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A Review on Quality by Design

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Abstract: *Pharmaceutical Quality by Design (QBD) is a systematic approach to development that begins with predetermined objectives and emphasizes the understanding of production and processes and process control, based on sound science and quality risk management. Quality purchasing design (QBD) is emerging to increase the promise of providing safe and effective medicines to customers and promises to improve the efficiency of product quality. Quality means eligibility for use. The quality of the medication means that the product provides therapeutic benefits to the label reproducible and free from contamination on the label. In vivo or in vitro performance test can be evaluated for drug production. Dietite by Quality guarantees the performance of the product in vitro and the performance of the in vitro product in the in vivo product. "So the quality design is related to the product."*

Keywords: Quality by design, Benefits of Qbd , Elements Of Quality by design , Application of Qbd

I. INTRODUCTION

The basic concept of QbD is "The Quality cannot be tested into the product, but it should be built into it." The design space is defined as a manufacturing area of the product including Equipment, Material, and Operators and Manufacturing Conditions. The design space should be well defined prior to regulatory approval. Working with design space is not considered as a change, but working out of design space is considered as a change. Different variables are monitored for their effect of product quality when the manufacturing is done out of design space. All these variables are assessed and conclusions will be drawn which serves as a tool to QbD. All these data are included in the regulatory submission dossier The pharmaceutical product formulation can be developed based on the data obtained from product development studies. The process variables that are emerged during development stages will serve as a source for QRM. Before conducting the development studies the QTPPs of the product must be determined and having the final product quality in mind and evaluation is performed to obtain the desired quality of product. The QTPP of product includes design space, specifications and manufacturing controls.

1.1 Objectives of QbD

- The main objective of QbD is to achieve the quality products.
- To achieve positive performance testing.
- Ensures combination of product and process knowledge gained during
- Development.
- From knowledge of data process, desired attributes may be constructed.

1.2 Benefits of QbD

- Batch failures must be eliminated, and deviations must be kept to a minimum, in order to avoid regulatory issues.
- Empowerment of technical personnel
- a quick-response system that is agile and flexible.
- Many businesses want to reduce waste and project rejections while increasing manufacturing efficiency.
- Create a scientific knowledge base for all products.
- On science-related topics, collaborate more closely with industry.
- Ascertain that all data is consistent.
- Include a risk assessment and management component.

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- Reduce the amount of time spent testing the final product.
- The ability to make a decision on a release date quickly.

1.3 Benefits of Implementing QbD for FDA

- Ensure scientific foundation for review
- Provides for better coordination across review, Compliance and inspection
- Improves information in regulatory submissions
- Provides for better consistency
- Improves quality of review (establishing a QMS for CMC)
- Provides for more flexibility in decision making
- Ensures decisions made on science and not on Empirical information
- Involves various disciplines in decision making
- Uses resources to address higher risks

1.4 Benefits to Industry

- 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
- Allow for possible reduction in overall costs of Manufacturing –less waste
- Ensure less hassle during review –reduced Deficiencies –quicker approvals
- improves interaction with FDA –deal on a science level Instead of on a process levelAllows for continuous improvements in products and Manufacturing process.

1.5 Pharmaceutical Development

Widely used in pharmaceutical development and Manufacturing.

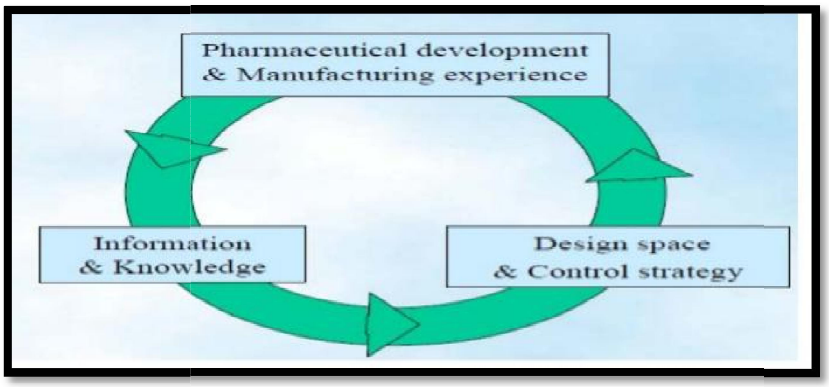

Figure: Pharmaceutical developments

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1.6 Used in PAT

A system for designing, analyzing and controlling Manufacturing through timely measurement of critical Quality performance attributes of raw and in process Materials and processes with the goal of ensuring final Product quality.

