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Quality by Design: A revolutionary concept of pharmaceutical product development in modern era

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Abstract

Quality by Design (QbD) has become a new concept for development of quality pharmaceutical products, It is an essential part of the modern approach to pharmaceutical quality, QbD is a best solution to build a quality in all pharmaceutical products but it is also a major challenge to the Pharmaceutical industry whose processes are fixed in time, despite inherent process and material variability, Under this concept of QbD throughout designing and development of a product, it is essential to define desire product performance profile [Target product Profile (TPP), Target Product Quality Profile (TPQP)] and identify critical quality attributed (CQA). On the basis of this we can design the product formulation and process to meet the product attributes.

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This leads to recognize the impact of raw materials [critical material attributes (CMA)], critical process parameters (CP P) on the CQAs and identification and control sources of

variability. QbD is an emerging idea which offers pharmaceutical manufacturer with increased self-regulated flexibility while maintaining tight quality standards and real time release of the drug product, this paper discusses the pharmaceutical QbD and describes how it can be used to develop the pharmaceutical products well within the specified period of time.

Introduction

Dr. Joseph M Juran proposes first the theory of Quality by design (QbD) is a concept first According Dr. Juran that quality of the product only can be obtained by proper. The US Food and Drug Administration (FDA) always supports the adoption of QbD principles by pharmaceutical manufacturer in drug product development, manufacturing, and regulation. FDA's believes that end testing cannot improve the quality of the product but proper qbd design can definitely improve quality on QbD began with the recognition that increased testing does not necessarily improve product quality. Quality must be built into the product. ICH Q8(R1)guideline, describes QBD as "quality cannot be tested into products, i.e., quality should be built in by design" According to ICH Q8 QbD is defined as A systematic and organised approach for development of pharmaceutical product.
For proper QbD we all need proper evaluating of product and process variable which has influence on the ultimate product quality. For developing QBD ONE SHOULD HAVE KNOWLEGE on other FDA proposes guideline of: Pharmaceutical Development and Quality Risk Management.

Quality risk management (QRM), as defined in International Conference on Harmonization's (ICH) Q9 document (1), is designed to ensure that drug critical quality attributes (CQAs) are defined and maintained from phase to phase during drug development and manufacturing and changes in drug-product formulation, definition, analytical method, and associated process changes are understood and managed to ensure patient safety and drug efficacy. An effective QRM process can further ensure the high quality of the drug product to the patient by providing a proactive means to identify and control potential risks to quality during development and manufacturing. Risk can be defined two ways. First, as the combination of the probability of occurrence of harm and the severity of that harm, or second, as the potential influence of product and process factors on CQAs and the uncertainty of that influence. The first definition is traditional and takes into account potential failures and adverse events. The

second takes into account influence of factors relative to CQAs and how well we evaluate or know the influence of those factors on the CQAs of the drug product. In modern drug development, it is often the second definition that is a problem in that we don't know what we don't know. As we complete development activities, the risk goes down because our knowledge and evaluating of the factors associated with unit operations and analytical methods go up relative to product acceptance and all. into the QRM process. The major benefits of QRM and risk assessments are to improve the ability to develop drug products and drug substance and answer the question, "When, what, how much, and where do we need additional development?" Development activities reduce potential risks to safety and efficacy and help to achieve the benefits of the drug for the targeted indication. (2-4)

QbD has four vital components

1. Defining the Product Design Goal

In this step, it defines the Quality Target Product Profile (QTPP) and identifies all the critical quality attributes (CQA) for the product. The QTPP have several factors that explain the desired product and the CQAs include the product characteristics that have the most impact on the product quality. It also provides the framework for the product design and evaluating. The components are characterized and the compatibility of the components is evaluated.

2. Discovering the Process Design Space

Evaluating the organization processes is the vital to defining the design space. ICH Q8 defines design space as an “established multidimensional combination and interaction of material attributes and/or process parameters demonstrated to provide assurance of quality.” Critical process parameters (CPPs) are identified by determining the extent to which any process variation can affect the quality of the product. When the organization defines the design space, the organizations are able to anticipate issues and plan how to control the process.

3. Evaluating the Control Space

Based on the process design space, a well-executed control space also can be defined. This helps the organization to evaluate the processes in a way that ensures product quality from various known variability of the production process. This organized approach will keep the complex production processes under control. Plotting the output of the organization process and comparing it to such a reference will give a clear indication of whether the organization process is in control. One technique to help avoid such a disparity is to conduct a Design of

Experiments (DOE) study on the organization product in the development stage. Considerable wasted effort can be eliminated with such an approach as can any unexpected adverse outcome from the lack of control space evaluating

4. Targeting the Operating Space

The operating space is the important set of parameters, evaluated statistically, that help the organization to find any natural variability in CPPs and CQAs. For generic products, the operating space must be within the control space and should allow a reference product to be tested with the parameters. For new products, the operating space must be within the design space and compliant with regulatory guidelines. Innovators can get a competitive advantage by thoroughly exploring the design space, including testing multiple batches of formulations to truly refine their product

THE BENEFITS OF QbD

Proper implementation of QbD can potentially provide many important benefits for pharmaceutical product development. (5-10)

• More effective utilization of product development time and costs

• It will help to comply various FDA submission guidelines and regulation

• Time taken for Regulatory approval will be less.

QbD can potentially provide various benefits in manufacturing. Even after regulatory approval, routine QC testing may find an out of specification (OOS) result. For a company who are not using QbD approach, an OOS result can be difficult to find the root cause. Although in popular belief Qbd may have major financial burden for the company but in real it may have many financial and operational benefits. Implementing QbD in different phase requires a dedicated and sustained commitment by an organization. Evaluateing the effort necessary to implement QbD is a vital component to successful adoption. Some of the most common problems to adoption include:

• Lack of evaluating of the process and its benefits

• Organizational apathy to change

• Continuous change in priorities

• Unavailability of resources and expertise in QbD.

Conclusion

Quality by design is a common evaluating on the concepts of ICH Q8, Q9 and Q10 and will be important in the process of formulation. The review article explores the effective use of

target product profile including various form of risk assessment. In addition the article also explains the vital critical material attributes of critical process parameters. The application of QbD principles and tools to drug product and process development is also evaluated here. It can be concluded Quality by Design (QbD) principles and tools, play an important role in facilitating a higher level of process evaluating and create opportunities for investigation and developing control strategies in various formulation and process development.

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