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Review Paper

A Comprehensive Overview on Quality by Design in Pharmaceutical Industries

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ABSTRACT

Pharmaceutical has vast areas of formulation and development which design different formulations for different disease conditions and their treatment. Each product developed in the pharmaceutical has to pass the standard prescribed in the monographs. QbD plays an important role in drug product development that is very important because it ensures the stability, safety, and quality of the product. The product quality should be best so that it has per patient compliance. QbD ensures all the safety procedures in the industries that make the stable and good quality and validate the procedure. It also helps in the design of the product and its procedures. It controls all the manufacturing processes and understanding that develops the best quality product. Its modern approach in the pharmaceuticals which aims to develop and design a quality product using its manufacturing process that is intended to deliver constantly and shows good performance. Quality by Design (QbD) is a methodical approach to drug development that emphasizes comprehending and managing the production process to guarantee constant product quality. Critical Quality Attributes (CQAs), Critical Material Attributes (CMAs), and Critical Process Parameters (CPPs) are all identified in this examination, which offers a thorough summary of QbD concepts. It talks about how to optimize pharmaceutical formulations and manufacturing processes by using risk assessment tools, Design of Experiments (DoE), and multivariate analysis. It is emphasized how important regulatory guidelines—like those provided by the International Council for Harmonization (ICH) Q8–Q11—are to maintaining compliance and improving product lifecycle management. Additionally, the study examines how QbD might enhance product effectiveness, lower variability, and speed up regulatory approvals. The difficulties in putting QbD into practice, such as the lack of resources and the complexity of data processing, are also discussed. Insights into the strategic application of QbD to improve pharmaceutical product development and production are the goal of this research.

INTRODUCTION

Quality by Design plays a vital role in the holistic approach to the development of different dosage forms that ensure the quality of the pharmaceuticals. This approach helps to increase the efficiencies, and flexibility and provide regulatory relief to the drug development that offers the business benefits to the product throughout the life cycle. This concept should be embraced by the pharmaceutical industries because of improves the robustness of the manufacturing process and facilities that help in the continuous improvement of the shape and size of the product that enhances the quality and productivity. Before

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the introduction of this concept, it is mediatory to accept that the quality of the product should be designed and built during the manufacturing process (Woodcock, 2004). QbD fundamentally meant building a quality product not testing it. This is a good business & science project because of complete product and process understanding. The comparison before without the processes approach, QbD possesses greater opportunities for developing and designing an efficient and flexible system that increases the efficiency of the product, reduces the cost, minimum chances of project rejections, and less waste product will produce. This approach solves all the problems that were related to the quality of the pharmaceutical product as poor design, safety, efficacy, and quality. Thus, due to it, it's clear that by analyzing the product the quality could not be improved. It ensured the consistent incorporated risk management and information (Bruttin & Dean, 1999). "Quality by Design" is a method of conveying a good scientific understanding of the essential process steps (*as shown in fig. 1*) & aspects that aid in product quality, design, and control testing based on scientific limits during the development stage, using knowledge gained from the product's life cycle to work on continuous environmental improvement. QbD is a term used to describe the pharmaceutical development process for the formulation development and manufacturing process to maintain product quality standards.

Continuous Improvement of Hallmark of QbD

The QbD enhances the identifying ability of the root cause that fails the manufacturing process, and manufacturing environment to give the development activities, and efficiency of manufacturing increase (*as shown in fig. 2*), it also has an objective to enhance the root cause, post-approval change management to provide a return of investment by of batches. It increases the development capacity, speed, and design of formulation and transfers the resource to the upstream protective mode from the downstream corrective mode.

Design

The product is designed differently to acquire the patient compliance and requirement performance that consistently meets the quality product attribute, process parameters, and starting raw materials on the quality product is understood; process variability of the critical sources can be identified and controlled (*as shown in table 1*). The process was previously reviewed and adjusted to ensure a constant level of quality throughout time.

According to the FDA PAT Guideline, the system for designing, analyzing, and controlling the manufacturing through timely measurement of critical quality and performance of the new in-process materials and processes with a goal that ensuring the safety of the final product (Swan, 1999).

