AMJ Australasian Medical Journal [AMJ 2022;15(1):312-314]

A review on quality by design (QbD) - Its significance and applications

Tejaswini Gangaraj*, Sahoo NK

Department of Marri Laxman Reddy Institute of Pharmacy, Dundigal, Hyderabad, Telangana, India

REVIEW

Please cite this paper as: Tejaswini G, Sahoo NK. A review on quality by design (QbD) - Its significance and applications. AMJ 2022;15(1):312-314.

Corresponding Author:
Gangaraj Tejaswini
Marri Laxman Reddy Institute of Pharmacy,
Dundigal, Hyderabad,
Telangana, India.
Gangaraj_tejaswini85@gmail.com

ABSTRACT

The pharmaceutical Quality by Design (QbD) 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. The basic concept of QbD is "The Quality cannot be tested into the product, but it should be built into it." Quality by design is a direct relation to Product performance. The review paper includes the development process of QbD, significance and various applications in the pharmaceutical industry[1]. The process includes the quality target product profile (QTTP), critical material attributes (CMAs), quality risk management (QRM), Design space, comprehensive control strategy, and finally lifecycle management. The importance of QbD design is that it offers various advantages over the traditional approaches for the testing and development of drug quality. QbD has its perspectives to contribute the drug design, development, and manufacture of high-quality products. Applications of QbD to pharmaceutical processes (formulation development), analytical development are briefly discussed using few examples[2]. A harmonized pharmaceutical quality system applicable across the lifecycle of the product emphasizing an integrated approach to risk management and science should be built up leading to better quality medicines to patients.

Key Words

Quality By Design (QbD), Quality Target product and drug profile, Quality Risk Management, Product Performance

Introduction

Why is quality so important in pharmaceutical industry?

Quality is "Standard or suitability for intended use." This term includes such attributes as the identity, potency, and purity[3].

"Mere analysis of final product will not work but the quality should be designed in the product."

Quality by Design

According to ICH q8 guidelines, QbD is defined as, "A systematic approach to development that begins with predefined objectives & emphasizes product, process understanding & process control, based on sound science & quality risk management.[4]"

Objectives of quality by design

1. To ensure the quality products.
2. From this knowledge & data process measurement & desired attributes may be constructed.
3. Experimental study would be viewed as positive performance testing of the model ability through Design space.
4. Ensures combination of product & process knowledge gained during development.

Lifecycle of quality by design

1. **Target product profile:** TPP is defined as, "A prospective summary of the quality characteristics of drug product that ideally will be achieved to ensure the desired quality, taking in to account safety & efficacy of drug product."(ICH Q8).
2. **Quality Target Product Profile (QTPP):** The Quality Target product profile is a term that is an ordinary addition of TPP for product quality. It guides formulation scientists to establish formulation strategies and keep formulation is well-organized.
3. **Critical Quality Attributes (CQA):** According to ICH Q8 R2 "A CQA is a physical, chemical, biological, or microbiological property or characteristic that should be within an appropriate limit, range, or distribution to ensure the desired product quality".
4. **Risk assessment:** Risk assessment is the linkages between material attributes & process parameters.
5. **Control strategy:** Control strategy is defined as, "A designed set of control, derived from current

product and process understanding that assures process performance and product quality."

6. **Continuous improvement throughout product life cycle:** Product quality can be improved throughout the product lifecycle[5].

Statistical Tools Used in Quality by Design

Design of Experiments (DoE)

DoE is a structured, organized method for determining the relationship between factors affecting a process and the response of that process.

Methodology of DoE: Choose experimental design→Conduct randomized experiments→Analyse data→Create multidimensional surface model.

Types of DoE

i. Screening experiments: A special extreme type of fractional factorial. Often used at the start of an experimental sequence; few experimental runs but yields important information about key variables.
ii. Fractional factorials: Less runs (than full factorials) but less information, too. Studies a predetermined fraction of a full factorial.
iii. Full factorials: Generates lots of information but requires many runs. Usually used to study variables at 2 or 3 levels (settings).
iv. Response surface analysis (RSA): An optimizing design in which the main independent variables are already known. Limited runs, highly selective information.

Application of DOEs: Scope out initial formulation or process design, Optimize product or process, Determine design space, including multivariate relationships.

Chemometrics and modelling

Chemometrics is the science of relating measurements made on a chemical system or process to the state of the system via application of mathematical or statistical methods[6].

Applicable to any multivariate data: Spectroscopic data & Manufacturing data.

Chemometric analysis is empirical, relates multivariate data to single or multiple responses, utilises multiple linear regressions to multivariate data.

Statistical process control

Statistical process control (SPC) is the application of statistical methods to identify and control the special cause of variation in a process.

Common cause variation: Random fluctuation of response caused by unknown factors.

Special cause variation: Non-random variation caused by a specific factor.

Applications of Quality by Design in Various Fields of Pharmaceutical Industry

1. **In analytical department:** For Chromatographic technique- determination of purity, In screening of column used for chromatography, In development of HPLC method for drug products/substances, In capillary electrophoresis, In stability studies, In UHPLC technique.
2. **For hyphenated technique:** In LC–MS method development
3. **In bio-analytical method development**
4. **In dissolution studies**
5. **For spectroscopic measurements:** In handling complex spectroscopic data, In mass spectroscopy and IR spectroscopy.
6. **Pharmaceuticals:** In modified release products, In sterile manufacturing, In solid oral dosage form, In gel manufacturing, in Tableting process.
7. **Biopharmaceuticals:** In manufacturing of protein, In production and characterization of monoclonal antibody, In nano-medicine.

Conclusion

QbD involves thorough understanding of process through science and risk based approach. Statistical methods and tools are essential to maintain a process that is in control and capable of producing appropriate high quality product. Design of Experiments provides an effective and efficient way to simultaneously test for factor effects and interactions and to describe causative relationships between process parameters or input materials with the quality attributes.

References

1. Mogal V, Dusane J, Borase P, et al. A review on quality by design. Pharm Biol Evaluations. 2016;3(3):313-9.
2. Kumar VP, Gupta NV. A Review on quality by design approach (QBD) for Pharmaceuticals. Int J Drug Res Dev. 2019;9(3-s):1137-46.
3. Sangshettia JN, Deshpande M, Zaheer Z, et al. Quality by design approach: Regulatory need. Arab J Chem. 2017;10(S2):S3412-25. doi: https://doi.org/10.1016/j.arabjc.2014.01.025
4. Chavan SD, Pimpodkar NV, Kadam AS, et al. Quality by Design. Research and Reviews: Journal of Pharmaceutical Quality Assurance. 2015;1(2).
5. The windshire group. Overview of statistics used in QbD throughout the product life cycle. The windshire group, LLC. 2014.
6. Chen C, Moore C. Role of Statistics in Pharmaceutical

Development Using Quality-by-Design Approach – An FDA Perspective. FDA/Industry Statistics Workshop. 2006.