Chapter 10

Quality by Design in Pharmaceutical Formulation

Sundaramurthy Vivekanandan
Bluefish Pharmaceuticals Pvt. Ltd, India

ABSTRACT

Quality by design (QbD) is a systematic, scientific, risk-based approach to product development and manufacturing process to consistently deliver the quality product. In this chapter, application, benefits, opportunities, regulatory requirements involved in quality by design of pharmaceutical products are discussed. In quality by design approach, during development, the developer defines quality target product profile (QTPP) and identifies critical quality attributes (CQA). Critical process parameters (CPP) of unit operations which impacts critical quality attributes need to be identified to understand the impact of critical material attributes (CMA) on quality attributes of the drug product. Quality by design approach is defined in ICH guidelines Q8 – Pharmaceutical Development, Q9 – Quality Risk Management, Q10 – Pharmaceutical Quality System. This chapter describes the implementation of new concepts in quality by design like design of experiments to achieve design space, control strategy to consistently manufacture quality product throughout the product lifecycle.

INTRODUCTION

Quality by design is a systematic approach to product and process design, development that begins with predefined objectives and emphasizes product and process understanding and process control, based on sound science and quality risk management (ICH Q8(R2)).

FDA had provided detailed description to Quality by Design in 2004 via ‘pharmaceutical cGMPs for 21st century – a risk based approach’

FDA faced issue of increase in number of regulatory variations to registered New Drug Applications (NDAs) and Abbreviated New Drug Applications (ANDA’s) in 2007. FDA had observed that, the applicants had focused more in chemistry section of dossier and least priority provided to manufacturing process and product development. Hence, FDA decided that, more controls were required on drug product manufacturing process and the qualitative, quantitative composition. In 2005 FDA had insisted the applicants to submit chemistry manufacturing control (CMC) section with an application of QbD as part of New Drug Application and Abbreviated New Drug Application (Patricia Van Arnum et al., 2007).
IMPORTANCE OF QUALITY BY DESIGN APPROACH

Quality must be built in drug product development as well as during manufacturing process (ICH Q8(R2) 2017; Robert A. Lionberger, Sau Lawrence Lee, LaiMing Lee, Andre Raw, and Lawrence X. Yu 2008). Quality can not be improved by testing finished product or by performing in-process tests. In traditional pharmaceutical manufacturing process, the manufacturing process controlled through fixed parameters or range with additional in-process testing at different process stages. Whereas Quality by Design approach defines design space and control strategy to maintain design space to ensure quality of finished product (Lan Zhang, Shirui Mao et. al., 2017; Jaiprakash N. Sangshetti Mrinmayee Deshpande Zahid Zaheer Devanand B.Shinde Rohidas Arote. et al., 2017). This infers that, QbD approach helps to develop quality product through consistent, robust process. The same is depicted in Figure 1.

QbD ultimately helps to implement ICH Q8, Q9 and Q10. ICH released ‘Q8(R2) Pharmaceutical Development’ in 2009, ‘Q9 Quality Risk Management’ in 2005 and ‘Q10 Pharmaceutical Quality System Guidelines’ in 2008 (Rathore et. al., 2009). ICH released Q8/Q9/Q10 Questions & Answers (R4) in 2010 to emphasis details about design space, real-time release testing and control strategy (ICH Q&A 2010). Now FDA has increased implementation of QbD concepts in drug product development made by the applicants from January 2013 (Jaiprakash N. Sangshetti Mrinmayee Deshpande Zahid Zaheer Devanand B.Shinde Rohidas Arote. et al., 2017).

ELEMENTS OF QUALITY BY DESIGN IN PHARMACEUTICAL DEVELOPMENT

Various elements of Quality by Design system (Vemuri Pavan Kumar, N. Vishal Gupta 2015; Jaiprakash N. Sangshetti Mrinmayee Deshpande Zahid Zaheer Devanand B.Shinde Rohidas Arote. et al., 2017; Lawrence X.Yu et. al., 2008) are listed below and the same is shown in Figure 2.

1. **QTPP**: Identify the Quality Target Product Profile (QTPP) by defining desired drug product characteristics.
2. **CQA**: Identify Critical Quality Attributes (CQA’s).
3. **CPP & CMA**: Identify Critical Process Parameters (CPP’s) and Critical Material Attributes (CMA’s).
4. **Risk Assessment**: Perform risk assessment by linking CMA’s and CPP’s to CQA’s to assess impact of these parameters on QTPP.

*Figure 1. Traditional system Vs QbD approach*