International Journal of Trend in Scientific Research and Development (IJTSRD)
Volume 7 Issue 1, January-February 2023 Available Online: www.ijtsrd.com e-ISSN: 2456 – 6470

"Current Approach of Quality by Design" An Overview

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ABSTRACT

In this Analysis, we'll look at how QbD is being practised right now. QbD represents a cutting-edge methodology for enhancing the safety and efficacy of pharmaceuticals. Quality by Design (QbD) is a relatively new idea in the pharmaceutical industry, but it has quickly become an integral aspect of the current approach to quality. Quality by Design relies on the ICH Guidelines as its basis. Guidelines Q8 for Pharmaceutical Development, Q9 for Quality Risk Management, and Q10 for Pharmaceutical Quality Systems from the International Council for Harmonization (ICH) served as inspiration for this document. QbD is the most effective method now available for improving the quality of all pharmaceutical goods, but it poses a significant problem for the pharmaceutical business, whose procedures are traditionally static. Eventually, despite inevitable process and material variation, It is crucial to establish the desired product performance profile [Target product Profile (TPP), Target Product Quality Profile (TPQP)] and to pinpoint the attributes of quality that are most important to the product's success throughout the QbD process (CQA). We may then use this information to tailor the product's composition and production method to those characteristics. This results in the identification and management of sources of variability and an understanding of the effect of raw materials [critical material attributes (CMA)] and critical process parameters (CPP) on critical quality attributes (CQAs). To which the process and technique of development must have access. Quality-by-Design (QbD) encompasses the processes of drug development and manufacturing. that guarantees the product meets the standards set out in advance.

How to cite this paper: R. Kavi Bharathi | R. Sanil Kumar | Shantaram Nangude ""Current Approach of Quality by Design" An Overview" Published in International Journal of Trend in Scientific Research and Development (ijtsrd), ISSN: 2456-6470, Volume-7 | Issue-1, February 2023, pp.1374-1384, URL: www.ijtsrd.com/papers/ijtsrd53873.pdf

IJTSRD53873

KEYWORDS: *Quality By Design, Pharmaceutical Quality, ICH Guidelines, Quality Target Product Profile, Critical Quality Attributes, Critical Material Attributes, Critical Process Parameter, Process development, Product Specification*

1. INTRODUCTION

QbD encompasses the entire process of creating a product, from the first idea to the final packaging. The FDA administration announced a new effort in 2002. (cGMP for the Twenty First Century: A Risk based Approach).The Food and Drug Administration (FDA) launched this project to showcase a new regulatory framework centered on quality by design (QbD) risk management and quality system.

The primary goal of pharmaceutical research and development is to create a high-quality drug and a development process that consistently produces the desired results.

In today's pharmaceutical industry, Quality by Design (QbD) is an emerging idea for the creation of high-quality goods. The Quality-by-Design (QbD) method is used in the pharmaceutical industry to achieve the desired results in both product design and production. The design adheres to the ICH requirements (Q8, Q9, and Q10) that are necessary to carry out a pharmacological procedure.

Monitoring and optimising process and formulation parameters live throughout production is a crucial aspect of quality by design (QbD). QbD requires a thorough understanding of how these factors impact product qualities. Possible gains in productivity, regulatory relief, and flexibility, as well as long-term economic benefits for the company, might result from switching to a new method of drug development.

Pharmaceutical Quality by Testing: Raw material testing, drug substance production, a consistent drug product production procedure, in-process laboratory testing, and final product testing all play a role in this system's commitment to high quality products

Pharmaceutical Quality by Design: ICH Q8 outlines An objective-driven technique of development that uses scientific rigour and quality risk management to place a premium on knowing one's stuff and keeping one's methods tightly under wraps.

What Is QUALITY?

The fitness of a drug substance or drug product for its intended purpose. Identity, power, and pristineness are all hallmarks of this incumbent (ICH Q6A).Product or service qualities and attributes that contribute to meeting the customer's expressed or implicit demands (ISO).