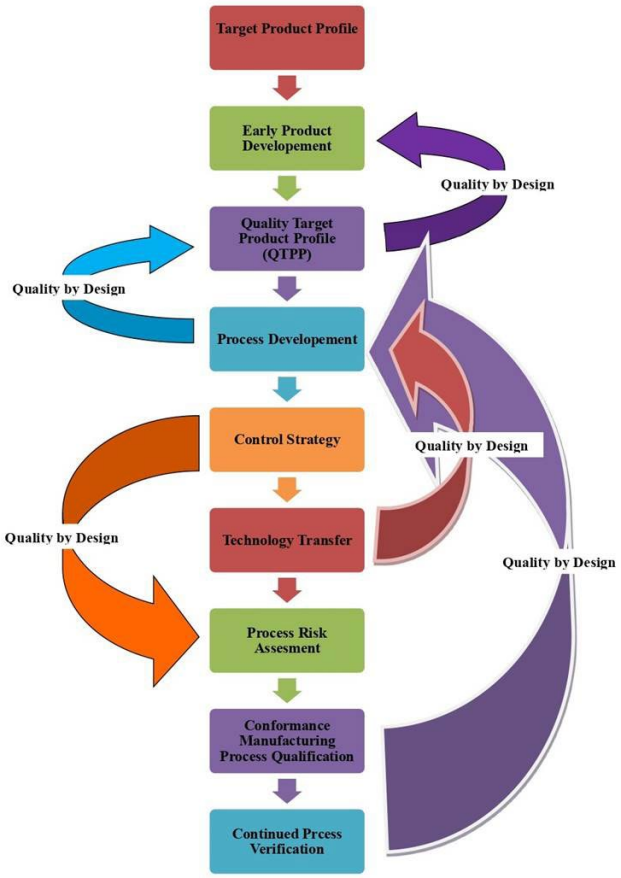

Figure 1: Process Development and Control Strategy in QbD

Table 1: Advantages of QbD before and after use in pharmaceuticals

Sr. No.	*Aspects*	*Before QbD*	*After QbD*
1.	Pharmaceutical Development	Empirical	Systematic and multivariate experiments
2.	Process Control	In the process of testing, manual analysis wide and reduced response	PAT is used for the feedback & forwarding of feed in real time
3.	Manufacturing Process	Fixed	Adjustable with the design space
4.	Control Strategy	The intermediate and final product was tested	Risk-based parameters, real-time release
5.	Life Cycle Management	Reactive to time problems and out-of-specification	Continual improvement
6.	Product Specifications	For the quality control	Overall, the control strategy based on the products

Benefits of Quality by Design

Benefits for industries

Quality by Design (QbD) is a methodical strategy that prioritizes cooperation between manufacturing and research to improve pharmaceutical development's efficacy and efficiency. A deeper comprehension of the product and manufacturing process is made possible by this sophisticated method, which guarantees a superior design with fewer difficulties and a lower requirement for manufacturing supplements. By facilitating the seamless incorporation of new technologies, QbD minimizes regulatory inadequacies and review process challenges. It lessens the load of validation by encouraging ongoing development and offering a greater degree of certainty over product quality. QbD helps to minimize deviations, avoid expensive investigations, and prevent problems linked to regulatory compliance by emphasizing a full understanding of the production process and product characteristics. Furthermore, it enhances the overall quality and uniformity of pharmaceutical goods by giving technical staff members a clear framework and greater understanding of the production process.

Benefits for FDA

Pharmaceutical assessments are far more thorough and of higher quality when a scientific review methodology is used. This approach promotes a more organized and methodical evaluation procedure and guarantees more uniformity in regulatory assessments. It improves the overall safety and effectiveness assessment of pharmaceutical goods by successfully managing increased risks. Furthermore, by enhancing the caliber and thoroughness of the first regulatory submission, a well-organized scientific review lessens the requirement for post-approval regulatory filings. Additionally, it increases decision-making flexibility, enabling more intelligent and flexible regulatory measures (Hussain, 2003).

Elements of Pharmaceutical Quality by Design

An applicant approaches the QbD for identifying the characteristic of the product development to critical quality on behalf of patient compliance and converts them into the drug product critical quality attributes (CQAs), this helps in developing good relationships between the formulation, manufacturing process and, CQAs for the delivery of good quality products to the patient (Knapp, 1998).

QbD has the following elements which are discussed below –

- A QTPP is used in identifying the different CQAs of the pharmaceutical products.
- It helps in product design which includes the identification of CMAs.
- Product design consists of the identification of the critical process parameters (CPPs) and helps in the linking of the scale-up principle with CMAs and CPPs with the CQAs.
- The control strategies involved in the specification of all the APIs and excipients that are used in the drug product help in controlling all the processes and steps involved in the manufacturing process.
- It increased the capability of the process and continued the improvement.

Quality Target Product Profile (QTPP)

QTPP is the tool that is applied for the development of strategies for product development. The term explains itself clearly that planning with the end in mind which is the natural extension of the quality product (Lionberger *et al.*, 2008). According to the FDA, "the TPP provides the information about the drug development program and gives the accurate statement to the drug at the time of development. This was developed according to the key section in labeling and development activities of the drug for the specific intended concept to inclusion in drug labeling (Potter *et al.*, 2006)."

QTPP is a prospective summary of the drug product that consists of the quality characteristic that is ideally achieved to ensure the desired quality of the product in the account of safety and efficacy of the product. In new drug development, the QTPP evolves and refined the product as the development process progresses. It is a quantitative and qualitative description of the design goals and strategies before the knowledge and process experience or availability of equipment and facilities that can affect the QTPP (Potter *et al.*, 2006). It involves in identification of different aspects of the critical quality attributes that include the purity, potency, pharmacokinetic profile, shelf

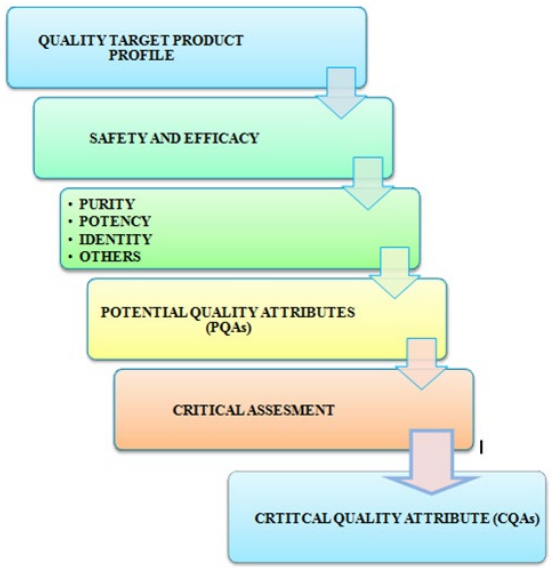

Figure 2: Process of determining Critical Quality Attributes (CQAs) in Drug Development

life, and the sensory properties of the formulated drug products (*as shown in fig. 2*). Design of the developed drug product based on the QTPP form.

