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Product quality by process analytical technology and quality by design- A short communication

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ABSTRACT

A Systematic approach which is based on scientific knowledge and concept of quality risk management which leads to development which emphasizes on process and product undertaking an starts with a predefined objectives is usually called as QBD, which now aims at pharmaceutical development to design a quality product and the entire manufacturing process aiming to produce according to the standard and specifications to consistently deliver product intended, the knowledge is purely base on scientific approach, QbD is not only limited to production but is also extended to analytical procedures and methodology, the article relates to a short communication about A QBD its approach, history and its basic elements. The product procedures now need to comply till the end of the entire procedure s rather than only at the beginning and that's where QbD plays important role throughout the method life cycle also it give added advantage is to include the procedure to discovering and minimizing the sources of viability which may lead to inferior quality and procedure and products.

Keywords— *QbD, PAT, ICH, Quality Control*

1. INTRODUCTION

The intended performance of the product which has to be delivered consistently is mainly due to the products which are of high quality by design and superior manufacturing process which is now the ultimate aim of all pharmaceutical firms dealing with product development[1]PAT(Process Analytical Technology)[2] and QbD are the simple scientific tools which is implemented by firma to develop very effective economical analytical method ,which can be applied throughout the product cycle not only at the beginning in order to facilitate regulatory flexibility too in all the analytical procedures. Quality, safety and efficacy are the fields which are now more focused on. To achieve this in one's own frame method, design space and freedom to change method parameters are usually sought at and all this is together referred as method operable design region [3].The emphasis throughout to obtain method performance which is optimal as well to undergo rigorous evaluation and searching alternative methods basically defines the goal of QbD and its methodology. [4]

QbD approaches to synthesis of active pharmaceutical ingredient is with example usually followed by guidelines clearly mentioned by ICH Q11.Similarly, Guidelines Q8 to Q11 have all described and briefly discussed QbD techniques in formulation development and various synthetic processes, The ICH basically guides the concepts of analytical quality by design for drug and its related parameters and others substances, therefore QbD is tool and quality is the core by which this tool functions in pharmaceutical industry. It has been a mandatory procedure even in USFDA approach [2], therefore even now the generic companies are implementing this QbD approach for their formulation development.

US FDA has initiated the services of Quality by Design (QbD) and was indeed marked as one of the most important landmarks in quality. In fact, it started as early as 2013 by FDA. The concept emphasized on monitoring all the procedure through control strategy, viewing critical process parameters and increase of product process and product understanding through risk management. The aim was for more of customer satisfaction as there was consistency in all the commercial manufacturing. The beginning of the journey toward the implementation of QbD, which was initiated by US FDA also lead to the process of Process Analytical Technology" (PAT), which will guide the pharmaceutical firms about generic and the advantage of PAT in real time release too. Quality for pharmaceutical in 21st century, a risk based approached was first step towards the goal of establishment of quality, which is QbD.

To come to conclusion after reaching to root because is limited and in large scale suggests an addition of more relevant data which is impossible without quality product and understanding of procedures and this is the role of QbD its final role is to increase the real cause of root analysis and changes made after changes managed. [5]

1.1 Definition of QBD

A process having predefined approach and objectives and implies on product and process understanding, based on scientific approach along with quality risk management in a very systematic way is defined as QbD.

1.2 Advantages of QBD

An extremely efficient agile flexible manufacturing tool which without excessive regulatory taxation produces high quality drug product

- Is economic and cost efficient of industry
- It has a GMP inspection of approval after the process and focuses on PAI
- Product quality is totally assured
- The manufacturing process is efficiently increased
- The regulatory process and manufacturing process are totally in sync after the approval to
- Complications are eliminated or minimized in the beginning
- There is always scope of improvement
- Innovations are welcomed always
- Regulatory procedures are too efficient
- First cycle improvements are encouraged

1.3 Objective of QBD

- Ensures combination of quality product along with scientific and process knowledge
- The given data and process should be in such a way that it should desired attributes should be constructed
- Main aim is quality product and process characteristics for new estimation during the processes.

