How Can Quality by Design Enhance Biopharmaceutical Manufacturing in India? Exploring Strategies and Outcomes.

Research dissertation presented in partial fulfilment of the requirements for the degree of MSc in Pharmaceutical Business and Technology (QQI)

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CANDIDATE DECLARATION

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I certify that the dissertation entitled: “How Can Quality by Design Enhance Biopharmaceutical Manufacturing in India? Exploring Strategies and Outcomes.” submitted for MSc in Pharmaceutical Business and Technology is the result of my own work and that where reference is made to work of others, due acknowledgment is given.

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LIST OF ABBREVIATIONS

QbD - Quality By Design

QTPP - Quality Target Product Profile

CQA - Critical Quality Attributes

CMA - Critical Material Attributes

CPP - Critical Process Parameters

ICH - International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use

TPQP - Target Product Quality Profile

EMA - European Medicines Agency

US FDA - U.S. Food and Drug Administration.

CDSCO - Central Drugs Standard Control Organization

GMP - Good Manufacturing Practices

PAT - Process Analytical Technology

DoE - Design of Experiments

RSM - Response Surface Methodology

API – Active Pharmaceutical Ingredient

REM - Hazard Estimation Matrix

FMEA - Failure Mode Effect Analysis

NIR – Near Infrared Spectroscopy

QRM – Quality Risk Management

TPP – Target Product Profile

AQbD - Analytical Quality by Design

ATP – Analytical Target Profile

CMM – Continuous Method Monitoring

QbT – Quality By Testing

NDA – New Drug Application

FFD – Fractional factorial Designs

PBD - Plackett-Burman Designs

PP – Process Parameters

FA – Formulation Attributes

RA Methods - Risk Assessment Methods

CCD - Central Composite Design

rQbD - Retrospective QbD

R&D – Research & Development

USP - US Pharmacopeia

PICS - Pharmaceutical Inspection Co-operation Scheme (PIC/S)

DBT India - Department of Biotechnology

CII - Confederation of Indian Industry

DMAIC - Define, Measure, Analyze, Improve, and Control

MODR - Method Operational Regions

GDPR - General Data Protection Regulation

CPV – Continuous Process Verification

SPC - Statistical Process Control

SME - Small and Medium Enterprises

ABSTRACT

This study investigates the integration and impact of Quality by Design (QbD) principles within the Indian biopharmaceutical manufacturing sector. As the industry expands, driven by the demand for affordable biologics and the necessity to meet stringent international quality standards, QbD emerges as a pivotal approach. This research evaluates the current level of QbD integration, explores specific strategies employed by manufacturers, and analyses the outcomes on product quality, regulatory compliance, and operational efficiency. It also identifies significant barriers to QbD implementation, including technical expertise gaps, high upfront investment costs, and regulatory challenges. The study is based on a comprehensive survey conducted among industry professionals. The survey employed structured questionnaires designed to collect quantitative data on the perceptions, experiences, and practices related to QbD implementation within the sector. Data analysis was performed using statistical methods, including descriptive statistics to summarize the data and inferential statistics to explore relationships between variables, assess the impact of QbD practices, and identify significant trends within the industry. The findings reveal that while QbD is widely recognized for its potential, its implementation remains in the early stages across much of the industry. The results highlight the need for enhanced training, investment in advanced technologies, and stronger regulatory alignment to facilitate broader and more effective QbD adoption. These insights are intended to guide policymakers, industry leaders, and regulatory bodies in strengthening the Indian biopharmaceutical sector through the effective application of QbD principles.

Keywords: Quality by Design (QbD), Indian biopharmaceutical industry, regulatory compliance, operational efficiency, technical challenges, survey research, statistical analysis, descriptive statistics.

CHAPTER ONE

INTRODUCTION

1.0 Background of Study

India's biopharmaceutical sector is expanding and changing quickly, becoming a significant player in the international market. The capacity of this industry to create reasonably priced biologics, such as vaccines, monoclonal antibodies, and biosimilars, is what accelerates its growth. However, this expansion demands compliance with strict international quality standards and legal obligations. Quality by Design (QbD) is one strategy that shows a lot of promise for reaching these criteria.