QTPP identifies the CQAs of the drug products

QTPP deals with the quality characteristic of the pharmaceutical product that is used to ensure the achievement of the desired quality, safety, and efficacy of the product (Nosal, 2007). To develop an effective and safe product, here are the following parameters of QTPP that include Clinical investigations, alternative routes of administration, dosage forms, and drug delivery systems are only a few of the applications for pharmaceutical goods (Tong *et al.*, 2007). A key factor in guaranteeing both patient safety and therapeutic efficacy is dosage strength. Furthermore, the closure mechanism and container have a significant impact on the medicinal product's stability and integrity. Changes in the drug moiety's rate of dissolution have a substantial influence on the pharmacokinetic and aerodynamic properties of the dosage forms, which can affect drug absorption and overall therapeutic results. Therefore, in order to fulfill the standards for the planned marketed goods and guarantee consistent performance and patient benefit, it is imperative to maintain suitable drug product quality criteria.

The next step in the product development is the identification of the CQAs which conclude the quality attribute of the product that includes physical properties such as shape, color, odor, score configuration, friability, degradation products, drug release or dissolution studies, assay, residual solvents, content uniformity, moisture content, and microbial limits (Berridge, 2007).

Critical Quality Attributes (CQAs)

According to **ICH Q8 (R2) –** It is the appropriate range or limit or distribution of the physical, chemical, biological, and microbiological characteristics or properties to ensure the quality of desired products. It is usually combined with API, excipients, in-process materials, and the drug products for example the solid oral dosage form is typically the aspects that affect the purity, release, strength, and stability of the drug product whereas the sterility and clarity of the parenteral products as well. It also includes other properties like bulk density and particle size distribution that also affect the drug product quality (Reed, 2005).

ICH Q9 stated the potential drug substance used in CQA that guides the process of formulation and development. The exclusion and inclusion can be performed for the known drug samples that increase the method of process used for preparation and development enlisted in the list of potential CQAs (Hlinak *et al.*, 2006).

Using quality risk management, the pharma product may be prioritized using the list of possible CQAs for the evaluation that will come after. The appropriate CQAs can assess the extent of identifying the iterative process of quality risk management and experimentation through which the variation might influence the quality of the drug product. A good quality attributes management system and appropriate formulation process; design and development are used to achieve all target attributes using these target elements (Juan *et al.*, 2011).

The degree of variability in pharmaceutical goods is mostly determined by the analytical methodology's capabilities. Analytical procedures' inherent variability is directly impacted by the products' inherent variability (Juan *et al.*, 2011). Numerous factors, such as equipment, operators, and sample properties, contribute to this variability and the overall quantitative variations seen throughout analysis. Product qualities play a crucial role in the formulation process, and in order to comprehend and manage these variances, research into them using design of experiments (DOE) is necessary. By accurately assessing product variability, a well-designed analytical procedure guarantees consistent product quality and adherence to regulatory criteria.

Product Design and Understanding

Over the decades, the main objective of the QbD was to focus on the process design, understanding, and controlling the quality as they are discussed in the ICH Q8 (R2). These points are the most important aspects of the QbD that help to design the product that meets the desired criteria that fulfill the patient needs through the clinical studies and maintains the optimized therapeutic activity throughout its shelf life that was determined by the stability studies (Terry, 2010). The main objective of the product design was to develop and formulate the optimized product that delivers the desired QTPP over the shelf life of the product. Product design has the key elements which are discussed below –

- Characterization of the drug using the biological, physical, and chemical parameters.
- Selection and identification of the excipients having different grades and types.
- Interactions studies between the drug product and excipients.
- Identifications and optimization of the CMAs of drugs and excipients.

A typical pharmaceutical manufacturing process consists of several unit tasks that interact to produce the required product quality. To complete unit operations, batch or continuous production techniques might be employed. Mixing, milling, granulating, drying, compressing, and coating are a few examples of discrete unit processes that include physical or chemical changes (Wagdy *et al.*, 2013). A process is often considered to be well-understood when all important sources of variability have been identified and explained, variability has been controlled by the process, and product quality attributes can be accurately and reliably predicted (Alex *et al.*, 2012).

Process parameters are factors that affect a process step or unit operation, such as the input operating parameters

(such as speed and flow rate) or process state variables (such as temperature and pressure) (Xiaoming *et al.*, 2012). Finding every known process parameter that might affect the result is crucial to ensuring optimal process performance. Scientific knowledge and a comprehensive risk assessment should be used to identify high-risk characteristics. It is essential to set boundaries or values for these important variables. Validating these criteria is aided by testing, such as Design of Experiments (DoE). First-principles models that connect Critical Material Attributes (CMAs) and Critical Process Parameters (CPPs) to Critical Quality Attributes (CQAs) should be used to evaluate the data's scalability (Sheryl *et al.*, 2011). In order to create the "process design space" for important parameters, a control plan should specify acceptable ranges (Anurag *et al.*, 2011).