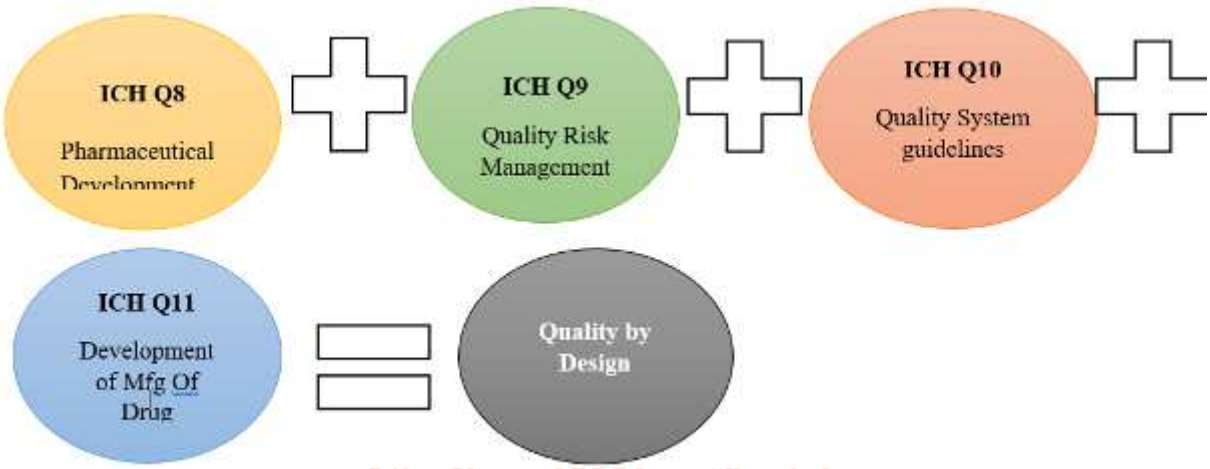
What Is QUALITY by DESIGN?

Management of Quality Risk as a Tool for Securing Procedures (ICH Q9).

Life Cycle Management (LCM) benefits from having a stronger understanding of both the technique and the product since it allows for more control over the variables. QbD's creator, Dr. Joseph M. Juran, says, "Quality cannot be tested into things; it is to be included by design. “One approach is to design a control plan that is based on an in-depth knowledge of each product and method.

Quality-by-Design (QbD) is a technique to regulatory control that has been incorporated into the quality guidelines of the International Conference on Harmonization (ICH) since 2005. This approach includes,

Q8: Pharmaceutical Development
Q9: Quality Risk Management
Q10: Pharmaceutical Quality System guidelines



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Quality by Design means -designing and developing formulations and manufacturing processes to ensure a predefined quality.

Quality by Design needs– understanding however formulation and producing method variables influence product.

Quality by Design ensures – Product quality with effective management strategy.

Quality-by-Design implementation is facilitated in **Stage 1 (Process Design)** of the **Process**

Validation Lifecycle

2. COMPONENTS OF QbD:

QbD has four key components

Defining the Product Design Goal

In this section, you will specify the Quality Target Product Profile (QTPP) and construct a comprehensive list of Critical Quality Attributes (CQAs).The CQAs are a reflection of the aspects of the QTPP that have the greatest impact on the quality of the product. They lay the groundwork for the product's development and comprehension.

We define the components and evaluate their compatibility with one another.

Discovering the Process Design Space

The key to establishing the design space is an understanding of your processes.

By "proven multidimensional combination and interaction of material characteristics and/or technique parameters incontestable to create assurance of quality," ICH Q8 describes what constitutes a design space.Using essential process parameters, one may estimate how much a method modification might effect a specification (CPPs). Mapping your operational area considerably improves your capacity to anticipate problems and set up methods for keeping control. Real-world experimental data, product-use history, or published works can all serve as guides for determining the range of available parameters.

Understanding the Control Space:

An effective control space is often mapped out in accordance with the method design space.

Because of this, you may learn your processes in great detail, which reduces the impact of the manufacturing process's inherent unpredictability on product quality.

You may maintain complete command over your state-of-the-art production method by always following these prescribed processes. To visualise the concept of a control space study, imagine the end result of a tightly regulated process as a reference product data set consisting of closely packed information points.

