to improve processes). Fig. The Juran’s Trilogy



II. KEY ELEMENTS OF QUALITY BY DESIGN



2.1 Target Product Profile (TPP)

Under this title, purpose is an important word. A goal is nothing more than the result we want to achieve. Therefore, we focus on a drug profile or target product that provides the desired quality, safety and protection. Efficiency. The TPP is defined as “a prospective summary of the quality characteristics of a medicinal product that are ideally achieved to ensure the desired quality, taking into account safety and security”; effectiveness of the drug. » (ICH Q8) The target product profile must include the following:

- Dosage form
- Route of administration
- Dosage

- Pharmacokinetics
- Stability

TPP is intended for patient and patient use. Label-based concepts because they identify the desired performance characteristics of a product in relation to patient needs. It is organized by key sections on the drug label. Pharmaceutical companies use the desired information on the label to develop a target product profile. The TPP is then used to influence the design and safety of clinical trials. ADME and drug design, especially QTPP.

2.2 Quality Target Product Profile (QTPP)

The QTPP is a quantitative surrogate for scientific safety aspects. Efficiency that can be used to design and optimize formulation and manufacturing. Processes. It must contain quantitative targets regarding impurities, stability and performance requirements of the specific product. The QTPP is not a specification as it covers studies such as bioequivalence or stability that are not carried out in series. The QTPP should only consider the effects of the product that are relevant to the patient.

Product Profile Quality Target is a term that is simply an addition to TPP for product quality. Guides formulation scientists in determining formulation strategies and maintaining good formulation organization. QTPP is associated on the label with identity, name, dosage form, purity and stability.

2.3 Critical Quality Attributes (CQAs)

CQA has been defined as “a physical, chemical, biological or microbiological property or characteristic that must be within the appropriate limits, ranges or distributions to provide the desired product quality.” The identification of CQAs is done through a risk assessment according to ICH Q9. Critical quality attributes are generally associated with the drug substance, excipients, intermediates and drug product. Critical quality attributes include properties that provide the desired quality, safety and effectiveness. CQAs for biotechnology products generally address aspects that affect the purity and stability of the product. Drug product CQAs can be identified from the Target product profile. Use of strong risk estimation methods for identification of CQAs is new to the QbD standard.

2.4 Critical Material Attributes (CMAs)

Material attributes can be auxiliary raw materials, pharmaceutical substances, reagents, solvents, packaging and others. Labeling materials. Material properties can be quantified and analyzed. is usually correct, but can sometimes change with further editing.
E.g. Impurity profile, porosity, specific volume, sterility.

2.5 Critical ProcessParameters (CPPs)

Process parameters include all operational input parameters for system or device operation (e.g. mixing speed, flow date, etc.) and process state variables (e.g. temperature, pressure, etc.). It

must be controlled to achieve the desired product quality and process uniformity.

2.6 A Design Space

Design space is defined as “the multidimensional combination and interaction of input variables (e.g., material attributes and process parameters) that are proven to produce quality.” The relationship between process inputs and critical quality attributes can be described in design space. A design space is a way to represent an established understanding of a process. The design space is the direct result of DoE data analysis and analysis. verified models such as first principle models.

2.7 Control Strategy

A control strategy is defined as “a set of designed controls based on current understanding of the product and process that ensure process efficiency and product quality.” The control strategy aims to ensure that a product is continuously produced to the required quality. Once a sufficient understanding of the process has been achieved, a control strategy must be developed to ensure that the process remains under control within normal variations in material properties. a process that supports the areas. The control strategy can include raw material control, process control and monitoring, space design for single or multiple operations, and end product specifications used to ensure consistent quality.

III. PHARMACEUTICAL QUALITY BY DESIGN TOOLS

3.1 Riskassessment :

The FDA defines risk management as a strategic safety program designed to reduce product risks through the use of one or more interventions or tools. This is a comprehensive process for assessing, monitoring, communicating and reviewing risks to the quality of a medicine throughout its life cycle.

Quality risk assessment should be scientifically based and ultimately related to patient protection, and the effort, formality and documentation of the quality-related risk management process should be proportionate to the level of risk.

The aim of ICH Q9 is to provide a systematic approach to quality risk management and does not specifically address risk assessment in product development. However, the risk assessment tools defined in ICH Q9 also apply to

risk assessment during product development. The purpose of risk assessment prior to development studies is to identify potentially high-risk formulations and process variables that could affect the quality of the drug product. This helps prioritize the research to be conducted and is often due to gaps in knowledge or uncertainty. Test results determine which variables are critical and which are not, making it easier to determine a control strategy. The result of the risk assessment is the identification of the variables that need to be investigated experimentally. ICH Q9 provides a non-exhaustive list of common risk assessment tools as follows: Basic methods to facilitate risk management (flowcharts, checklists, etc.) Fault tree analysis, risk classification, filtering, preliminary threat analysis, threat analysis, critical control points, failure mode impact analysis, failure mode, impact and criticality analysis, functional analysis and functional threat analysis. Support statistical tools. It may be useful to adapt these tools for use in specific areas related to the quality of pharmaceutical substances and medicines.