A thorough, scientifically grounded method for developing and producing pharmaceuticals is called Quality by Design (QbD). Instead of depending just on testing the final product, it stresses building quality into the process from the beginning. Understanding the links between Quality Target Product Profile (QTPP), critical quality attributes (CQAs), critical material attributes (CMAs), and critical process parameters (CPPs) is the main goal of the QbD framework, as described by the International Conference on Harmonization (ICH) standards Q8, Q9, Q10 and Q11. The International Council for Harmonization (ICH) offers crucial regulations to guarantee the safety and quality of pharmaceuticals. Pharmaceutical development is the main emphasis of ICH Q8, which places a strong emphasis on an extensive understanding of product and process design for reliable quality. Quality risk management is covered by ICH Q9.A thorough pharmaceutical quality system is outlined in ICH Q10, which encourages consistent manufacture of drugs of superior quality and ongoing improvement. The research and manufacturing of drug substances are guided by ICH Q11, which outlines the fundamentals of process development, control, and lifecycle management to guarantee the quality of the substance (Sachin L. Darkunde, 2020).

A drug product's intended quality attributes are outlined in detail in the Quality Target Product Profile (QTPP), which is intended to guarantee the product's safety and effectiveness. It takes into account factors including strength, dose form, intended use, pharmacokinetic characteristics, container closure method, and quality standards like stability and sterility. The development of new products is based on QTPP, which directs the formulation and optimization of the medication to satisfy therapeutic and regulatory objectives. Particle size, drug release, stability, and other physical, chemical, biological, or microbiological characteristics that must be regulated to guarantee the intended product quality are known as critical quality attributes or CQAs. They are impacted by both the drug ingredient and excipients and are essential for preserving the safety and effectiveness of the medicinal product. The term "critical material attributes" (CMAs) refers to the crucial characteristics of raw materials and excipients that, in order to guarantee product quality, must be kept within certain bounds, such as moisture content or particle size. These characteristics are crucial for reliable medication manufacture and have a direct impact on CQAs. The primary elements of the manufacturing process that have an impact on CQAs are known as Critical Process Parameters, or CPPs. Temperature, flow rate, and mixing speed are a few examples. To guarantee that the process yields the required level of uniformity and quality in the finished product, CPP control is essential. Achieving the Target Product Quality Profile is aided by the identification and management of CPPs (TPQP). This knowledge aids in the development of reliable procedures that frequently yield high-quality output (Sirohiwala *et al.*, 2023).