To determine if your method is state-of-the-art, you can plot your findings and compare them to those of a recognised industry leader. Doing a Design of Experiments (DOE) study on your product while it's still in development is one technique to help prevent this discrepancy.

This strategy has the potential to eliminate the hassle and extra effort caused by a lack of understanding of the control space.

Targeting the Operating Space

The operational area is the range of values within which the CPP and CQA can vary naturally, as established by scientific analysis.

It is important for a generic product's operating environment to be inside the control space so that a reference product may be evaluated using the same conditions.

The new product's operating space should be included in the design space and conform to applicable regulations. Advantages may be gained by innovators who thoroughly try out several iterations of their designs and compositions.

3. ELEMENTS OF QbD:

The section that follows elaborates on potential approaches to gaining a lot of systematic, increased the understanding of the product and method under development.

ICH Q8: Pharmaceutical development Should include,

1. Quality Target Product Profile (QTPP's)
2. Critical Quality Attributes (CQA's)
3. Risk Assessment
4. Design Space
5. Control Strategy
6. Product Lifecycle Management and Continual Improvement

QUALITY TARGET PRODUCT PROFILE (QTPP'S):

When combined with other elements of the QbD methodology, the QTPP provides the basis for the product's conceptual design. The focus is mostly on security and efficiency.

An expected profile of a drug's quality features that must be met to guarantee the desired level of quality, with attention given to the drug's safety and effectiveness: ICH Q8 (R2) (R2) Considerations for the QTPP's might embrace

- Intended clinical use, including administration route, dosage type, and delivery methods.
- Dosage strengths • Container closure system
- Aspects of pharmacokinetics that are affected by the release or distribution of therapeutic moieties (e.g., dissolution, aerodynamic performance)
- Quality standards for the drug product (including sterility, purity, stability, and drug release) that meet regulatory requirements and are suitable for the product's intended market.

BENEFITS OF QUALITY TARGET PRODUCT PROFILE:

1. Identifies risks and sophisticated methods to optimally control Tools/enablers (Similar as integration of QbD and biopharmaceutics).
2. Generates and enables know biopharmaceutical.
3. A recursive, literacy-based life-cycle method for better patient outcomes through informed decision making and treatment planning.
4. To create, test, and produce a pharmaceutical product in accordance with QTPP's with specifications (similar to dissolution/release acceptance criteria) that are in line with the product's desired in vivo performance.

CRITICAL QUALITY ATTRIBUTES (CQA's):

To ensure that a product meets its quality requirements, it must have particular values for what are called Critical Quality Attributes (CQAs). ICH Q8 (R2) (R2).

In the pharmaceutical industry, CQAs are often associated with the following: active pharmaceutical ingredient (API), inactive pharmaceutical ingredient (IPA), intermediate (in-process component), and drug product.

Common critical quality attributes (CQAs) of "Solid oral medicinal forms." include product purity, strength, drug release, and stability.

Furthermore, CQAs for "Other delivery techniques," such as aerodynamic properties for inhaled products, might incorporate product-specific requirements.

Sterility and adherence of transdermal patches for intravenous administration.

The HPTLC procedure's most crucial quality assurance elements are the TLC plate, mobile phase, and injection concentration.