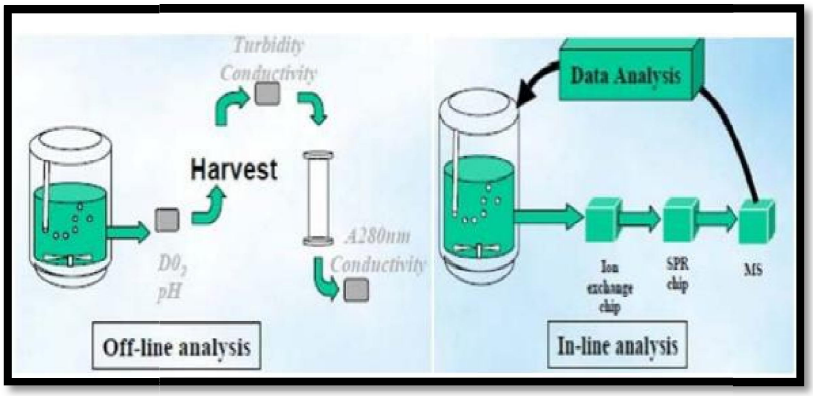

Figure: Off – line and On- line Analysis

For experimental design

A structured organized method for determining the Relationship between factors affecting a process and the Output of that process.

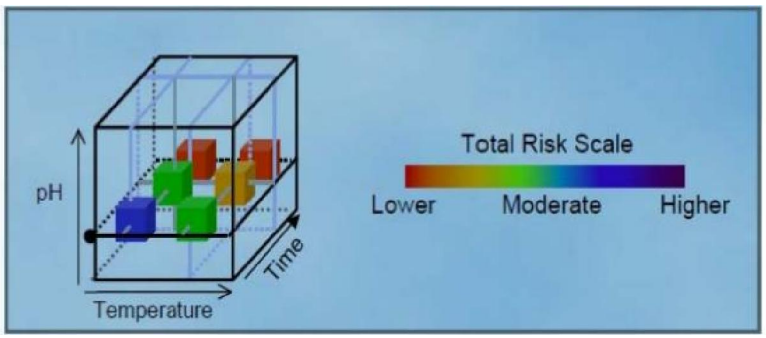

Figure: For Experimental design

II. KEY ELEMENTS OF QbD

- Because quality, safety, and effectiveness can now be linked, the TPP can be refined. As a starting point for product planning and development, the standard characteristics of the product are identified.
- Characteristics of importance Material properties that must be within acceptable limits, ranges, or distributions are known as attributes.
- In Risk Assessment, CPPs and material attribute compared to CQAS. The CPPs will be determined through The use of risk assessment tools like the FMEA or the bone diagram. ICH Q9 lists the risk management tools that will Be used.
- An important connection between CQAs and CPPs can be established and represented in a stylistic area through the use of experiment style possible
- The company's long-term strategy in the event of an unexpected event, it is important to identify and address the problem as soon as possible.
- Management of the product lifecycle and continuous improvement in quality .

III. TPP

The TPP specifies how a drug product should look for purposes of labelling and drug development. The product's intended use, target audience, administration route, and other critical features and quality design are all defined by TPP.

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3.1 Target Quality Product Profile (TQPP)

The term TQPP may be a logical follow-up to the term TPP when discussing product quality. The QTPP is required in order to comprehend and trace data that cannot be passed down from one generation to the next. This is accomplished by laying out the desired characteristics of a drug product while also considering the product's potential side effects and safety concerns. TQPP's indefinite-quantity type and purity include quantity, strength, instrumentation closure system, and identity",

3.2 CQA's

CQA can be applied in a variety of ways to ensure a product's quality, safety, efficacy, and stability (certificates of conformity, or CQA for short). It is also possible to define, measure, and monitor the final product's quality to ensure that it remains within acceptable limits. Quality attributes include clinical safety and efficacy, as well as the parameter boundary approaching failure. Manufacturing is also a quality attribute. It's possible that the criticality of the APT manufacturing process will change, raising the criticality risk level.

3.3 Critical Material Attributes (CMAs)

It is critical to fail when a true change in a parameter causes it impossible for a product to meet a QTPP. It's important to consider how much adjustment one is willing to make as well as the uniqueness of each input material when deciding which parameters are important. CMAs that fall within an acceptable range or ranges must meet drug substance, excipient, and in- process material quality.

3.4 CPP's

This means that any measurable input or output of a method step must be managed in order to achieve the required product quality and method consistency. Each item in this read would be a method parameter. Here's how it'd work: Parameters are examined before or during procedures that can have a significant impact on the appearance, purity, and yield of the finished product.