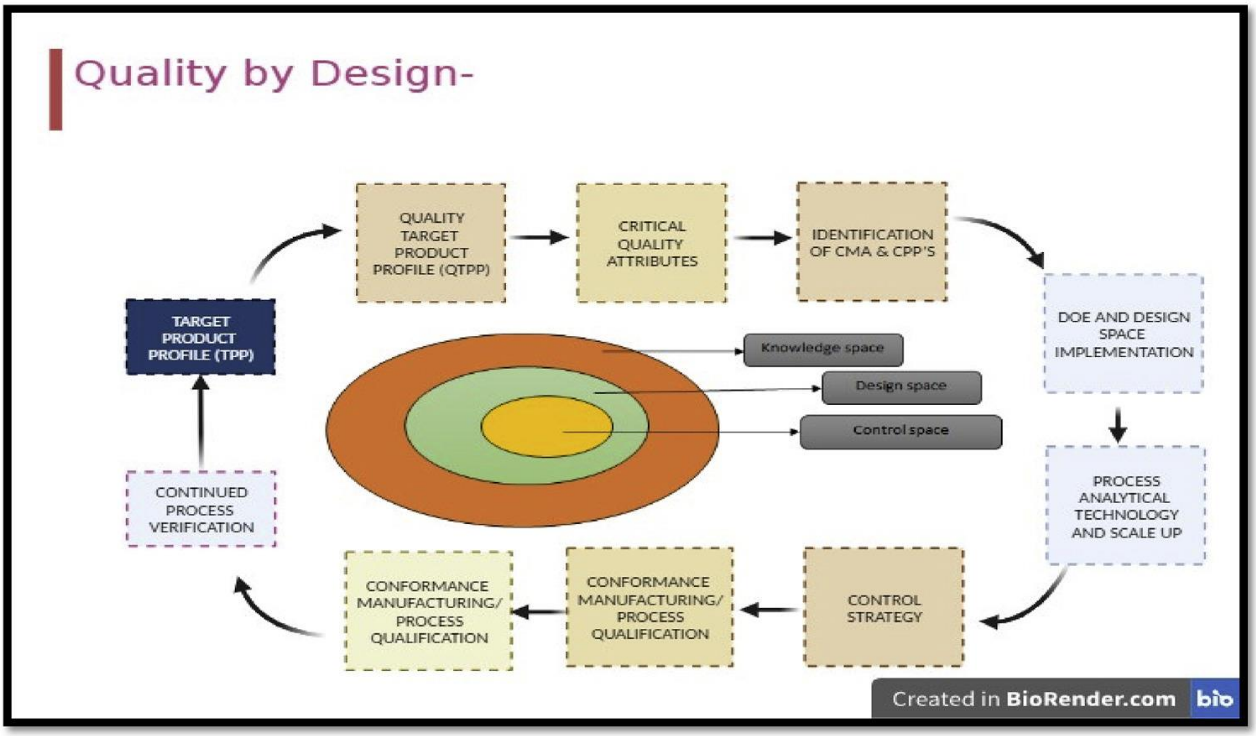

Figure 1 Quality By Design System (Khan *et al.*, 2024)

To guarantee constant drug quality, the European Medicines Agency (EMA) supports Quality by Design (QbD) in pharmaceutical applications. To limit variability and satisfy predetermined quality requirements, QbD applies statistical, analytical, and risk-management techniques throughout the design, development, and manufacturing phases. To identify crucial material properties and process parameters and enable continual improvement, it combines multiple-variate analysis, process-analytical chemistry, and knowledge-management systems. The ICH guidelines Q8, Q9, Q10, and Q11 provide a detailed explanation of QbD principles, which were first introduced in guidelines from 2009 to 2012. The EMA's PAT team was established in 2003 to support QbD and make sure the regulatory network is ready for QbD submissions. From 2011 to 2016, a joint pilot program with the US FDA harmonized QbD implementation and promoted high-quality medicines in the EU and US, which resulted in ongoing collaboration in continuous manufacturing and emerging technologies (EMA, 2024).

The application of QbD to the production of biopharmaceuticals is still in its early stages in India. To promote the implementation of QbD, the Central Drugs Standard Control Organization (CDSCO), India's main regulatory authority, has aligned its recommendations with global norms. In spite of this governmental backing, QbD implementation presents a number of challenges for Indian biopharmaceutical companies. These difficulties include a lack of technical know-how, the requirement for a large initial outlay, and problems with the quality of raw materials and supply chain management (Roy and Gupta, 2021).

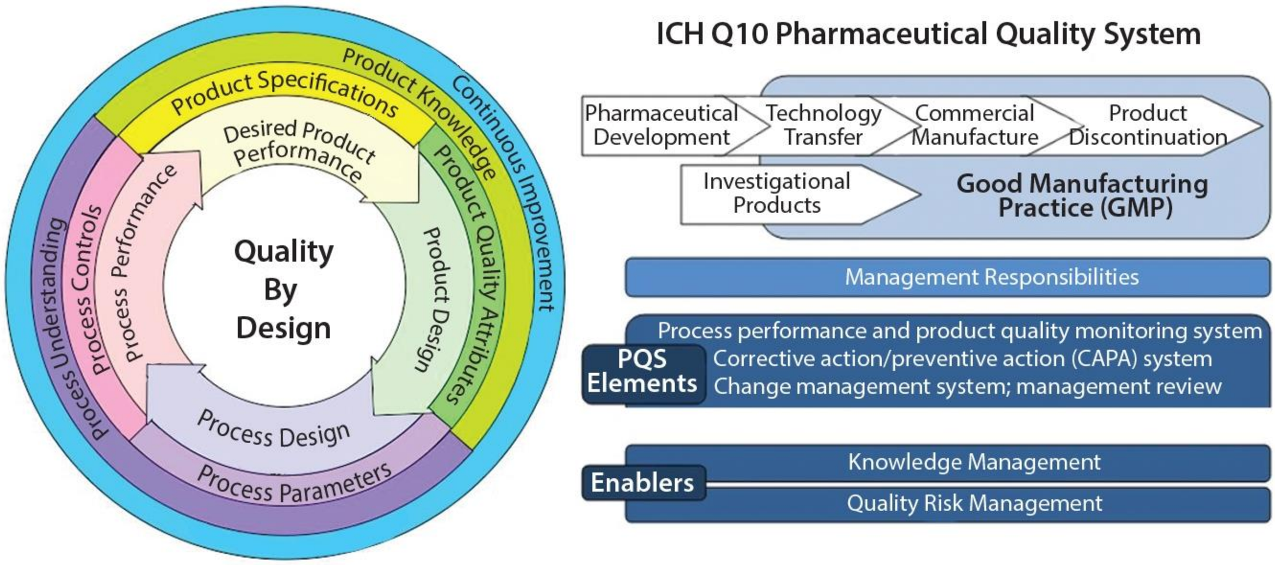

Figure : 2 Challenges in Implementing Quality by Design(Michael Torres, 2015)