Critical Material Attributes (CMA)

- Identification of important medicinal product quality attributes It's crucial to analyse the relationship between drug substances and drug products (Bhambure *et al.*, 2011).
- The drug substance's intended quality was determined by taking into account its use in drug products as well as knowledge of its physiochemical, biological, and microbiological properties and characteristics that could influence the development of the drug product, such as the drug substance's solubility, which influences the dosage form choice (Enikó *et al.*, 2010).
- The rationale for selecting the excipients' kind, grades, and amounts. Understanding which material attributes contribute the most to the excipient's functioning is critical to success.
- Critical quality aspects such as solubility resolution rate, chemical, and physical stability, and manufacturability will be influenced by the choice of the correct salt solid form particle size, shape, and degree of aggregation (bonding index flow filterability) (Parks, n.d.).

Critical Process Parameters (CPP)

A significant process parameter, according to the ICHQ 8(R2), is variability, which has an influence on a critical quality characteristic and should be monitored or controlled to guarantee the process achieves the appropriate quality. It is in charge of ensuring that the CQAs are met, as well as identifying possible CPPS through risk assessment (Nosal, 2006).

Categories of Parameters

- Unclassified parameters are the unknown criticalities. In this parameter, there is a need for additional data that is used to classify the unclassified parameters that are critical or non-critical.
- Critical parameters are critical at the time when the change in the product causes failure to achieve the QTPP.
- Non-critical parameters observed in the potential of the operating space and no change caused due to interaction that doesn't fail the QTPP and established the suitable range.

When CPPs are altered with regular operation ranges, they have a direct and considerable impact on CQAs. The type of equipment and its settings, as well as the working circumstances of the equipment and the surrounding environment, such as moisture temperature, should all be taken into account (Morris, 2004). Process capacity should be investigated to demonstrate a process's repeatability and consistency. A statistical evaluation of the inherent process variability of a certain attribute is called process capacity. The most often used formula for process capability is Six Sigma. A given attribute's tolerance value is divided by its process capability to get the process capability index (FDA CDER, 2004).

ICHQ10 specifies that the condition of control must be maintained. A mechanism for assessing the effectiveness and quality of processes should be developed and put into place by pharmaceutical companies. To create a control plan, the process performance and quality monitoring system should incorporate quality risk management (U.S. Food and Drug Administration, n.d.).

Six Sigma & QbD

Motorola coined the phrase Six Sigma in the 1980s, and it refers to the use of a component-based technique to reduce variability in production and optimize processes. Six Sigma has focused on the continuous improvement of an existing process, using the DMAIC technique (D-Define, M- Measure, A Analyze, I-Improve, C-Control) (*as shown in table 2)*. In the pharmaceutical sector, technologies such as Design of Experiments (DoE) and Control Charts are employed at various phases throughout the product lifecycle. Early Six Sigma practitioners developed an extra set of tools and practises known as Design for Six Sigma as a result of their recognition of the costs associated with bad product design (DFSS) (Callis *et al.*, 1987).

PMADV (D-Define, M-Measure, A-Analyze) is the approach used by DFSS. D-Design, V Verify is used to design new processes and is also used when there is no process or

Table 2: Comparison of DMAIC and DMADV in Process Improvement and Design

DMAIC	*DMADV*
An incremental improvement system for current processes that aren't meeting specs. D - Define M - Measurea A - Analyze I - Improve C - Control	An improvement system for creating new high-quality processes or products. D - Define M - Measure A - Analyze D - Design V - Verify

when an existing process has been developed using DMAIC but still does not meet the acceptable level.

DFSS also provides the tools and a systematic method for efficiently generating new processes, reducing the work, time, and costs associated with designing and eventually manufacturing the new product continuously (*as shown in table 3*). The primary assumption of DFSS is that to successfully develop the requisite goals, it is necessary to first understand the process and product, to identify and manage crucial material and process factors (U.S. Food and Drug Administration, 1995).

For instance, QbD is a methodical approach to development that emphasizes product and process understanding, process control built on solid science, and risk management in the pharmaceutical industry. QbD starts with specified goals. The DFSS technique is well-suited to the QbD framework of generating reliable products with thorough process knowledge (Wu & Khan, 2009).

The DFSS and QbD share a philosophy based on the idea that applying systematic and structured aspects to product development will increase the amount of process knowledge gained by the development team, allowing them to make better decisions and increasing the likelihood of developing a quality product that will perform as intended (Woodcock, 2004).

Control Strategy

Control strategy is defined as the set of plans of controls that are derived from the current product and understanding process that assure the performance of the process and good quality product. It requires ensuring that the materials and process are within the limit range which also helps in avoiding the defect and maintains the desired quality (*as shown in fig. 3*). It is the quality-by-design process that is established by an assessment of the risk that takes into consideration CQAs and the capability of the process. It includes different elements that help ensure the quality of the product such as input material, process controls and monitoring, design space to final product specification (Rathore & Winkle, 2009).