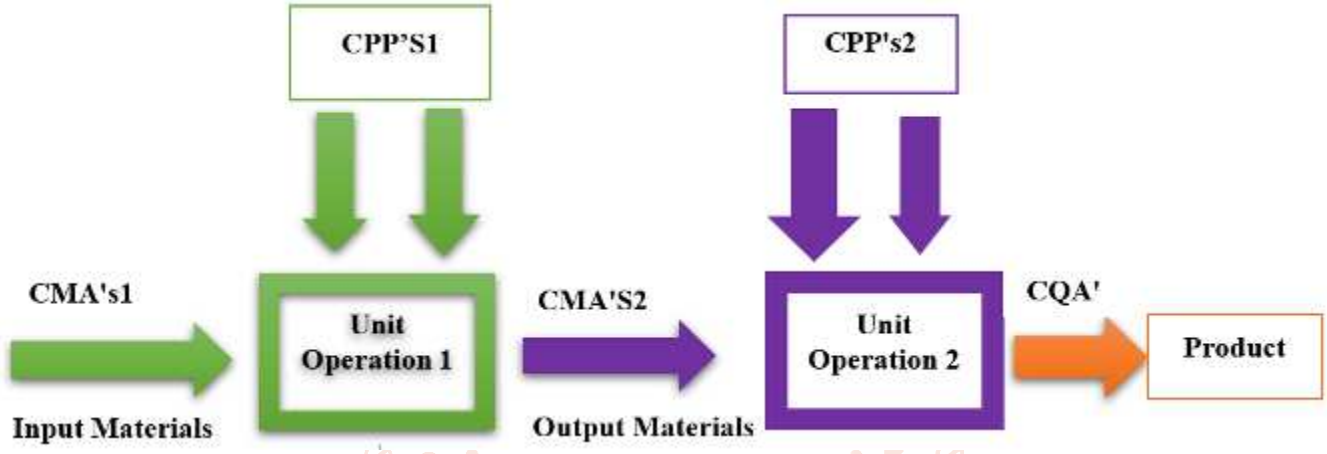
Amount, time, and reagent for developing and detecting colour on plates.

Clinical relevance includes both risk-free use and high product performance. Hence, it's crucial to think about factors that might stand in as surrogates for performance while developing an oral CR medication. This can be anything from the rate of drug release to the potency of the medication to the concentration of the polymer to the viscosity of the polymer to the glass transition temperature (Tg) of the composite or any combination of these and other characteristics.

Table 2.1: QTPP Component and CQA'S Components

QTPP Component	CQA's
Dosage Form & Strength	Assay (Efficacy)
Appearance & Identity	Impurities (Safety)
Pharmacokinetics	Content uniformity (Efficacy)
Dissolution, Content Uniformity	
Impurities & Residual Solvents	

CTORS AFFECT DRUG PRODUCT CQA's:



CRITICAL MATERIAL ATRIBUTES (CMA's):

A Crucial Manufacturing Attribute (CMA) is a property of an input material (drug ingredient, excipient, or in-process material) that must be maintained at a consistent value to ensure product quality.

The CMA, and by extension the CQA of the drug product, may have an impact on the material properties of the drug product, including excipients, drug components, reagents, solvents, packaging, and labelling.

CRITICAL PROCESS PARAMETERS (CPP's):

A critical process parameter is defined by ICH Q8 as "a process parameter whose variability impacts a critical quality feature and, hence, must be monitored or managed to assure that the process produces the required quality" (R2). direct impact on the CQA ratings. What's more, you can keep an eye on and tweak something called a Process parameter (PP) (adjusted).

When a process parameter has a great deal of influence over a critical quality attribute, we call it a critical process parameter. By risk assessment and experimental efforts, CPPs make sure the best CQA and CPPs are selected from a pool of possible PPs.

RISK ASSESSMENTS:

The method of risk assessment is an important scientific tool in the field of Quality risk management (QRM).

Understanding and anticipating sources of variability in the manufacturing process is a primary goal of risk assessment in pharmaceutical development, with the end goal being the implementation of an appropriate control strategy to ensure that the drug product's CQAs are within the desired requirements.

Input-process-output diagrams, Ishikawa diagrams, risk rating and filtering, and so on are common examples of such tools.

A method for evaluating and rating potential dangers is known as "risk filtering and ranking."

Ranking the risks associated with complex systems usually necessitates the consideration of a wide variety of quantitative and qualitative criteria associated with each risk. The risk assessment can be determined by various methods which are as follows:

1. Failure Mode Effect Analysis (FMEA)
2. Failure Mode Effect And Criticality Analysis (FMECA)
3. Fault tree Analysis (FTA)
4. Hazards Analysis and Critical Control Point (HACCP)
5. Hazards Operability Analysis (HOA)
6. Preliminary Hazard Analysis (PHA)

COMPONENTS OF RISK ASSESSMENT:

There are three components of risk assessment, that is, Risk identification, Risk analysis and Risk evaluation

Risk Identification: The risk assessment team assigned to this initiative first prepared a list of all operations and associated supporting systems that had potential impact on product quality.