Over 90% of the contents of each pill or tablet we take come from excipients, yet historically, regulatory attention has not placed much emphasis on their quality. In the production of pharmaceuticals, excipients are inert materials used with the active component of a drug. They help maintain the drug's stability and improve absorption, taste, and overall safety and efficacy of the medication, among other functions. Binders, fillers, flavouring agents, preservatives, and disintegrants are examples of excipients (Kar *et al.*, 2019). Numerous medication recalls have resulted from this negligence, which has been connected to uneven excipient quality and poor product design. The Quality by Design (QbD) strategy needs to be applied early in the drug development lifecycle to overcome these issues. This sector of the pharmaceutical industry is being improved by new laws and programs that enforce stricter adherence to Good Manufacturing Practices (GMPs). It is crucial to comprehend the application of QbD in the Indian biopharmaceutical industry for several reasons. It can offer success stories and best practices that can serve as a guide for other producers. It assists policymakers and regulatory agencies in determining which sectors require assistance and action. Moreover, it advances international cooperation and standardization by adding to the corpus of information on QbD worldwide (Das, 2018).

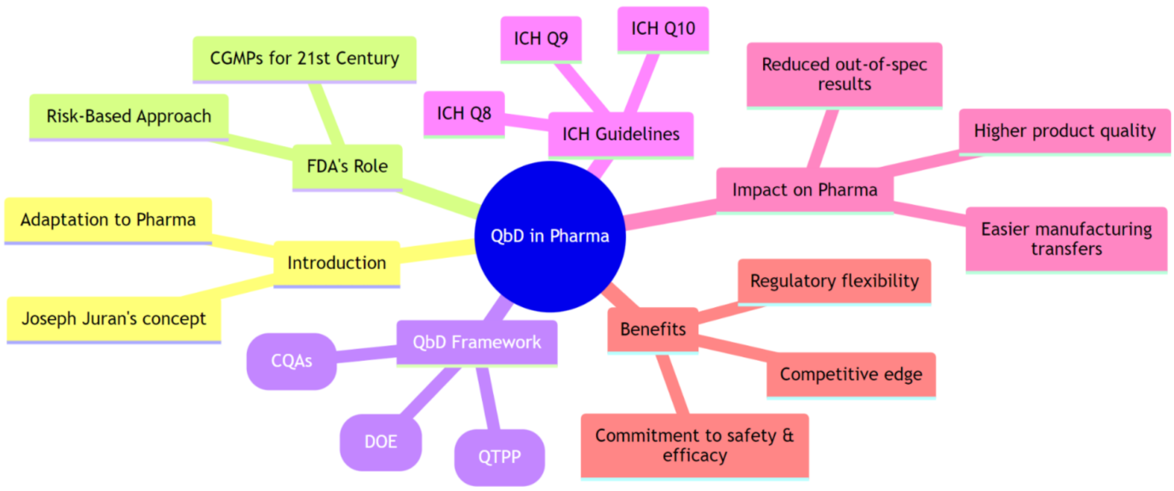

Figure :3 Functional and Regulatory model for QBD in Pharmaceutical manufacturing

(Chandramouli R, 2023).

This thesis investigates the use of QbD to biopharmaceutical production in India, looking at methods and results to enhance medication efficacy and safety by careful process design and strict quality control from the start. Through an analysis of QbD implementation tactics and results, this research seeks to support ongoing innovation and quality improvement in biopharmaceutical production in India. In order to increase India's competitiveness in the global market, it aims to guarantee the manufacture of biological products that are safe, effective, and of the highest quality and adhere to international standards.

1.1 Aims and Objectives

1. To assess the present state of Quality by Design (QbD) integration in Indian manufacturing processes for biopharmaceuticals.
2. To examine the specific approaches used by Indian biopharmaceutical producers to apply QbD guidelines.
3. To investigate the results of QbD adoption, with particular attention to how it affects product quality, regulatory compliance, and operational effectiveness in India.
4. To determine and investigate barriers, technological and regulatory, that stand in the means of QbD implementation in Indian biopharmaceutical manufacturing.
5. To offer suggestions for removing limitations that have been found and improving the effective utilization of QbD in Indian biopharmaceutical production.

