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Review Article

Process Analytical Technology (PAT) in Pharmaceutical Development and its Application

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ABSTRACT

Process Analytical Technologies (PAT) are used to provide and inform timely analysis of critical quality parameters with the end goal of improving final product quality as well as reducing manufacturing costs, thereby significantly benefiting the Pharmaceutical Industry in manufacturing area. The potential for improved operational control and compliance resulting from continuous real-time quality assurance was highlighted as a likely benefit that would result from PAT implementation. It is a very new topic and a various work has been done on this topic by academic and industrial contributors in the last decade. In this paper, we will start with brief PAT concepts, Introduction, Historical view, Regulatory view, PAT tools, Pat implementation and a review of their application in the wider pharmaceutical industry. The first steps in an Analytical Quality-by-Design (AQbD) method development include understanding the analysis needs (e.g., purpose, specificity, sensitivity, cycle time, on-line/off-line, qualitative/quantitative, accuracy, precision) and selection of the technique that will meet these criteria. One set of analytical tools applied during the development and scale-up of drug substances and dosage forms include in-situ analytics, chemometrics and modelling i.e., Process Analytical Technology (PAT) tools. Pharmaceutical companies face many challenges and problems while implementing PAT into their new and pre- existing manufacturing processes. This article discusses the challenges and problem encountered. The scope of this article is to introduce the reader to PAT. It, however, is a wide – ranging subject, which is expanding rapidly.

Keywords: Process analytical technology, Quality by design, critical quality attribute.

INTRODUCTION

Historically, pharmaceutical production involves the manufacture of the finished product, followed by laboratory analysis to verify quality of the product. The disadvantages associated with this approach are continual process optimization, recurring manufacturing difficulties, and the possibility of failed batches. The Food and Drug Administration (FDA) is inviting discussions throughout the pharmaceutical industry concerning a new mode of operation, which will address these concerns. This mode of operation is known as Process Analytical Technology (PAT). Process analytical technology (PAT) is a key element of the "Pharmaceutical Current Good Manufacturing Practices (CGMPs) for the 21st Century - a Risk Based Approach" initiative announced by the FDA in August 2002 to improve and modernize pharmaceutical manufacturing. [1]

The PAT initiative was first proposed by the United States Food and Drug Administration's (FDA), Centre for Drug Evaluation and Research (CDER) with the objective of achieving good health and cost benefits by application of modern process control and tests in pharmaceutical manufacturing industries. [2]

Quality-by-Design (QbD) is well-established in development and manufacture of pharmaceutical drug substance and drug product and is discussed in ICH Q8, Q9 and Q11. The outcome of QbD is a well-designed and understood quality product that consistently delivers the continuous performance. The knowledge obtained during development helps in justify the establishment of a design space, (process) control strategy and set point within the (regulatory approved) design space. Materials made within the design space will produce an acceptable product, and the changes within the design space are (regulatory) acceptable. These same principles and concepts have been applied to the development of analytical methods, and termed Analytical QbD (AQbD). Analogous to process QbD, the aim of AQbD is to design a well-understood, robust method that consistently delivers the necessary performance as described in the analytical target profile (ATP). One set of analytical tools used in support of pharmaceutical development and control include insitu analytics, chemometrics and modelling i.e., Process Analytical Technology (PAT) tools. Process analytical technology (PAT) can be defined as "a system for designing, analyzing, and controlling manufacturing through timely measurements (i.e., during processing) of critical quality and performance attributes of raw and in-process materials and processes, with the goal of ensuring final product quality". [3]

This definition (and relation with QbD) has been debated and described in many venues (e.g., conferences, social media, article etc.). In these enthusiastic discussions, one point that is frequently overlooked is that PAT tools are firmly attached in the pharmaceutical workflows that underpin development and scale-up, for both drug substance and dosage forms. The term Process Analytical Technology (PAT) was introduced by the US FDA as an initiative to bring an improved understanding of pharmaceutical manufacturing processes to increase the quality of their products. [4]