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Quality by design (QbD) in the field of pharmaceuticals - A Review

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ABSTRACT

The profile of the target product includes all the characteristics of the product like chemical properties, constituents of the product, physical state and formulation of the product, state of the product at which the highest efficacy and lowest efficacy is obtained. The medical benefits that can be achieved by the use of the product, site of application of the product, pharmacokinetic and pharmacodynamics of the product, aerodynamics, toxicology, purity rates, sterility etc. For the development of manufacturing process, many factors should be clearly understood, which includes the necessary means of the manufacturing of the selected product, the ultimate goal of the manufacturing, what are the drawbacks that have been encountered. in the past manufactured products-during and after production, how to overcome those loop wholes, what are the all useful techniques that may or may not be economic that can be employed in this manufacture developing process etc. For achieving all these, there should be a number of experts in manufacturing who are hired for this process, as it is always dealt with immense importance and economy. Quality by Design is a very novel approach for making advances in the field of medicine, which can be said as therapy with pharmaceutical advances can cure anything. But, very innovative thoughts by the experts and in-depth research and understanding of the therapeutic moiety of an organism and the disease can help in this advancement.

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INTRODUCTION

Quality by Design is defined as the efficiency of the product enhanced by how it is made or produced (Kumar and Gupta, 2015). In simple, quality can be defined as the high standard of the product. In terms of pharmaceutical field, being dealt with medical devices, medications, contamination is a significant drawback. Thus, a product which is known to have no contamination and known to produce the desired effect at a defined time is said to be a quality product (Nasr, 2004). Thus, standards that a pharmaceutical product should meet include level of contamination, reproducibility, efficacy and therapeutic benefit of the product. Many other parameters define the quality of a pharmaceutical product (Food and CDER, 1995). As many of the parameters like stability, reproducibility, efficacy, safety, economic benefits can be achieved in the field of pharmaceutical products by making innovations in the Design of the product, Quality by Design is considered to be an essential concept in the name of development in medical advances (Food and CDER,

Table 1: Scope for Quality by Design (QbD)

Date	Guideline reference	Scope
Aug 2009	ICH Q8	Pharmaceutical development
Nov 2005	ICH Q9	Quality risk management
Jun 2008	ICH Q10	Pharmaceutical quality system
Jan 2011	FDA	Process validation. General principal and practices
Dec 2011	ICH Q8/Q9/Q10	Guide for implementation
March 2012	EMA/CHMP/QWP/811210	Real time release testing
March 2012	EMA/CHMP/QWP/CVMP/70287 (draft)	Process validation
May 2012	ICH Q11	Development and manufacture of Drug substance (Woodcock, 2004).

1997a).

Benefits that can be achieved by Quality by Design process

There are several been some useful outcomes from Quality by Design, which includes

1. The process of the product can be made to get better understood by the processor or the health care professional.

2. When the stability of the product is increased, it automatically decreases the number of failures among the batches of production.

3. It gives immense economic benefits from its reproducibility (Food and CDER, 1997b).

4. Any product after a particular improvement in quality by Design will give its high efficiency and effective control.

5. It can also increase the regulatory approach flexibility.

6. It also increases the additional opportunities for advancements in the medical field (Food and CDER, 2004). Scope for quality by Design is shown in Table 1.

Various steps involved in the process of Quality by Design development

Identification of target product profile (TPP)

Using the property like with the link drugs developed, labelling of the drug, the target of the product profile is identified. Target profile can be said as the heart of the product that is aimed to be re-designed for improving its quality in various aspects (Food and Administration, 2004). It should be all of first identified to see if any chances for modification is available.

The profile of the target product includes all the characteristics of the product like chemical properties, constituents of the product, physical state and formulation of the product, state of the product at which the highest efficacy and lowest efficacy is obtained (ICH Q8 (R2), 2009). The medical benefits that can be achieved by the use of the product, site of application of the product, pharmacokinetic and pharmacodynamics of the product, aerodynamics, toxicology, purity rates, sterility etc.

Drug Substance and Excipient Properties

Besides the target of the product, the excipient substances play a significant role in the success of a product. For example, many products which are to be delivered in oil medium are hydrophilic which cannot be dissolved in oil medium (hydrophobic) without the help of excipient that masks the dissolution process of the target substance (Food and CDER, 2004). Similarly, to attain a high rate of bioavailability to achieve therapeutic ranges of a drug in the biological fluids, by skipping or reducing the effect of the first-pass metabolism, excipients are of significant importance (Woodcock, 2004). All the critical factors of the excipients that are to be assessed are chemical, physical properties, toxicity, and rate of clearance by pharmacodynamics and pharmacokinetic parameters of the substances (Yu *et al.*, 2007).

Formulation Design and Development

As per the regulations and norms of FDA and the rules, not all the studies can be carried out in a human species, due to many factors like dealing with life-threatening diseases management, complications of the experiment conducted, and various toxicity profiles of the products. Many in vitro models have been developed to effectively implement this process (Nasr, 2004), which includes arti-

ficial tools and machines that have been designed to evaluate various kinetics and dynamic properties of the substances which includes dissolution, flexibility, and solubility, rate of diffusion, concentration, sterility and purity. Nowadays, artificial models have been developed for assessing the dynamic properties, which includes artificial heart, kidney models, where the machine designed acts as a live organ. This is also known as "Organ Chip Model", where a chip acts as a complete organ appropriately (Food and CDER, 1995).

Use of overages

Overages are the substances which have the property to increase the self-life of the substance. But, the use of overages to improve the life of the substance is not highly recommended in the field of science due to its toxic effects. If there is no other chance to formulate a therapeutic product without overages added in it, then the available amount of overages as given by FDA can be added in the formulation (Food and CDER, 1997b).

Manufacturing process development

Manufacturing process development is one of the most crucial parts of the Quality by Design. It is evident that without progress in the process of manufacturing, the Quality by Design cannot be achieved (Food and CDER, 2004).

For the development of manufacturing process many factors should be clearly understood, which includes the basic process of manufacturing of the selected product, the ultimate goal of the manufacturing, what are the drawbacks that have been encountered in past manufactured products- during and after production, how to overcome those loop wholes, what are the all useful techniques that may or may not be economic that can be employed in this manufacture developing process etc (Woodcock, 2004). For achieving all these, there should be a number of experts in manufacturing got hired for this process, as it is always dealt with immense importance and economy.

Design of experiments

Experimental Design can be defined as the protocol of the whole process that should be employed for achieving Quality by Design. It should be done after completely understanding the need, the process involved in it, outcome required, human empowerment for the experiment and economic burden (Nadpara *et al.*, 2012; Glodek *et al.*, 2006).

Critical quality control parameters

Every system will have some parameters to assess the quality of the same. Similarly, after the redesigned product production, to check for the outcome of the desired characteristics by all changes made during the process, few parameters should be set as critical tools for assessing the quality which is known as "critical quality control parameters". This may include, means for checking the reproducibility of the designed product, economic input and benefit by marketing, therapeutic advances and others (Jadhav *et al.*, 2014).

Quality by Design is a very novel approach for making advances in the field of medicine, which can be said as therapy with pharmaceutical advances can cure anything. But, very innovative thoughts by the experts and in-depth research and understanding of the therapeutic moiety as well as an organism and the disease, can help in this advancement.

CONCLUSIONS

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 the past and sets future regulatory expectations. QbD can be viewed as a process defined by a 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.

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Conflict Of Inteterest

The authors declare that there are no Conflicts of Interests

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