1.4 Principle of QbD

One: The base of evaluation for risk to QbD should be based on scientific knowledge and it should be ultimately linked to protection of patient in case of usage of product

Second: The level of risk involved should be matched to the level of effort, documentation and formality

ICH guidelines	Key elements
Q8	**Pharmaceutical development** (a) The critical quality attributes (CQAs) is identified by the quality target product profile of the drug product. (b) Critical material attributes (CMAs)are identified by product design and its understanding. (c) The linking of CMAs and CPPs to CQA are done through understanding scale up principles, along with process design and its understanding (d) The manufacturing process should have total control strategy and specification on drug product, excipients, drug substances. (e) There should be improvement and process capacity continually.
Q9	Quality risk management (a)The level of risk taken for the process should comply with the level of effort put and also the level of documentation and formality involved for the quality risk management. (b)The ultimate aim will be favorable to the patients and evaluation of risk to quality must be based on knowledge which is totally of scientific origin.
Q10	Pharmaceutical quality systems (a) A management system with a strong change (b) The process performance and product quality should be reviewed by management system (c) The plan should have preventive and corrective action (d) 4. The level of risk taken should always match the risk formality and documentation involved
Q11	Manufacture and development of drug materials a substances

Traditional approach vs. QbD approach

Aspect	Current	QbD
Pharmaceutical development	Optimization is maximal and focus is on random and empirical forms.	Control strategy and robustness is mainly focused base on multivariate and systemic
Manufacturing process	Fixed	The company usually manages quality system which is Adjustable within design space.
Process control	Process involving in procedures	The process operations are trended and tracked and are utilized with the help of PAT
Product specification	Batch data is the basis of quality control which is the primary source	The desired product performance is usually controlled by overall quality control.
Control strategy	By getting tested and doing inspections.	Real time release is possible only by control strategy which is risk based.

2. ANALYTICAL QUALITY BY DESIGN (AQbD)

This is the latest approach which requires very few resources than the traditional validation approach where the quality is not compromised at all, basically AQbD is a method validation approach, which acts over a range of entire APIs batches as compared to other analytical methods ,without the need of any revalidation it applies both the extreme knowledge of MODR and DoE for designing method validation of all APIs. This method provides information , on measurement control strategy and also has scope for continuous improvement base on ICH validation and also due to interaction and measurement of uncertainty.

The need of guidelines regarding documentation of knowledge generated during method development and product development prompted the need to find suitable rationale to justify it, which lead to the combined approach of QbD and AQbD which not only gives an insight of understanding of methodology increased basis of knowledge sharing and practical development of high performance methods based on scientific knowledge and automated rationale, the hindrances to the pathway are implementation of harmonization technologies its concepts along with the industrial and regulatory agencies training concepts and education with available human resources meant for industries and other regulatory agencies ,based on dynamic control strategy which is excellent in terms of returns of investments low product recall or nil rejects or any changes post production, moreover it achieves lots of operative elasticity, efficient regulatory oversight, regulatory filing, reduces consumer generated skepticism reduces time to reach market saves significant resources as testing is only real-time. The various tools utilized by AQbD are ATP, CQA, Method Optimization and Development with DoE, MODR, and Control Strategy with Risk Assessment, Method validation, and continuous improvement as depicted in the flow chart.

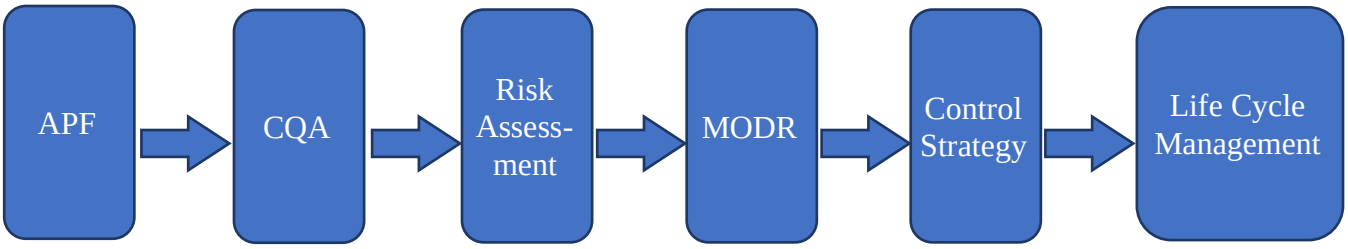

Fig. 1: Flow chart depicting AQbD

2.1 ATP

A tool to attain QTPP which is the result of methods used in the process of analytical method development which is in turn defined by analytical target profiles ,it can also be used in developmental approach which were used traditionally or as a component of QbD approach that can be used in establishment of any analytical methodology. To measure the CQAs of drug product the method requirement can be also described by ATP.

The selection of analytical techniques like gas chromatography, ion chromatography, HPLC,HPTLC and other procedural requirement like assay and test for purity is usually covered by ATP it also covers the selection of target analytics like API and impurities.

2.2 CQA

The Chemical and physical property of the drug substance along with the impurities are described by CQA analytical method development also it defines terms like pH values, boiling points, charged functional groups, solubility, polarity. The detection method, color for reagent development time taken for plate development, injection time and volume mobile phase TLC plate are basically CQa for HPTLC. Temperature of oven its program injection concentration, its temperature and flow rate of gas, concentration of sample and diluents uses comes under the category of CQA of GC. The elution method, organic modifier, diluents used, column use, PH of mobile phase used buffers used in mobile phase is the CQa of HPLC –UV or RID. The CQa for various analytical procedures are made of methodology and measured parameters, in order to ensure the desired product quality the limit or range should remain in specified limit, The biological, chemical, physical or microbial property is define by ICH FOR CQa in Q8.