1.2 Research Questions

1. To what extent is Quality by Design (QbD) integrated into Indian biopharmaceutical manufacturing procedures currently being carried out?
2. What specific strategies do Indian biopharmaceutical companies employ to apply QbD principles?
3. In Indian biopharmaceutical production, what are the effects of QbD execution on product quality, regulatory compliance, and operational efficiency?
4. What are the main statutory and technical hurdles preventing QbD from being used in Indian biopharmaceutical manufacturing?
5. What suggestions are there to improve the successful application of QbD in Indian biopharmaceutical manufacturing and overcome any challenges that have been identified?
6. How has the adoption of QbD in India been affected by the recent harmonization of CDSCO recommendations with worldwide standards?

7. What are the technical and financial understanding prerequisites for the biopharmaceutical sector in India to successfully deploy QbD?
8. How does the overall performance of QbD in pharmaceutical development and production depend on the quality of the excipients?
9. What is the potential for enhancing QbD techniques in Indian biopharmaceutical production through international collaboration and information sharing?

1.3 Research Hypothesis

This study assumes that certain techniques, such as multifaceted analysis, process analytics, and knowledge-management technologies, are essential for Indian biopharmaceutical producers to successfully use the concepts of Quality by Design (QbD). It is projected that the Indian biopharmaceutical industry will see notable gains in product quality, regulatory compliance, and operational efficiency as a result of utilizing such strategies. Biopharmaceutical companies can improve product quality, comply with regulatory standards set by organizations like the CDSCO, and optimize resource utilization by streamlining operations and proactively addressing critical quality attributes and process parameters through methodical process design and proactive handling. With recommendations to promote wider adoption of QbD principles and improve competitiveness and innovation in the industry, this study aims to bring insight into best practices and implementation-related issues related to QbD.

1.4 Scope and Limitations of the Study

This research offers a thorough examination centered on the implementation of Quality by Design (QbD) in the Indian biopharmaceutical industry. It assesses the degree of QbD adoption that is currently occurring in Indian manufacturing processes, looks at particular strategies and methodologies that manufacturers use, and looks into the effects that QbD implementation has on operational effectiveness, regulatory compliance, and product quality. In addition to comparing Indian practices with international norms and analyzing the effects of harmonizing CDSCO recommendations with global standards, the report identifies regulatory and technical hurdles to QbD adoption. It also evaluates the financial and technical requirements for a successful QbD deployment, looks into the significance of excipient quality, considers how international cooperation might advance QbD techniques, and offers suggestions for enhancing QbD's efficient application in Indian biopharmaceutical production.

The study does, however, have a few limitations. The study's geographic scope is restricted to the biopharmaceutical industry in India only, and its conclusions might not generalize to other countries. Due to differences in scale and capacity, the depth of study may be impacted by restricted access to sensitive or proprietary company data. Additionally, the difficulties and methods that have been identified may not apply to all biopharmaceutical businesses in India. The findings' applicability and relevance may be impacted by prospective changes in national and local laws over the study period. Variability in the infrastructure of different firms and the fluctuations in technology might cause variations in the results of QbD implementation. The amount of data that can be gathered and analysed may be limited by resource limitations, and even with efforts to maintain objectivity, researcher bias may affect how qualitative data is interpreted. Furthermore, certain discoveries may go out of date rather soon due to the biopharmaceutical industry's rapid evolution.

1.5 Relevance of Study

This study's scope includes a comprehensive analysis of Quality by Design (QbD) integration in the Indian biopharmaceutical sector only. Its objectives are to assess the degree of QbD adoption that is already occurring, explore certain strategies such as process-analytical techniques and multivariate analysis, and assess the effects on product quality, regulatory compliance, and operational effectiveness. The report highlights legal and technical barriers, offers suggestions for getting beyond them, and compares Indian procedures with international norms. In addition, it analyses the impact of recent regulatory alignments, appraises technical and financial requirements, and focuses on how excipient quality affects QbD success. The goal of this strategy is to increase QbD implementation and raise Indian biopharmaceuticals' level of global competitiveness. The significance of this resides in leading industry participants and policymakers towards enhanced manufacturing procedures, guaranteeing better, safer, and more effective biopharmaceutical commodities that satisfy international requirements. The fact that the study's conclusions might not apply to nations other than India is one of its limitations.

1.6 Outline of Dissertation

The following describes how the study is organized. The six chapters that make up the thesis's major body.

The study's goals and objectives are outlined in Chapter 1, which also includes analysing the effects of QbD on product quality and operational efficiency, as well as assessing the degree of QbD integration at the moment and looking into certain implementation methods. It emphasizes the study's relevance to international norms and its focus on the Indian context. The research hypothesis and study significance are presented at the end of the chapter.