3.2 Design of Experiments (DOE) :

Experimental design: deals with the planning and execution of experiments to analyze the data obtained in order to obtain valid and objective conclusions. This tool is very effective in identifying all the factors that collectively influence outcome responses.

Role of DOE –

- Obtain maximum information from a minimum number of experiments.
- Study effects individually by changing all operating parameters simultaneously.
- Consider the variability of experiments, operators, raw materials, or the processes themselves.
- Identify interactions between process parameters

3.3 Process Analytical Technology (PAT) :

A system for design, analysis and production control through timely measurement of the critical quality and performance characteristics of raw materials, materials and processes in a process to ensure product quality.

PAT Objectives:

- 1) Building Quality
- 2) Improve understanding and control.
- 3) To reduce process variability.
- 4) Increase process reliability.

PAT Tools:

- Multidimensional Design Tools.

- Process analysis (online, online, online)
- Continuous improvement and knowledge management
- Process control tool

IV. ADVANTAGES

4.1 Continuous improvement:

QbD can ensure safe and efficient drug supply and significantly improve the quality of production. It is based on the principle of continuous improvement and the growing need for manufacturing companies to better understand products and benefit from the growing knowledge base that develops over a product's life cycle. For example, in development, designs of experiments (DOEs) are useful for determining the influence of important factors and interactions.

4.2 Change Control

The QbD approach aims to improve change support capabilities. If quality is built throughout the product development process, only minor changes may be required to update regulatory documentation following changes to the manufacturing process. In fact, extensive knowledge of the process and its parameters has already been acquired and data collected to support possible updates. This differs from the old approach, which avoided changes due to their potential negative impact on product quality

4.3 Failure Prevention:

A QbD approach can enable production teams to better understand the parameters of the development process. Has extensive knowledge of how process parameters work and how they relate to each other. This can also reduce the risk of batch failures due to unexpected causes, as all possible interactions are already assessed and known. This can have the added benefit of reducing overall costs.

4.4 Consistency :

Integrating quality into the process ensures greater batch-to-batch consistency. This proven consistency will help increase regulators' confidence in the robustness of the process and product. This could allow for less intensive regulatory oversight during registration as well as a reduction in the number of submissions and applications post-approval.

4.5 Right first time :

One of the goals of the QbD approach is to increase the chances of a product registration being

successful “first time.” QbD ensures that all sources of variability affecting the process are identified, explained and managed with appropriate measures. This ensures that the products always meet predefined specifications and are “perfect at first sight”. Immediate success means companies not only manage their resources profitably, but also ensure that efforts are focused on the right areas.

4.6 Reduced control :

Comprehensive knowledge of the processes ensures a good assessment of the quality of the manufactured products before testing, as a quality assurance mechanism is already integrated. This reduces the need for inspections of intermediate and final products as real-time checks take place in the process itself. This reduces production, testing and release times for both manufacturing companies and their customers while reducing cost.

V. SOFTWARES

- 1) Design of Expert®(DOE)
- 2) MODDE®
- 3) Unscramble ®
- 4) JMP®
- 5) Statistica ®
- 6) Minitab ®

VI. CASE STUDY

6.1 Capsule development :

A comparative study using the traditional and QbD approaches for two products: Tradium and Qbidium .

They were available in the same capsule dosage form and had the same manufacturing process, but QbD was implemented only in Qbidium . The Tradium studies began with the creation of a general product description and were poorly defined in the production process; They also left out a critical factor in the manufacturing process and were an afterthought after a long period of regulatory scrutiny.

In the case of Qbidium, the QbD principles were adequately implemented and risk assessment studies on the characteristics and use of the software were conducted to understand critical ones Factors The time required at the beginning of Qbidium development seems to be longer, but the insights gained are faster and can be processed more reliably.

6.2 Formulation development of orally dispersible tablets

Charoo et al. investigated the development of dispersible diclofenac tablets based on a QbD approach. QTPP explained. Pharmaceutical active ingredients, excipients and process properties were determined based on QTPP, pre-formulation studies and previous experience. The significance of the threats and the probability of occurrence were assessed and a risk classification was created. Specific CQAs such as appearance, hardness, friability, dissolution, content uniformity, and disintegration time were further investigated in a series of factorial studies. The control strategy was developed after assessing the residual risk and assessing its acceptability. The amount of disintegration product and compression pressure were found to be CPP in terms of their effect on disintegration time and tablet dissolution. By using different combinations of hardeners and disintegrants, the desired disintegration times could be achieved over a larger area of the installation space. To achieve homogeneity of the mixture, a combination of mixing time, mixing speed and drug particle size was selected as CPP. At a compression force of less than 7.6 kN, the tablets had an acceptable disintegration time and content uniformity. Design space compatibility provided the flexibility to release batches in real time.