Table 3: Correlation between DFSS & QbD

DFSS	*QbD*
Define the purpose of the project and the requirements of customers	**QTPP –** To define the purpose of the project and the requirements of customers
Measure – Agree on customer specifications to fulfill the needs	**CQAs -** Agree on customer specifications to fulfill the needs
Analyze – Processes, products, methods to meet the specifications	**Materials Attributes** - Processes, products, and methods to meet specifications
Design – Processes, products, and methods to meet specifications	**Design Space -** Processes, products, and methods to meet specifications
Verify - Processes, products, and methods to meet specifications	**Control Strategy -** Processes, products, and methods to meet specifications

Product Life Cycle & Continuous Improvement

The process life cycle can increase product quality. Companies can examine current approaches to increase product quality, and process performance has been reviewed to ensure quality consistency. Periodic maintenance can be accomplished using the company's internal quality system (Alex *et al.*, 2012). The goal of a contemporary quality system is to prove efficiency by streamlining a process and minimizing wasted efforts in manufacturing. QBD focuses on product quality as well as continual process improvement and variability reduction. The Quality System procedure is the backbone of continual improvement. It aids in the "identification and implementation of specific product quality improvements, process improvements, and variability improvements, therefore boosting the capacity to consistently meet quality requirements (House, 2011)."

Drug Substance and Excipients

Testing is used to keep an eye on the quality of raw materials, such as those used to make medications and excipients. If they satisfy further criteria like USP for drug substances or excipients, as well as manufacturer-planned and FDA-approved parameters, they can be used in the creation of the product. The method of producing drug substances is also carefully inspected because it's not obvious if the standards alone will be sufficient to ensure quality (André *et al.*, 2011). QbD examines the qualities that are essential to patient satisfaction, transforms them

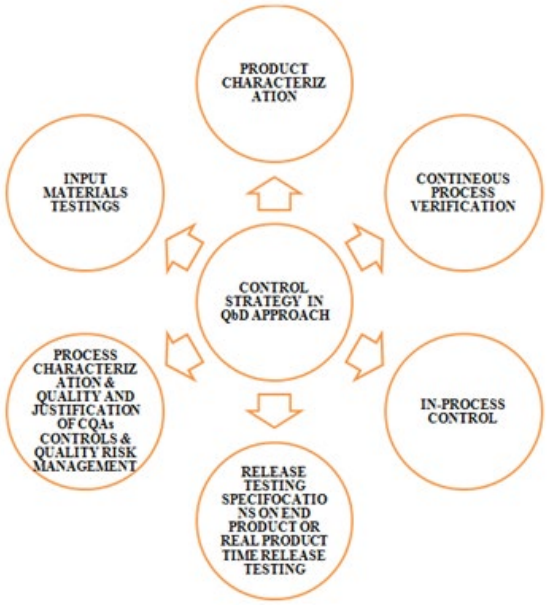

Figure 3: Representation of some examples of Control Strategy in the advancement approach of the development (QbD)

into qualities the medication product ought to possess, and identifies the significant process variables that may be changed to reliably produce a therapeutic product with desired properties (*as shown in fig. 4*). This is done by establishing the relationship between product features and formulation and manufacturing process factors (such as excipient and medication component quality and process parameters) (Joseph *et al.*, 2011).

Drug Substances

The relationship between physicochemical and biological qualities helps in enhancing product performance and manufacturing efficiency. The quality and physical qualities of beginning and source materials are critical in drug substance product development and manufacturing (Warren, 2009). The choice of beginning and source trials should be based on adherence to relevant principles as part of the manufacturing process development criteria. Solubility, for example, is one of the physicochemical and biological qualities that must be investigated. The size of the particles, crystal characteristics, biological activity, water content, and permeability are all factors to consider. The paper explains how to link material characteristics and process parameters to drug-substance CQAS, how to apply Quality Risk Management to assist process parameter life cycle management, and how to offer a Design Space for a biotechnological product unit oration. ICH QUI also serves as a guide for drug substance makers when drafting a submission as part of the drug substance application process, regardless of whether they use a traditional or improved approach to design and development (Deliang & Yihong, 2010).

A Starting Material is a material with certain chemical characteristics and structure, and it is used as a "significant structural piece." A commercially accessible chemical is defined as one that is offered as a commodity in a pre-existing market. Chemicals created via bespoke syntheses were not regarded as commercially available and should be justified when employed as Starting Materials, in addition to their intended usage in the non-pharmaceutical sector. Starting materials are classified as synthetic, semi-synthetic, and biotechnological/biological, according to the standard (*as shown in fig. 5*). The principles for synthetic drug substances include the knowledge that early in the manufacturing process, changes in material characteristics, and operating circumstances have a lesser ability to affect drug substance quality (Betterman *et al.*, 2012). Regulatory authorities should offer an adequate account of how impurities are created, how the bowing process influences impurity formation, destiny, and purge, and if the control method is appropriate.

Excipients

Excipients are widely known to be a primary cause of variability. The purpose and utility of excipients determine the characterization and comprehension of their features. The knowledge and information on drug-excipient compatibility are useful for designing formulations and manufacturing procedures. These details may have come from both theoretical and experimental research. It is well understood that a mechanistic knowledge of degradation kinetics is more useful in forecasting stability than experimental data obtained under artificial stress settings.

