

Quality by Design: A Brief Introduction

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Editorial

Quality by Design (QbD), a concept introduced by Dr. Joseph M. Juran, emphasizes the design of quality into product. Quality-by-Design is defined as “a systematic approach to pharmaceutical development with predefined objectives”. This approach emphasizes product and process control, based on sound science and quality risk management. A high quality drug product, as defined by Janet Woodcock (Director for the Center for Drug Evaluation and Research), is a product free of contamination which can consistently deliver the clinical performance and therapeutic effects as indicated in the label [1]. It was recognized that the quality of product doesn't improve with increased testing. Following equation indicates the factors affecting quality.

Pharmaceutical Quality=f (drug substance, excipients, manufacturing, packaging).

QbD is a systematic approach to pharmaceutical product development and requires a thorough understanding of the critical factors affecting product's quality. It demands an understanding of product and process controls. Information included in International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), ICH Q8, Pharmaceutical Development, along with ICH Q9, Quality Risk Management, and ICH Q10, Pharmaceutical Quality Systems demonstrates how implementing quality by design ensures the quality of product. Some of the advantages of QbD include improved product design, reduced manufacturing issues, assessment and lowering of risk, and improved post-approval change management [2].

A Critical Process Parameter (CPP) is a factor which has an impact on a critical quality attribute and, hence, should be monitored to ensure that the process produces the product with desired quality. Critical Quality Attribute (CQA) is a physical, chemical, biological, or microbiological property or characteristic that should be within an appropriate limit to ensure the desired product quality [3].

Design of Experiments (DoE) and Process Analytical Technology (PAT) are the tools that can be used in Quality by Design. ICH guidance Q8 defines design space as “the multidimensional combination and interaction of input variables (e.g., material attributes) and process parameters that have been demonstrated to

provide assurance of quality”. A design space is determined at a lab scale and is scale and equipment dependent. This needs to be appropriately justified when using at a commercial scale [4].

For generics, few aspects of QbD include identifying and defining the target product profile (TPP), risk assessment, and identifying the critical quality attributes (CQA) of the product which must be controlled to meet the quality of the product. It also includes developing a control strategy for the manufacturing process controls and further monitoring the process to ensure product quality. A generic sponsor uses control strategy which includes monitoring of input controls, process controls to ensure that the quality of the product remains consistent when scaling up from exhibit batch to commercial batches. The limits established for the design space must also assist to form the basis for establishing the acceptance criteria for process validation. In order to ensure that the established process controls helps in achieving the product quality, process validation needs to be demonstrated. Subsequent to the process validation, regulatory filing shall include the acceptable ranges for all the critical operating process monitoring plan. After the approval, the critical quality attributes will be further monitored to ensure the performance of the process within the defined acceptance variability. QbD thus ensures the product quality by controlling the formulation and process variables [2]. This approach also helps for flexible regulatory approaches.

Quality by Design is an approach to reduce product variability and failures which helps in achieving high quality pharmaceutical products.

References

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