2.3 Risk management

A safety program which is strategically designed to decrease any product risk is defined as risk management by FDA, throughout the entire life cycle of the product [6] the assessment done to control communicate and review of risk done in a specific systematic way is process of risk management. CQA and input process are linked by it . Risk management tools available are:

(a) Pareto analysis
(b) Ishikawa or fish bone analysis
(c) Pareto analysis.

2.4 MORD

When the quality of the method and the robustness do not get significantly effected on by the method variables then it is coming under a safety zone called as MORD which is basically an experimental safety zone .It is a multivariate scientific approach base on risk management where the different variable method on the method is evaluated by its effect to obtain results and to check on the performance .Various factors which effect the product performance like concentration of reagents during extraction ,volume of extraction, temperature of extraction, heating time during extraction, the type of column used ,flow ,size of sample are also connected within it. MODR is result of small robustness of the method which are in reference and also to the method in references which are connected to the apparatus and to the method development used. The results for Design of experiment DoE

is used ,which provides information on variables used ,for prediction and optimization of analytical response in the technique the experimental designs like OD-optimal design, FD-factorial design, CCD- central composite design ,Box-behnken Design-bbd are employed by it. The clarifications of different CQAs on analytical procedure and its influence are also helped.

2.5 Method control strategy

In order to assure that ATP requirements will be met during the various analytical methods transfer as well as in routine use a planned set of control is used which serves for all purpose of variation is usually referred as method control strategy, which is a planned set of controls. It is derived from current product and assures process performance by understanding process and product quality too (ICH Q10). The system suitability parameters or the continuous monitoring is attained by it in routine use, this is not a onetime procedure but an exercise which has to be performed throughout the different stages of product development in its life cycle.

2.6 Life cycle management

To ensure fitness of quality product for its intended uses in method validation, transfer and verification with the key steps in analytical methods for particular analytical methods which includes all elements of AQbD comes under the term "LIFE CYCLE MANAGEMENT OF ANALYTICAL PROCEDURE". it continues with all the methods used with the commencement and establishment of ATP. It is the main focus of performance for the qualification like precise studies ,site of use and all other routine studies to ensure that the method utilized is under control throughout [7] by getting involved in various activities which are under verification continuously to provide complete assurance.

3. CONCLUSION

Application of QbD principles facilitates and finally leads to the development of quality products. Which is taken care throughout the procedures and finally extremely beneficial to the patients, still there are lots of confusion among regulatory bodies, academicians, industry experts, scientists on the real aspect of QbD in spite of latest researches an publications hence this short communication intents to describe the importance and objectives of QbD its details, elements and explanation of its implementation tools.

4. REFERENCES

[1] Nadpara NP, Thumar R V, Kalola VN, Patel PB. (No Title) [Internet]. Vol. 17, International Journal of Pharmaceutical Sciences Review and Research. 2012 [cited 2020 Mar 14]. Available from: www.globalresearchonline.net

[2] Raman NVVSS, Reddy Mallu U, Reddy Bapatu H. Analytical Quality by Design Approach to Test Method Development and Validation in Drug Substance Manufacturing. 2015 [cited 2020 Mar 15]; Available from: http://dx.doi.org/10.1155/2015/435129

[3] Analytical Quality by Design (AQbD) in Pharmaceutical Development | American Pharmaceutical Review - The Review of American Pharmaceutical Business & Technology [Internet]. [cited 2020 Mar 11]. Available from: https://www.americanpharmaceuticalreview.com/Featured-Articles/144191-Analytical-Quality-by-Design-AQbD-in-Pharmaceutical-Development/

[4] Vogt FG, Kord AS. Development of quality-by-design analytical methods [Internet]. Vol. 100, Journal of Pharmaceutical Sciences. John Wiley and Sons Inc.; 2011 [cited 2020 Mar 15]. p. 797–812. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21280184

[5] Yu LX, Amidon G, Khan MA, Hoag SW, Polli J, Raju GK, et al. Understanding pharmaceutical quality by design. Vol. 16, AAPS Journal. Springer New York LLC; 2014. p. 771–83.

[6] Gandhi A, Roy C. Quality by Design (QbD) in Pharmaceutical Industry: Tools, Perspectives and Challenges. 4:11.

[7] Ganorkar A, Gupta K, Gupta Biomed Sci KJ, Res T. Analytical Quality by Design: A Mini Review. [cited 2020 Mar 16]; Available from: http://biomedres.us/submit-manuscript.php

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