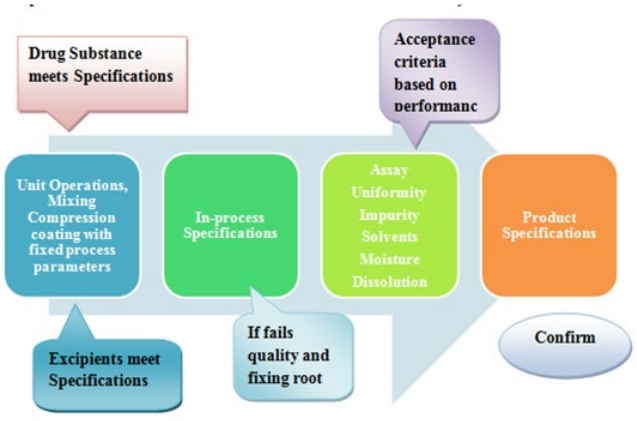

Figure 4: Quality by Design (QbD) Workflow in Pharmaceutical Manufacturing

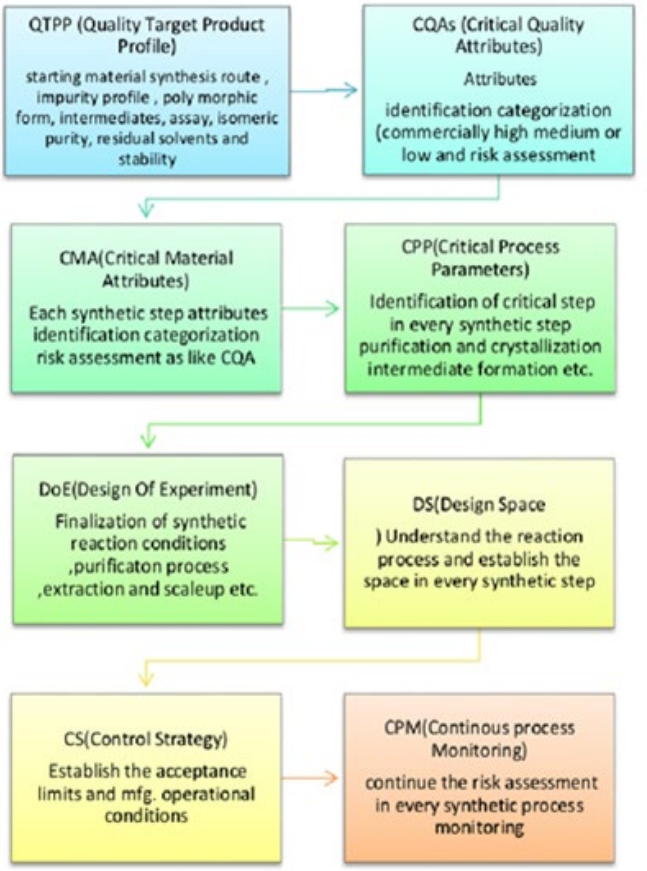

Figure 5: Drug substance synthesis in the QbD approach

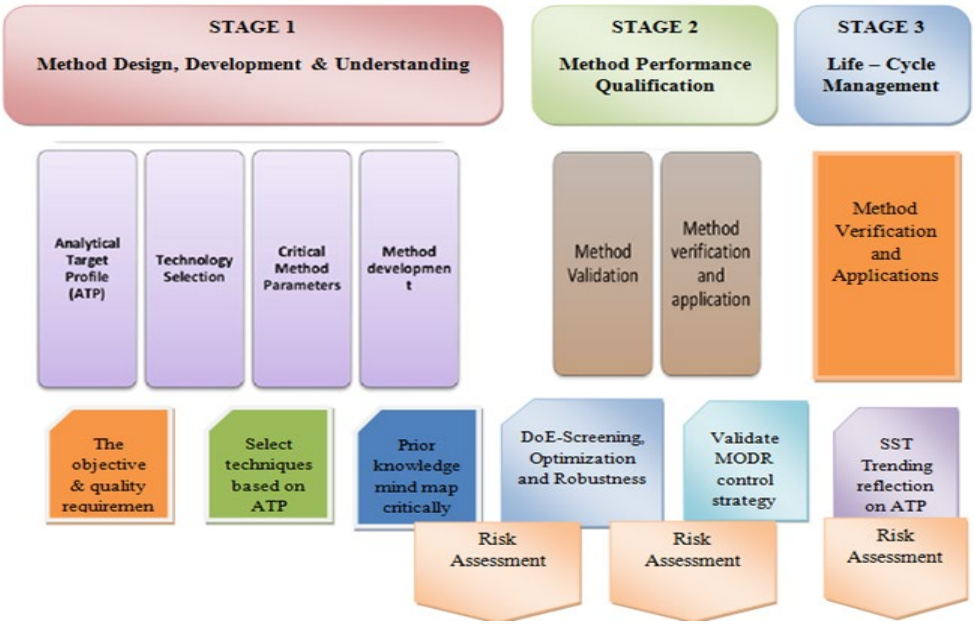

Figure 6: Stages in Analytical Method Design, Qualification, and Verification

Stages involved in the role of excipients in Quality by Design

Excipients must be established and approved by pharmaceutically affiliated producers and distributors to ensure the quality and safety of the completed product. Excipients were characterized as qualitative categories for the objectives and functions of an excipient in a medicinal product, and they served as the justification for their presence in the formulation.