Risk Analysis: The Risk Analysis stage of the QRM process estimates the potential harm(s) associated with each potential risk.

Risk Evaluation: The analysis may be qualitative or quantitative in nature, or a combination of the two to determine the significance of the risk.

DESIGN SPACE:

Many input elements (including material characteristics) and process parameters have been proven to interact in order to achieve quality assurance. If you keep inside the constraints of the design, no one will notice that you changed anything. If you make a change that takes you outside of the approved design space, you will need to go through the post-approval change process. After an application is submitted to regulators, the proposed design space is examined and authorised [ICH Q8(R2)].A design space may be built for a single unit operation or for the ensure process.

TOOLS APPLIED IN QbD APPROACH:

DESIGN OF EXPERIMENT (DoE)

Methodical experimentation is used to maximize results. We are well-versed in using Minitab and Statistica for DoE in product development, and we have the necessary resources to do so.

Design of experiments done by **2 methods**

Screening: Methods used to uncover crucial elements by a comprehensive screening of a big pool of candidates with a minimum of experimentation. The primary goal of these designs is to isolate single-effect variables, rather than examining their interplay.

Placket-Burman and fractional factorial designs are frequently employed for such research Optimization: The most popular types of experiments studied for optimization include full factorial designs, surface response approaches (such Central composite and Box-Behnken), and mixed designs. It is probable that substantial effects and interactions, as well as quadratic and cubic factors, are required to generate curvature in these designs. Such configurations are employed only when a select number of constituents that seem to contribute to the process or formulation have been discovered.

CONTOL STRATEGY:

Controls designed to guarantee the effectiveness of the procedure and the quality of the end product in accordance with ICH Q8 (R2) and Q10.The ability to evaluate and guarantee product quality based on process data, which typically includes a suitable blend of quantifiable material attributes and process controls. This skill can be put to use before, during, or after the manufacturing process.

Under the framework of the QbD paradigm, the control strategy is determined by conducting a risk assessment that takes into consideration both the criticality of the CQA and the competence of the process. The control approach may have the following components at your discretion: (but not limited to)

1. Procedural Control
2. In-process Control
3. Batch release testing
4. Compatibility testing
5. Process Monitoring It is worth noting that the use of risk assessment in creating the control strategy is unique to the QbD approach.

LIFECYCLE MANAGEMENT AND CONTINUES IMPROVEMENT:

Differentiating itself from the traditional approach, which necessitates a halt in the process at some point, the QbD strategy enables continuous improvement over the whole product life cycle. By keeping tabs on how things are going, quality may be kept at a constant level. Based on regular commercial production experience, including risk assessment and communication between the plant, quality assurance, quality control, R&D, and Applied R&D.

4. CURRENT APPROACH OF QbD IN PHARMACEUTICAL DEVELOPMENT:

The Current Approach Quality by Design (QbD) From Development to Manufacturing

Quality by Design takes into account all of the most important parts of the pharmaceutical manufacturing process. In the process of developing new drugs, a methodical and multivariate approach is utilised to build an efficient process design. This design is founded on an analysis of the risks that are connected with the various stages of the process.

Table 4: Current Approach vs QbD Approach

CURRENT APPROACH	QbD APPROACH
Quality assured by Testing & Inspection	Quality built into Product & Process by design based on Scientific understanding
Data intensive Submission-Disjointed information without "Big picture"	Knowledge rich Submission-showing product knowledge & process understanding
Specifications based on Batch history	Specifications based on Product performance Requirements
Quality built into Product & Process by design based on Scientific understanding	Flexible process within design space, allowing continuous improvement
Focus on Reproducibility-often avoiding or ignoring variation	Quality built into Product & Process by design based on Scientific understanding
Use of statistical process control unit method is limited	Use of statistical process control unit method is predominant
Empirical Development	Systematic development
Product specification are primary means of control	Product specification are of the overall quality summary
Validation of manufacturing process is primarily based on initial full-scale batches	Life cycle approach to validation of manufacturing process and continuous verification

