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QUALITY BY DESIGN APPROACHES TO ANALYTICAL METHOD DEVELOPMENT: A MINI REVIEW

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ABSTRACT

(QBD) Quality by design is a systematic approach to and drug development. Predefined product specifications are done by, planning, developing, manufacturing respectively. Science risk-based management approaches are used for a predefined product. Analytical development method based on the same principle of QBD known as AQBD. The Traditional approach and analytical approach are specified in QBD. Analytical profile, risk Assessment, different critical quality attributes are used for various analytical techniques. Method validation and control strategy is put in place. Design space for the development of a product is required according to ICH Q8 guideline i.e. method operational design region. Analytical techniques are streamlined pathways for new drug development. Gives a new effective and unique approach.

KEYWORDS: Quality, Analytical QBD, CQA, MODR.

INTRODUCTION

ICH Q8 guidelines define QBD as, "A systematic approach to development that begins with predefined objectives and emphasizes product and process understanding and process control, based on sound science and quality risk management." QBD is nothing but the relation between predefined product specifications in order by planning, developing formulations,

manufacturing procedures. It mentions an integrated approach towards drug development. For the best quality of the drug, the importance of QBD is increased in search of new drug development in the pharmaceutical industry. FDA or more and regulatory agencies take the follow up of drug development data, to prove them or to answer them we need to go towards a risk-based scientific and integrated, proactive approach. At the level of industrial concepts the understanding of product, manufacturing process, development as to build quality in drug. As quality by testing is competed by designing. Newly the concepts of QBD are extended up to analytical techniques. Principles of QBD are applied to the analytical development method and termed Analytical QBD (AQBD).

HISTORY OF QBD

The operation window was introduced in 1950. The term quality by design was given by Joseph M Juran in 1970. After that in 1990 QBD term was popularized. Then it was firstly introduced in 2004 into the chemistry, manufacturing, controls review process by USFDA in Cgmp.

BUILDING BLOCKS OF QUALITY BY DESIGN

➢ Regulatory Flexibility, Design space ➢ Specifications ➢ Controls ➢ Lifecycle management ➢ Support a. DOE b. QRM c. PAT ➢ Knowledge a. Process options b. Process parameter c. Material attributes

TRADITIONAL APPROACH QBD

It is based on the principle of the empirical approach. End product testing assures the quality of a product. Specifically, data for submission are included in a traditional approach. Considers batch history mandatory for specification. It is a limited and simple process, identified the frozen process. Mainly focusing on less variation or ignoring variation and reproducibility.

ANALYTICAL APPROACH QBD

It is based on the principle of the systemic approach. It mainly focuses on robust and cost-effective methods. The method development stage built the robustness and reproducibility method. Analytical profile assures the quality of product, the end product is submission is with knowledge of quality. Which is based on the method of performance of ATP criteria.

ADVANTAGES OF AQBD

1. Product design and process development.
2. Factual understanding of pharmaceutical methods and processes.
3. Scientifically based probability assessment.
4. Carries robust method.
5. Quality of the end is analyzed.
6. Gives required space for development.
7. A Control strategy is maintained by analysis.
8. Minimizes costly investigations and deviations.
9. Technical staff empowerment.
10. Regulatory compliance problems are avoided.
11. Fewer chances of batch failure.
12. A Flexible process allows continuous improvement.

CRITICAL QUALITY ATTRIBUTES (CQA)

CQA for analytical methods consists of method attributes and method parameters. Every analytical technique has a different CQA.

Analytical Technique	CQA
HPLC	▪ Mobile phase ▪ Buffer ▪ PH ▪ Diluent ▪ Column selection ▪ Organic modifier
GC	▪ Gas flow ▪ Oven temperature and program ▪ Injection temperature ▪ Sample diluent ▪ Concentration
HPTLC	▪ TLC plate ▪ Mobile phase ▪ Injection concentration and volume ▪ Plate development time ▪ Colour development method

METHOD OPERATIONAL DESIGN REGION (MODR)

According to ICH Q8 guidelines requirement of design space in product development, method operable design region can be established in the phase of method development.

MODR helps to carry out routine operations. This MODR is a source of robust and cost-Effective methods. The Establishment of the desired operating conditions is based on the understanding of the method of performance region. It serves as operating range same for critical method input variables and CQA, giving results similar to the standards in the ATP. Different input method parameters are allowed to be used in expected method performance criteria and method response which may be without resubmission to FDA by MODR.

PROCESS AND ANALYTICAL TECHNOLOGY

For the effective implementation of method analytical technology (PAT) system, parallel development of analytical QBD is extremely counseled. PAT relies on two major components: (a) Understanding of the scientific and engineering principles concerned manufacturing process; (b) Identification of the variables which affect product quality. In step with the bureau draft guidance, "the desired state of pharmaceutical manufacturing is that product quality and performance are ensured through the planning of effective and economical manufacturing processes" during which continuous and real-time quality assurance was counseled. Once the properties of the drug product elements area unit are understood, the process variables that management the relevant properties should be known. Identification of these variables essentially needs a variable approach. Now, pharmaceutical industries area unit ongoing of establishing specific method understanding and style process analytical management ways to create PAT approach simpler tool.