The literature on QbD concepts and their use in the pharmaceutical sector is thoroughly reviewed in Chapter 2. To identify best practices, success stories, and knowledge gaps, the chapter reviews prior research on QbD deployment both internationally and in India. This literature review provides background information for the study, emphasizing the significance of quality by design (QbD) and the obstacles that the Indian biopharmaceutical industry has in implementing these principles. The research design and methodology followed to carry out the study are described in Chapter 3. To ensure the validity and reliability of the study, the chapter describes the sampling techniques and participant selection criteria. It also covers the study's ethical considerations and the data analysis methods, such as statistical and thematic analysis. To meet the goals of the study, this chapter offers a defined framework for the research methodology and data analysis.

The results of the analysis are presented in Chapter 4, which also includes detailed evaluations of the individual answers to the different questions ,the results reported are interpreted and their implications are discussed about the goals and objectives of the study. The study's main conclusions are outlined in Chapter 5, which also highlights the importance of QbD in raising the quality and efficacy of biopharmaceutical production in India. The chapter offers concluding recommendations for improving QbD adoption in India and identifies topics that should be investigated in the future to improve knowledge and use of QbD principles in the biopharmaceutical sector. The research findings and their greater implications for the sector and regulatory organizations are brought together in this conclusion.

1.7 Chapter Summary

In the first chapter of the dissertation, Quality by Design (QbD) in India is introduced and its significance in achieving the high international quality requirements is highlighted. Using the ICH principles as a guide, the chapter explores the QbD framework with particular emphasis on the CQAs, CMAs, and CPPs (critical process parameters). It highlights the role that statistical, analytical, and risk-management techniques play in ensuring consistent drug quality through QbD, while also addressing the difficulties that India has had implementing the strategy. This chapter describes the goals of the research, which include assessing the state of QbD integration, investigating techniques for implementation, examining results, identifying difficulties, and putting forward a research methodology. The study's significance in improving biopharmaceutical manufacturing methods in India is emphasized as it presents the research hypothesis in its conclusion.

CHAPTER TWO

REVIEW OF LITERATURE

2.1 Introduction

Quality by Design (QbD), developed more than ten years ago as a concept by the esteemed quality expert Dr. Joseph M. Juran, marks a radical change in the way medications and cosmetics are manufactured. The idea that quality should be ingrained in a product's design from the outset, addressing possible problems at their source instead of using reactive post-production procedures, is fundamental to quality by design. The Food and Drug Administration (FDA) of the United States has endorsed Quality by Design (QbD) and is an advocate for incorporating these concepts into the research, production, and regulation of pharmaceuticals. This method acknowledges that quality assurance cannot be achieved by greater testing alone; rather, quality must be included in all phases of the product lifecycle.

The evolution of Pharmaceutical QbD has been guided by key regulatory frameworks such as ICH Q8 (R2) on Pharmaceutical Development, ICH Q9 on Quality Risk Management, and ICH Q10 on Pharmaceutical Quality Systems. These guidelines, along with supplementary documents like the ICH Q1WG on Q8, Q9, and Q10 Questions and Answers, provide comprehensive direction on implementing QbD practices. Additionally, the outcomes of FDA-EMA's joint assessments of QbD elements in marketing applications have further shaped industry practices and regulatory expectations (Yu et al., 2014).

The primary objective of pharmaceutical enhancement through QbD is to meticulously design both products and their manufacturing processes to consistently deliver intended performance standards. Insights met from extensive research and developmental experiences in the pharmaceutical field contribute critical analytical perspectives, facilitating the establishment of design parameters, specifications, and robust manufacturing controls (Bendale et al., 2015). These insights also form the basis for effective quality risk management strategies, underscoring the proactive nature of QbD in ensuring product quality.

Over the past decade, numerous studies have explored various facets of QbD in pharmaceuticals, ranging from detailed conceptual explorations to discussions on implementation challenges and scope. These studies have collectively had a profound impact on the pharmaceutical sector, influencing industry practices and regulatory standards. This literature review synthesizes these findings, providing a thematic analysis that highlights the advancements, challenges, and future directions in the application of QbD within the pharmaceutical industry (Aru *et al.*, 2024).