Sources of excipients related excipients risk management

Analytical Quality by Design (AQbD)

The goal of analytical Quality by Design (AQbD) is to build a robust approach that can be used throughout the life cycle of a drug product as well as on similar products using the same API. API, pharmacological contaminants, and biological metabolites may all be analyzed using analytical QbD (Jennifer *et al.*, 2008).

QbD in analytical method development and validations

Analytical procedures are fully integrated into the QbD paradigm, and they play a critical role in the development of application techniques. The major goal is to specify the use of analytical methods, starting with validation and assessing their suitability (Betterman *et al.*, 2012). The three steps are depicted *as shown in fig. 6.*

Applications of ATP

The executive of QbD helps to establish the best method technology to satisfy with the standard guidelines hence essential for the pharmaceuticals so that they easily accept the concepts of the QbD. Factors that enhance the robustness were always taken into consideration for the development of an analytical method of QbD.

- Determination of impurities
- Simultaneous analysis of API and its related Substances
- Multimolecular separations
- Natural product analysis
- Method optimization and applications to degradation kinetics

Conclusion

QbD plays a vital role in the development of good quality drug products which enhances patient compliance. It procedure and method help in ensuring the best techniques that can be useful for product development. The main aim of the modern approach is to develop and design the best quality drug product using its manufacturing process which will help in the constant release of the product and enhance its performance. The main goal of working on this modern approach is to develop a well-characterized method that is reliable to demonstrate a high degree of assurance that meets the predefined criteria when operated within defined boundaries. It is also involved in the development and evaluation of different analytical methods that going to be used in the product development process.

Abbreviations

Quality by Design (QbD), Food & Drug Association (FDA), Critical Quality Attributes (CQAs), Critical Process Parameters (CPPs), Critical Material Attributes (CMAs), Quality Target Product Profiles (QTPP), Potential Quality Attributes (PQAs), Design of Experiments (DoE), Critical Process Parameters (CPP), Define Measure Analyze

Improve Control (DMAIC), Define Measure Analyze Design Verify (DMADV), Analytical Quality by Design (AQbD), Analytical Target Profiles (ATP), International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), Process Analytical Technology (PAT).