5. BENEFITS of QbD:

1. Do away with all of the batch failures
2. Reduce the number of inconsistencies and enquiries that are expensive.
3. Prevent regulatory compliance difficulties
4. The emancipation of technical personnel 5. The improvement of production efficiency, the reduction of costs and the elimination of project rejections and waste
5. Increased awareness and comprehension of the procedure
6. Constant improvement
7. Provide a better design for the product, which will result in fewer problems throughout production
8. Makes it possible to make ongoing improvements to both the goods and the manufacturing process
9. Decreases the total quantity of supplements used in production
10. Needed for post market adjustments; reliance must be placed on processes as well as a knowledge of risks and measures to mitigate them.
11. Enables the application of innovative industrial technologies without attracting the attention of regulatory authorities
12. Provides for the possibility of a reduction in total production costs due to less waste
13. Reduces the amount of bother experienced throughout the review process, resulting in fewer defects and faster approvals.
14. Enhances interactions with the FDA by dealing with matters of a scientific nature rather than those of a procedural nature

6. APPLICATIONS OF QbD:

➢ Drug substance and excipient development

Use of high-quality raw materials, including the active pharmaceutical component and excipients, is crucial to the manufacture of superior finished products. Improve the quality of the raw materials supplied to the pharmaceutical industry by improving supplier adherence to QbD standards. Because of the wide range of quality in the finished goods that may be made from these basic materials.

The primary CMAs of a drug material are the particle size, physical shape, polymorphism, moisture content, and flow properties, all of which have an effect on the drug's disintegration, dissolution, compaction, and compression characteristics. CMAs of excipients, such as particle size, shape, viscosity grade, moisture content, flow ability, etc., also have a substantial impact on these CQAs. Also, the ICH Q11 advice states standards that are pertinent to the QbD requirements for the development of drug substances, including crucial measures on chemistry, manufacturing, and control methods.

➢ Analytical method development

Using a trustworthy analytical strategy is crucial for easing quality control monitoring and accelerating the product development cycle. Using QbD principles in this setting allows for the development of very robust analytical procedures predicated on either established goals or a quality target method profile.

Important analytical features may be identified, which in turn leads to the identification of vital method variables (CMVs), which can be used to enhance method performance for continual improvement within the design space.

In a nutshell, "quality by design," abbreviated as "QbD," is a "framework" that assists in locating the source of variability and working to reduce that source's impact on the process of establishing analytical procedures.

This goes beyond the typical validation technique that is advised by the International Conference on Harmonization (ICH).The federal authorities are pushing the pharmaceutical business to embrace the adoption of systematic QbD paradigms for the purpose of increasing analytical knowledge. While analytical QbD is not required, and there are currently no regulatory rules in place.

➢ Dissolution testing

Testing for dissolution, which is considered to be a quality control method, is helpful in monitoring the drug release profile of various dosage forms. This makes it easier for the manufacturer to make judgements on the qualification of the batches based on the criteria for release.

An effective, reliable, and predictable dissolving method is urgently needed in this setting. By minimising the influence of variables including medium type, composition, volume, apparatus choice, and operating circumstances on drug release performance, a QbD approach allows for more wiggle room in the course of dissolving process development.

Establishing a predictable in vitro/in vivo correlation is essential to achieving bio waiver status, which is a requirement of today's regulatory agencies for very robust medicinal products with an in vitro dissolution performance comparable to that of the reference listed product.

➢ Bioequivalence testing

The final evaluation of the product's performance in vivo is done with the use of bioequivalence testing, which also evaluates the plausibility of a match being made between the generic product and the reference product. In order to establish bioequivalence, crucial pharmacokinetic measures like the Cmax and AUC ratio between the test product and the reference product need to fall within the regulatory acceptability limit of 80%-125%.

In this context, quality-by-design (QbD) provides formulation development by establishing a relationship between the input product and the process parameters in order to maximize the in-vivo performance.

Due to a lack of practical knowledge in developing a direct link between the in vitro and in vivo product performance criteria, the notion only has a limited regulatory value. This is because of the lack of practical understanding.

➢ Stability testing

The application of the QbD principles in stability testing contributes to the establishment of specifications (temperature and humidity conditions, packaging materials, and so on) for the stability testing of the products as well as monitoring controls for determining the product shelf-life, levels of impurities, degradation products, and so on. The number of regulatory advantages that will accrue over the long run will increase as the notion becomes increasingly significant in product development.