2.2 Understanding Quality by Design (QbD)

The review paper by GK Raju clarifies the fundamental goals and components of the Quality by Design (QbD) framework in the pharmaceutical industry. QbD includes the design and comprehension of product and process characteristics, including Critical Material Attributes (CMAs) and Critical Process characteristics (CPPs), as well as the creation of a Quality Target Product Profile (QTPP) that specifies Critical Quality Attributes (CQAs).Its implementation is made easier by QbD techniques including Process Analytical Technology (PAT), Design of Experiments (DoE), risk assessment, and previous knowledge. The main objectives are to reduce product variability and defects, which will improve production and development efficiency as well as post-approval change management. Despite its potential, QbD adoption is still limited. Future studies should focus on refining these methodologies and ensuring broader regulatory and industry alignment to promote widespread adoption, thereby advancing pharmaceutical quality and efficiency (Raju, 2014).

“To optimize drug development processes by minimizing resources like time, money, and labour while ensuring high-quality outcomes, Singh and Sharma's article "Quality by Design (QbD) Approach in Pharmaceuticals: Status, Challenges and Next Steps" describes the QbD approach in the pharmaceutical industry. QbD, which has its roots in the ICH guidelines Q8, Q9, and Q10, focuses on the methodical identification of important quality attributes (CQAs) and how they affect the efficacy, safety, and quality of products. Significant steps include creating a target product quality profile (TPQP), ranking critical process parameters (CPPs) and critical material attributes (CMAs), and optimizing using response surface methodology (RSM). In contrast to traditional methods, QbD places more emphasis on process control and comprehension than end-product testing. Despite its benefits, the study lacks practical case examples, underestimates the complexity of integrating QbD across different stages of drug development, and does not sufficiently address the challenges of software implementation and regulatory compliance. Additionally, the generalizability of the findings may be limited by the absence of diverse pharmaceutical scenarios (Singh and Sharma, 2014).

In addition to stressing QbD's importance in guaranteeing product quality and regulatory compliance, the paper by Raghav et al. offers a thorough review of QbD in the pharmaceutical sector. Essential components including experiment design, method intent, and risk assessment are covered, with an emphasis on how they apply to different pharmaceutical processes and analytical methods. Continuous improvement is made possible throughout the product lifetime by integrating QbD concepts, improving efficiency, and lowering variability. The paper does, however, also identify some of the obstacles to the widespread implementation of QbD, such as disparate regulatory interpretations, internal company resistance, and technology limitations. Importantly, despite the advantages that Quality-by-Design (QbD) offers, such as fewer batch failures and improved process control, its practical application is complicated by resource requirements. Despite these challenges, QbD remains pivotal for aligning pharmaceutical development with regulatory expectations and achieving cost-effective, quality-driven production (Raghav *et al.*, 2014).

Pharmaceutical Quality by Design (QbD) is a complete strategy to ensure product quality by developing and understanding manufacturing processes, according to a review paper by Bendale et al. rather than testing things after they are created, QbD emphasizes integrating quality from the start. Finding the key process parameters (CPPs) and critical quality attributes (CQAs) for every unit operation are important elements. Significant advantages of QbD include improved product quality, cost effectiveness, and regulatory compliance. It is applicable to a number of industries, such as the creation of analytical methods, APIs, dissolution testing, stability testing, and bioequivalence research.. The ICH Guidelines Q8, Q9, and Q10, which offer frameworks for pharmaceutical development, quality risk management, and pharmaceutical quality systems, are the fundamentals of QbD. QbD can be difficult to adopt, despite its benefits. It necessitates a substantial upfront investment, in-depth product and process knowledge, and thorough risk assessment techniques like REM/FMEA. Furthermore, it can be difficult and resource-intensive to incorporate QbD concepts into current workflows, which may restrict its use in smaller businesses or underfunded research environments (Bendale *et al.*, 2015).

Quality by Design, or QbD, is a proactive and comprehensive approach to pharmaceutical development that combines process control and scientific knowledge to meet predetermined goals for product quality, according to an article by Sarasija et al. QbD guarantees reliable and consistent production by defining design spaces for critical process parameters (CPPs) and critical material attributes (CMAs) and by identifying critical quality attributes (CQAs) from the patient's point of view. Significant gains in product quality, regulatory compliance, and manufacturing efficiency have been demonstrated by the application of QbD. Nonetheless, obstacles including high expertise requirements, a large upfront cost, and the difficulty of incorporating QbD into current workflows continue to be obstacles. Subsequent research endeavors may concentrate on formulating more proficient and economical approaches for executing QbD within smaller pharmaceutical enterprises. Furthermore, investigating the use of cutting-edge technologies like machine learning and artificial intelligence in QbD may improve prediction and process optimization even further, opening the door to more creative and individualized pharmaceutical treatments (Sarasija *et al.*, 2015).