References

1. Woodcock, J. (2004). The concept of pharmaceutical quality. *American Pharmaceutical Review, 7*(6), 10–15.
2. Bruttin, F., & Dean, D. (1999). A risk-based approach to reducing the cost of compliance in pharmaceutical manufacturing. *Pharmaceutical Technology Europe, 11*(5), 36–44.
3. Swan, J. P. (1999). The 1941 sulfathiazole disaster and the birth of good manufacturing practices. *Science & Technology, 53*(3), May–June.
4. Federal Food, Drug, and Cosmetic Act. (n.d.). Chapter V, Subchapter A, Section 501(a)(2)(B).
5. Hussain, A. S. (2003, September 17). Quality by design: Next steps to realize opportunities [Presentation to the FDA Advisory Committee for Pharmaceutical Science: Manufacturing Science Subcommittee].
6. Knapp, J. Z. (1998). "Absolute" sterility and "absolute" freedom from particle contamination. *PDA Journal of Pharmaceutical Science and Technology, 52*(4), July–August.
7. Lionberger, R. A., Lee, L. S., Lee, L., Raw, A., & Yu, L. X. (2008). Quality by design: Concepts for ANDAs. *The AAPS Journal, 10*, 268–276. https://doi.org/10.1208/s12248-008-9026-7
8. Potter, C., Beerbohm, R., Coups, A., *et al.* (2006). A guide to EFPIA's Mock P.2 document. *Pharmaceutical Technology Europe, 18*, 39–44.
9. Potter, C., Beerbohm, R., Coups, A., & others. (2006). A guide to EFPIA's Mock P.2 document. *Pharmaceutical Technology Europe, 18*, 39–44.
10. Nosal, R. (2007, September). PQLI-criticality. In *ISPE PQLI Berlin Conference*.
11. Tong, C., D'Souza, S. S., Parker, J. E., & Mirza, T. (2007). Commentary on AAPS workshop dissolution testing for the twenty-first century: Linking critical quality attributes and critical process parameters to clinically relevant dissolution. *Pharmaceutical Research, 24*, 1603–1607. https://doi.org/10.1007/s11095-007-9280-x
12. Berridge, J. (2007, June). ICH Q8 & Q9 (+Q10) defined and undefined: Gaps and opportunities. In *ISPE PQLI Washington Conference*.
13. Reed, R. A. (2005, June). A quality-by-design approach to dissolution based on the biopharmaceutical classification system. In *DIA Annual Meeting*.
14. Hlinak, A. J., Kuriyan, K., Morris, K. R., Reklaitis, G. W., & Basu, P. K. (2006). Understanding critical material properties for solid dosage form design. *Journal of Pharmaceutical Innovation, 1*, 12–17. https://doi.org/10.1007/BF02784876
15. Juan, G. R., Marcel, B., Gonz, M., Josep, A., & Manel, A. (2011a). *Journal of Pharmaceutical Sciences, 100*, 4442.
16. Juan, G. R., Marcel, B., Josep, M. G., & Alez, M. A. (2011b). *Journal of Pharmaceutical Sciences, 100*, 4442.
17. Terry, M. (2010). *Chemical Engineering and Processing, 106*, 24.
18. Wagdy, H. A., Hanafi, R. S., ElNashar, R. M., & Aboul-Enein, H. Y. (2013). *Journal of Separation Science, 36*, 1703.
19. Alex, E., Pascal, V., Thomas, S., Hervé, E., Ralf, G., Claire, L. S., & James, S. (2012). Journal of Pharmaceutical Sciences, **101**, 3604.
20. Xiaoming, X., Antonio, P. C., Mansoor, A. K., & Diane, J. B. (2012). *International Journal of Pharmaceutics*, **434**, 349.
21. Sheryl, M., Fredric, J. L., Rita, L. W., Alavattam, S., Jagannathan, S., Stephanie, S., & Samir, U. S. (2011). *Journal of Pharmaceutical Sciences*, **100**, 3031.
22. Anurag, S. R., Rahul, B., & Ira, S. K. (2011). *LC GC North America*, **29**, 252.
23. Bhambure, R., Kumar, K., & Rathore, A. S. (2011). *Trends in Biotechnology*, **29**, 135.
24. Enikó, R. T., Orsolya, L., Eszter, S., & Julianna, L. R. (2010). *International Journal of Pharmaceutics*, **392**, 261.
25. Parks, T. (n.d.). A science and risk-based approach for establishing critical process parameters and critical intermediate quality attributes. Retrieved from http://www.pharmachemicalireland.ie/Sectors/IPCMF/IPCMFDoclib4.nsf/wvICCNLP/2E3576E6D5211C69802570BC004BA9F8/$File/12+-+CPP+Poster.ppt (Accessed November 21, 2007).
26. Nosal, R. (2006, October). Industry perspective of risk-based CMC assessment under QbD. *AAPS Annual Meeting*.
27. Morris, K. R. (2004). Risked-based development and CMC question-based review: Asking the right questions for process understanding, control, and filing. *FDA Advisory Committee for Pharmaceutical Science*. Retrieved from http://www.fda.gov/ohrms/dockets/ac/04/slides/2004-4052S1_12_Morris.ppt (Accessed November 21, 2007).
28. FDA CDER. (2004, September). Guidance for industry: PAT—a framework for innovative pharmaceutical development, manufacturing, and quality assurance.
29. U.S. Food and Drug Administration. (n.d.). *FDA guidance for industry and review staff: Target product profile - A strategic development process tool (Draft guidance).*
30. Callis, J. B., Illman, D. L., & Kowalski, B. R. (1987). Process analytical chemistry. *Analytical Chemistry, 59*(7), 624A–637A. https://doi.org/10.1021/ac00139a719
31. U.S. Food and Drug Administration. (1995). *Guidance for industry: Immediate release solid oral dosage forms scale-up and postapproval changes: Chemistry, manufacturing, and controls, in vitro dissolution testing, and in vivo bioequivalence documentation.*
32. Wu, H., & Khan, M. A. (2009). Quality-by-design (QbD): An integrated multivariate approach for the component quantification in powder blends. *International Journal of Pharmaceutics, 372*(1–2), 39–48. https://doi.org/10.1016/j.ijpharm.2009.01.002
33. Woodcock, J. (2004). The concept of pharmaceutical quality. *American Pharmaceutical Review, 7*(6), 10–15.
34. IBM Business Consulting Services. (2006). Transforming industrialization: A new paradigm for pharmaceutical development. Retrieved from https://www-935.ibm.com/services/us/imc/pdf/ge510-3997-transforming-industrialization.pdf
35. Rathore, A. S., & Winkle, H. (2009). Quality by design for biopharmaceuticals. *Nature Biotechnology, 27*(1), 26–34. https://doi.org/10.1038/nbt0109-26
36. Alex, E., Pascal, V., Thomas, S., Hervé, E., Ralf, G., Claire, L. S., & James, S. (2012). *Journal of Pharmaceutical Sciences, 101*(11), 3604. https://doi.org/10.1002/jps.23258
37. International Conference on Harmonisation (ICH). (n.d.). *Quality guidelines.* Retrieved from https://www.ich.org/products/guidelines/quality/article/quality-guidelines.html
38. House, I. (2011). *Process understanding: For scale-up and manufacturing method of active ingredients.* Wiley-VCH Verlag GmbH & Co. KGaA.
39. André, S. R., Robert, L., & Lawrence, X. Y. (2011). *Pharmaceutical Research, 28*(12), 1445.
40. Joseph, K., Beth, A. L., Jon, I. H., & Glenn, T. C. (2011). *International Journal of Pharmaceutical Sciences, 100*(12), 2222.
41. Warren, C. (2009). *Pharmaceutical Technology Outsourcing Research, 28*(4).
42. Deliang, Z., & Yihong, Q. (2010). *Journal of Validation Technology, Autumn,* 74.
43. Betterman, S. M., Levy, S. E., & Brown, B. A. S. (2012). *Journal of GXP Compliance, 16*(3), 34.
44. Jennifer, Q. L., Angela, L., Wendy, D., Marc, T., & Sherry, K. (2008). *Microscopy and Microanalysis, 14*(6), 1606. https://doi.org/10.1017/S143192760808046X

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