- **Clinical trials**

One of the topics that has received the greatest attention in recent years is clinical trials. The design and goals of a clinical trial protocol are investigated using this method. This is done by determining the aspects that are "essential to quality" and controlling the influence that risk has on the trial's quality.

As a result of the high costs associated with clinical trials, federal agencies have been putting an emphasis on the current opportunities provided by risk-based QbD monitoring of clinical studies. This is done in an effort to contribute to the achievement of the most favourable scientific outcomes possible in terms of product safety and efficacy.

7. FUTURE PERSPECTIVE OF QbD:

In the near future, the QbD will be used in a much more broad manner. It will also be implemented at the manufacturing facility at the same time. This is because event-based techniques are most commonly employed in the development sector, where it is now seeing widespread adoption. It will also be used at the actual manufacturing facility at the same time.

Everything will work out OK if we can keep up the current rate of production while staying within the capabilities of the current set of instruments. Nevertheless, as we reach the more advanced and impactful phase of the normal deliberate methods to PAT employing controlled protocols, this is often where we tend to be confronted with quite strong pushback.

A small but dedicated group of regulatory agencies, led by the European Medicines Agency, is starting to put the QbD idea into practise (EMA).

The European Union has "Real-Time Released" a document at the same time it was written. Submissions that aim to show their high quality to the European Medicines Agency (EMA) are always welcome.

Applications whose primary purpose is to promote the concept of quality have attracted the attention of the European Medicines Agency (EMA) (QbD).

A quality-intentional approach is an abstract methodology with the goal of guaranteeing the quality of medicines by the application of various forms of applied mathematics, analytical, and risk-management methodology in the phases of drug discovery, development, and manufacturing. The goal of developing this technology was to guarantee the efficacy of pharmaceuticals. Intentional quality is equivalent with quality on purpose.

The ICH guidelines Q8, Q9, Q10, Q11, and Q12 are frequently cited by both the US authorities and the EMA when addressing the implementation of QbD. Currently, "Q13- Continuous Manufacturing" and "Q14-Analytical technique Development" are being worked on by the International Committee for Harmonization (ICH).These new ICH tips square dimensions are expected to become available soon.

SOFTWARE USED FOR QbD:

Software such as Design Expert ®, Unscrambler ®, JMP ®, Statstica ®, and Minitab ®, amongst others, is available for use with quality by design. These and other software packages often give an interface guide at each stage of the product development cycle.

Software offers assistance for chemometric analysis by means of multivariate techniques such as MNLRA, PCA, and PLS, amongst others.

Software's of QbD

8. CONCLUSION

The current approach to pharmaceutical quality must always include "quality by design" as a vital component. This debate sheds light on the use of QbD, including but not limited to: There will be an emphasis placed on the significance of the Target Product Quality Profile in the process of formulating a quantitative performance objective for QbD, A mechanistic relationship between the product quality and the manufacturing process may be established through the identification of important material properties. Confirmation that the critical process parameters are also the same as the operating parameters, and that they should be paired with the critical material characteristics in order to define the link between the nputs and outputs of the unit operation. The operations pertaining to quality must make an effort to identify quality issues at an early enough stage so that corrective measures may be taken without compromising cost, schedule, or quality. Rather than only focusing on the resolution of quality issues, the priority should be placed on prevention. Because of this, the quality needs to be embedded into the product as well as the services through careful planning in order to avoid the impending failure. It is impossible to test quality into items; rather, quality must be built in or designed into products from the beginning. The QbD may be considered as a process that is defined by a series of document requirements; it is a quality management system that builds on previous regulatory standards and establishes expectations for the future. These documents reflect both a comprehension of the process as well as an organisation of that information. The QbD technique is helpful in determining and justifying desired product profiles, as well as gaining a knowledge of products and processes. In order to create new platforms for the production of pharmaceuticals, there is a requirement for active research programmes that get adequate funding. Its purpose is to improve understanding of the process, and it is modelled after already established guidance and reference papers. Within the realm of pharmaceutical processes, such as drug development, formulations, analytical method, and biopharmaceuticals, quality by design (QbD) has become an increasingly important concept. The regulatory requirements and focus on all aspects desired in a quality product are the primary reasons for the adoption of QbD. These include determining the drug product quality profile, prioritising input variables for optimization, modelling and validating the QbD methodology, and, finally, QbD validation, scale up and production, as well as soft-ware used for QbD

9. REFERENCES:

[1] Lan Zhang, Shirui Mao (2016). Application of quality by design in the current drug development: Asian journal of pharmaceutical sciences 12 (2017) 1–8.