3.5 Risk Assessment

When we talk about "risk," we're referring to both the possibility and the magnitude of harm. By assessing the risks involved, the overall quality of a technique or process can be improved. A risk assessment's goal is to identify the critical characteristics that influence the quality of a finished product. A risk assessment can help improve communication when the FDA, trades, R&D/prototype, and multiple production sites are all involved. The methods for determining risk are as follows: A few risk assessment methods are described in ICH guideline Q9:

- Failure Mode Effects Analysis (FMEA)
- Failure Mode, Effects and Criticality Analysis (FMECA)
- Fault Tree Analysis (FTA)
- Hazard Analysis and critical control points (HACCP)
- Hazard Operability AnalyFME
- Preliminary Hazard Analysis
- Risk ranking and filtering
- Supporting applied mathematics tools

3.6 Design Space

The multidimensional combination and interaction of input variables (such as material qualities) and method parameters unquestionably ensures that the quality will be done appropriately. Moving out of the designated planning area is required for the more time-consuming post-approval amendment process (Fig. 2). The relevant authorities must review and approve an individual's projection of the planning area. The area for the scientist's style could be Y = FifY=Fisa function of the (critical) method parameters and the (critical) quality attributes/material attributes (Process Parameters, Material Attributes).

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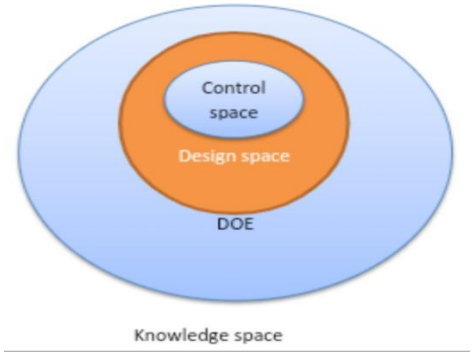

Figure: Design space

3.7 Control Strategy

A control strategy based on Extensive knowledge of the process and the product Includes control over the CMA of the input Materials and intermediates, control of the process Parameters, final drug product quality, and final Packaging. All these components of control Strategy are covered under process analytical Technology (PAT) Control space should be within the design space; it Is an upper and lower limit for raw material (or) a Process within which parameters and material are Regularly controlled, which assures the quality of The product. Every process has a control strategy right now. Fig. Shows a simplified quality Assurances diagram under the current regulatory Evaluation system. In this system, product quality is ensured by fixing The process to produce the active ingredient, raw Material testing, performing the drug product Manufacturing process as described in a fixed batch Record, in-process material testing, and end-product Testing. A factor identified to have risk has to be Controlled . Control strategy includes the following elements:

- Input material attributes (e.g., drug Substances, excipients).
- Equipment operating conditions.
- In-process controls.
- Finished product specifications

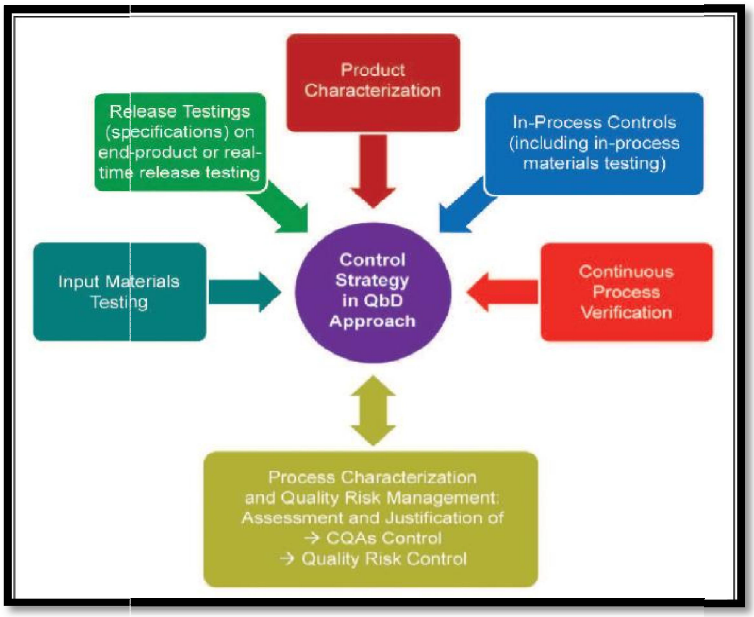

Figure: Control Strategy in Qbd

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IV. SIGNIFICANCE OF QBD

- Quality by Design means -designing and developing formulations and manufacturing processes to ensure a predefined quality.
- Quality by Design requires understanding how formulation and manufacturing process variables influence product quality.
- Quality by Design ensures Product quality with effective control strategy.

V. CONCLUSION

Quality by Design is intended to enhance process knowledge and is based on existing guidance and reference documents. QbD is a quality system that builds on past and sets future regulatory expectations; the QbD can be viewed as a process defined by series of document requirements. These documents organize and demonstrate process knowledge and understanding. QbD can be applied to legacy and new products, but the supporting document package may differ. The QbD suite of documents is "alive". They can and should be revised as the knowledge base changes. Ensures robust commercial manufacturing methods for consistent production of quality drugs. Ensures the consumers that therapeutic equivalent generics are manufactured every single time. QbD methodology helps in identifying and justifying target product profiles, product and process understanding. There is a need for vigorous and well funded research programs to develop new pharmaceutical manufacturing platforms.

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