RISK ASSESSMENT

Risk assessment strategy as laid out in the ICHQ9 guideline: "it is a systematic method for the assessment, control, communication and review of risks to the standard across the merchandise lifecycle". This step is important to succeed at a confidence level that the strategy is reliable. Once the technique is known, AQbD emphasizes detailed risk assessment of the factors that will cause potential variability within the technique, like analyst strategies, instrument configuration, measure and technique parameters, sample characteristics, sample preparation, and environmental conditions. Traditional technique development relied on testing the strategy when transfer whereas Analytical QbD demands the chance assessment step before technique transfer and throughout the merchandise life cycle. According to ICH Q9, risk assessment is disbursed in 3 steps viz., risk identification, risk analysis. One of the common ways that to perform risk assessment is to use a Fishbone Diagram, conjointly called Ishikawa consequently the chance factors square measure classified into the subsequent

categories: a) High-Risk Factors: e.g. Sample preparation methodology. This square measure is to be mounted throughout the strategy Development method. b) Noise Factors: This square measure was subjected to an associate degree MSA study. It can be done through staggered cross nested study style and variability plots, ANOVA, etc. These factors square measure subjected to robustness testing. c) Experimental Factors: e.g. Instrumentation and operation methods. Subjected to strength testing and acceptable vary is known. The third step is a Risk analysis that is finished through Failure mode and effects analysis (FMEA) and also the Matrix styles. Upon identification of the technique, AQBD focuses on detailed risk assessment of the factors of potential variability within the technique, like analyst ways, instrument configuration, mensuration and technique parameters, sample characteristics, sample preparation, and environmental conditions. Ancient technique development was supported testing the tactic when transfer whereas Analytical QBD necessitates the chance assessment step before technique transfer and throughout the product life cycle. Risk assessment strategy as laid out in the ICHQ9 guideline: "it is a systematic method for the assessment, control, communication and review of risks to the standard across the merchandise lifecycle. This step is imperative to succeed at a confidence level that the tactic is reliable. The first step that's Risk Identification is extraordinarily important to spot and rank potential risks. These risks may well be the methodology of operation of the instrument, characteristics of chemical agent, cycle time, etc. it's typically advisable to see a contingent methodology shut in the primary methodology fails. Flow charts and checklists square measure utilized to spot risk factors. The next step within the method is Risk Analysis. Tools that square measure used during this step include the Ishikawa os Diagram and therefore the CNX approach. The Cause and impact diagram or the Ishikawa Fishbone diagram compartmentalizes the risks into different classes looking at their supply. The other tool is that the CNX approach wherever C indicates the high-risk factors, N represents the potential noise factors and X is the factors that square measure to be experimented upon. According to this approach the chance factors square measure classified into the subsequent categories: I. High- Risk Factors e.g. Sample preparation methodology. This square measure is to be fastened throughout the Method Development method. II. Noise Factors: This square measure is subject to AN MSA study. Done through staggered cross-nested study style and variability plots. These factors are subjected to lustiness testing. III. Experimental Factors: e.g. Instrumentation and operation strategies. Subjected to strength testing and acceptable vary is known. The third step is a risk analysis that is finished through Failure mode and effects analysis (FMEA) and therefore the Matrix styles.

Control Strategy

A planned set of control(s) for all potential variation(s) assures that adenosine triphosphate demand would be met throughout analytical methodology transfer in addition to routine use. This can be earned with continuous watching of CMAs or system quality parameters. Management strategy isn't always a one-time exercise that's performed solely throughout method development however it will get modified with different stages of methodology lifecycle. Establishing a bearing strategy is of utmost importance whereas making certain that the strategy is playing as meant on a routine basis as goals represented in ATP, essentially it is a planned set of controls geared toward minimizing the variability within the method. The strategy is knowledge-dependent. Knowledge generated throughout technique development and technique verification forms the idea of the management strategy. An element known to own risk has got to be controlled. Additional attention is given to the high-risk factors. If the danger area unit is low and manageable then the strategy management strategy is outlined, which typically consists of applicable system suitableness check and verified time to time by having management over it so that technique delivers the fascinating technique attributes. Curiously, the management strategy of AQBD isn't completely different from the standard management strategy.

Life Cycle Management

Even when rummaging all the weather of QBD for a particular analytical technique, technique validation, verification, transfer area unit the key exercises that guarantee the fitness of the strategy for its supposed use. Combining together this can be termed as 'lifecycle management of analytical procedure', which starts with the institution of ATP and continues until the strategy is in use. The resultant confirmation with relevancy nucleotide is that the main focus for performance qualification, e.g., exactness study on the site of routine use. Continual verification involves activities, which offer the peace of mind that the strategy is under control throughout its lifecycle. Going through all the elements of AQBD for a particular analytical method the key steps that ensure fitness of the method for its intended use includes the method validation, verification, transfer. Combining all together is termed as 'lifecycle management of analytical procedure', which commence with the establishment of ATP and continues till the methods are in use. The resultant confirmation for ATP is the main focus of performance qualification e.g., precision study at the site of routine use. Continual verification involves activities, which assure that the method is under control throughout its lifecycle. Application to Analytical QBD ▪ Applied for development of the robust method. ▪

Applied to reduce and control sources of variability. ▪ Applied for the life cycle of the method. Application to industry ▪ Applied to reduce problems in manufacturing. ▪ Applied for better product design. ▪ Allow reduction in costs of manufacturing. ▪ Improve interaction with FDA ▪ Applied to reduce the number of manufacturing supplements for post-market changes. ▪ Ensure some problems during the review, reduce deficiencies. Conclusion QBD shows its importance in the pharmaceutical industry in the area of pharmaceutical processes like drug development, manufacturing, biopharmaceuticals, and analytical method. QBD is the main requirement of the ICH Q8. Development AQBD with MODR, Control strategy, Risk assessment, CQA shows the quality product designing. Commercial production is increased due to the various approaches of Analytical quality by design.

CONCLUSION

Different tools are used for the method development of analytical quality by design method like, ATP, CQA, MODR, Control strategy, Risk Assessment, Method validation. The non-variability and reliability in pharmaceutical industry are ensured by AQBD. The various approaches identifies a critical analytical factors. Aqbd contents provides better understanding of method improvement throughout the life cycle.

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