[2] Q8 (R1): Pharmaceutical Development, Revision 1. ICH Harmonized Tripartite Guidelines, International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use. 2007

[3] Q9: Quality Risk Management. ICH Harmonized Tripartite Guidelines. International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use. 2006

[4] Q10: Pharmaceutical Quality System. ICH Tripartite Guidelines. International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use. 2007.

[5] Mr. Rajesh Dumpala1, Ms. Jaini Bhavsar, Mr. Chirag Patil Quality by Design: A Present to Future Perspective International Journal of Trend in Scientific Research and Development; August 2020 Volume – 4 | Issue – 5: 878-885

[6] Dey Rumel Quality by Design – A new approach to drug development February 2018 International Journal of Drug Regulatory Affairs 3(2):8-16.

[7] Kiran Tambe, Smita Bonde A review on: Applications of pharmaceutical quality by design in product development World J Pharm Sci 2017; 5(1): 58-70

[8] Amit S. Patil, Anil M. Pethe Quality Design (QbD): A new concept for development of quality pharmaceuticals International Journal of Pharmaceutical Quality Assurance; 4(2); 13-19

[9] Sagar Kishor Savale Quality by Design (QbD) Approach used in Development of Pharmaceutical Formulations Asian Journal of Biomaterial Research 2017; 3(6):11-24

[10] Manohar D. Kengar*, Jameer A. Tamboli, Chandrakant S. Magdum Quality by Design- A Review June 2020 Vol 7, Issue 4

[11] Gandhi A, Roy C; Quality by Design (QbD) in Pharmaceutical Industry: Tools, Perspectives and Challenges; Pharma Tutor; 2016; 4(11); 12-20. 4.

[12] D. M. Patwardhan, S. S. Amrutkar, T. S. Kotwal and M. P. Wagh, Applications of Quality by Design to different aspects of pharmaceutical technologies: IJPSR, 2017; Vol. 8(9): 3649-3662.

[13] Aksu B, Yegen G. Global regulatory perspectives on quality by design in pharma manufacturing. Pharm Qual Des 2019;2019: 19-41

[14] Kadam VR, Patil MP, Pawar VV, Kshirsagar S. A review on: Quality by design (QbD). Asian J Res Pharm Sci 2017; 7:197-204.41.

[15] Hardik Patel, Shraddha Parmer, Bhavna Patel A comprehensive review on quality by design (QbD) in pharmaceutical July 2013 International Journal of Pharmaceutical Sciences Review and Research 21(1):223-236

[16] K Ramya sri, K Bhavani et.al An Outline of Quality by Design in Pharmaceutical Development April 2021Journal of Pharmaceutical Sciences and Research 13(4):200-205

[17] Helena B G., Claudia S., Sergio Paulo S. and Marcoreis S. Quality by Design in Pharmaceutical Manufacturing a systematic review of current status, challenges and future perspectives. European journal of pharmaceutics and Biopharmaceutics. 2020, 147, 19-37

[18] Patwardhan D M., Amrutkar S S., Kotwal T S. and Wagh M. Application of quality by design to different aspects of pharmaceutical technologies. International Journal of Pharmaceutical sciences and journal. 2017, 3649-3662

[19] Aayushi Rajora, Gurmeet Chhabra Quality by Design Approach: Regulatory need, Current and future perspective Asian J Pharm Clin Res, Vol 14, Issue 6, 2021, 29-35

[20] Gawade, A. Chemate, S. Kuchekar, A. Pharmaceutical Quality by Design: A New Approach in Product Development. Res Rev: J Pharm. Pharm Sci vol 2: 5-12 (2013)