VII. CONCLUSION

Quality is, by definition, an important element of a modern approach to pharmaceutical quality. Quality by Design aims to deepen process knowledge and is based on existing guidelines and reference documents. QbD is a quality system that builds on the past and guides future regulatory expectations; QbD can be viewed as a process defined by a set of document requirements. These documents organize and demonstrate knowledge and understanding of the process. QbD can be applied to both old and new products, but the support document package may differ. The continuation of the QbD documentation is “live”. They can and should be revised as the knowledge base evolves. It offers robust commercial manufacturing methods to ensure consistent production of high-quality medicines. It ensures that equivalent therapeutic generics are always produced for consumers. The QbD methodology helps to identify and justify target product profiles as well as product and process understanding. There is a need for vigorous and well funded research programs to develop new pharmaceutical

manufacturing platforms. The QbD process offers the chance for much greater regulatory flexibility within the future. the tactic performance criteria could potentially be registered instead of the tactic itself. the tactic used might be referred to as an example of the way to attain the specified method performance criteria. Any changes to the present method would be covered by internal change control procedures.

REFERENES

- [1]. Joseph M. Juran, A. Blanton Godfrey, "Juran's quality control handbook" fifth edition, McGraw-Hill, 1998, 2.5-2.8.
- [2]. <https://www.Juran.com/blog/the-history-of-quality>.
- [3]. Sharadha Param, Bhavna Patel, "comprehensive review on quality by design (QbD) in pharmaceuticals" 21(1), Jul – Aug 2013
- [4]. Shuling Kan, Jing Lu, Jianping Liu, unlin Wang, Yi Zhao "A quality by design (QbD) case study on enteric coated pellets: screening of critical variables & establishments of design space at laboratory scale" Issue-11
- [5]. July 2014, 1-9.
- [6]. Sushila D.Chavan, Nayana V. Pimpodkar, Amruta S. Kadam, Puja S.Gaikwad, "Research & reviews: Journal of pharmaceutical Quality assurance" Volume-1, Issue-2, October-December 2015, 18-22.
- [7]. Sarika Namjoshi, Maryam Dabbaghi, Michael S. Roberts, Jeffrey E. Grice and Yousuf Mohammed "Quality by design: Development of the Quality target product profile (QTPP) for semisolid topical product" March 2020, 6-10.
- [8]. Daniel Borchert, Diego A. Suarez-Zuluaga, Yvonne E. Thomassen and Christoph Herwig Risk assessment & integrated process modeling – an improved Qbd approach for the development of the bioprocess control strategy" Volume 7, Issue Aug 2020, 254–271.
- [9]. Vemuri Pavan Kumar, N. Vishal Gupta, "A Review on quality by design approach (Qbd) for pharmaceuticals" January - March 2015, Vol. 7, Issue 1, 32-44
- [10]. G. K. Raju, and Janet Woodcock, "Understanding pharmaceutical Quality by design" AAPS Journal, Vol. 16, July 2014, 12248-014-9598-3,771-780.15.
- [11]. Trevor Murphy, Niall O' Mahony, Krishna Panduru, Daniel Riordan, Joseph Walsh "Pharmaceutical manufacturing & the quality by design (Qbd), processanalytical technology approach"1-7.
- [12]. Akash S. Mali, Monali Jagtap, P Karekar, A Maruška, "A brief Review on process analytical technology (PAT) Review article" Vol 8, Issue 1, 2016,0975:7066,1-8.
- [13]. Sushila D.Chavan, Nayana V. Pimpodkar, Amruta S. Kadam, Puja S.Gaikwad, "Research & reviews: Journal of pharmaceutical Quality assurance" Volume 1, Issue 2, October-December 2015,18-22.
- [14]. Lawrence X. Yu, Gregory Amidon, Mansoor A. Khan,Stephen W. Hoag, James Polli,G. K. Raju, and Janet Woodcock, "Understanding pharmaceutical Quality by design" AAPS Journal, Vol. 16, July 2014, 12248- 014-9598-3,771-780.
- [15]. P.Abhinandan, Ramarao Nadendla "Application of Quality by Design & its parameters for pharmaceutical product" 2395-3411, Issue-Sep 2017, 505-513.
- [16]. Mahesh Shivhare, Graham McCreath "Practical considerations for DOE implementation in Quality by Design" June- 2010, 22-34.
- [17]. Isa Martins Fukuda1, Camila Francini Fidelis Pinto1, Camila dos Santos Moreiral, Alessandro Morais Saviano, Felipe Rebello Lourenço1, Design of experiment (DOE) applied to pharmaceutical & analytical Quality by Design (QbD)" 2018; 54:e01006, 1-15.
- [18]. Miryam Barad, "Design of experiments (DOE).A valuable multipurpose methodology" 5, Issue-2014, 2120- 2129.
- [19]. Izat N, Yerlikaya F, Capan Y, "A glance on the history of pharmaceutical quality by design. OA Drug Design & Delivery"2014 Jan 18, 1-8. [20]. Dr. Matteo Zacché, R&D Manager, Mattias Andersson, "The advantages of a 'Quality by Design' approach in pharma drug development" Jan 06, 2020 2 di 6