According to a review paper titled "A Review on Quality by Design" by Mogal et al., QbD has many advantages, including improved product quality, more regulatory flexibility, and increased productivity. It encourages innovation and continual improvement by helping businesses foresee and reduce risks, which reduces recalls and quality problems. Notwithstanding these benefits, implementing QbD has drawbacks, such as the requirement for a substantial time and resource commitment up front and possible organizational resistance to change. All things considered, QbD is an important framework that emphasizes risk management and science-based decision-making, supporting the changing pharmaceutical industry. Subsequent investigations may examine case studies of effective QbD deployment and enhance techniques to surmount adoption obstacles(Mogal *et al.*, 2016).

The integration of Process Analytical Technology (PAT) inside the Quality by Design (QBD) framework in pharmaceutical production is the main topic of the study paper by Trevor Murphy et al., named Pharmaceutical Manufacturing and the Quality by Design (QBD), Process Analytical technology (PAT) approach emphasizes how PAT-enabled real-time process monitoring and control may improve product quality, shorten cycle times, and streamline production procedures. The paper highlights the potential of NIR and Raman spectroscopy to provide continuous data for process knowledge and development and also explores their application in PAT systems. The upfront cost of sophisticated PAT systems and the difficulty of incorporating these technologies into current industrial settings present obstacles, too. Implementation challenges also include things like data management complexity, sensor accuracy maintenance, and calibration. The analysis indicates that QBD and PAT offer significant benefits in pharmaceutical development despite these obstacles, opening the door for more effective and compliance production procedures (Murphy *et al.*, 2016).

Quality by Design (QbD) is a science-based strategy that the pharmaceutical industry is progressively implementing to improve medication development and production, according to a study by Alam et al. The application of QbD to pharmaceutical quality assurance is examined in this paper, with a focus on defining the Target Product Profile (TPP), identifying Critical Quality Attributes (CQA), and putting Quality Risk Management (QRM) into practice. QbD tools, such Process Analytical Technology (PAT) and Design of Experiments (DOE), enable a thorough understanding of processes, guaranteeing regulatory compliance and consistent product quality. Enhanced productivity in production, lower costs, fewer product recalls, and simplified regulatory procedures are some benefits of QbD. Still, the study notes many drawbacks, including possible biases in the research papers chosen and the dynamic character of QbD procedures. Furthermore, it has been noted that evaluating formulation features and process parameters at the same time is difficult, making full integration of QbD difficult. The study also points out areas where raw material variability and environmental factors—both of which can affect product quality—have not been adequately taken into account. Despite these drawbacks, QbD continues to be a vital development in the pharmaceutical industry, supporting efficacy, safety, and regulatory flexibility (Alam *et al.*, 2016).

The article Overview of QbD: A Challenge to the Pharmaceutical Industry by Narke and Singh published in 2014 highlights the systematic method to finding important material qualities and process parameters of QbD, emphasizing its function from formulation and process development to regulatory approval. Nevertheless, one of the drawbacks is that QbD implementation initially requires a large investment in technology and experience due to its resource-intensive nature. Furthermore, it can be difficult to come to an agreement on design space and control mechanisms amongst various stakeholders, which slows down the pace of adoption and standardization. Despite all of these challenges, QbD has a lot to offer in terms of enhancing product quality and regulatory compliance (Narke and Singh, 2014).

Mistree et al.'s Quality by Design Approach for Pharmaceutical Product Development: A Comprehensive Review; of QbD which was published in 2020 highlights how crucial QbD is to contemporary pharmaceutical quality, compliant with ICH Q8, Q9, and Q10 requirements, and necessary for formulating procedures. To meet the regulatory standards needed for market approval, QbD principles and technologies are applied to the development of drug products and processes. In order to comprehend the links between input elements and critical analytical answers, QbD is also utilized in the creation and evaluation of analytical methods. This approach is similar to the process development methods found in ICH Q8 and Q9 (Mistree *et al.*, 2020) .

A study by Aru et al. Quality by Design (QbD) in pharmaceutical development: A comprehensive review; published on 2024 focuses on Quality by Design (QBD), a methodical, science-driven approach that guarantees constant product quality and revolutionizes pharmaceutical production. The report emphasizes the move toward a more methodical approach to the manufacturing of premium drugs in order to promote worldwide standardization and ongoing improvement. Some obstacles must be overcome in order to implement these changes, such as the industry's resistance to the anticipated changes. The combination of modern technology and global collaboration is anticipated to enhance QBD methodologies, guaranteeing an era of optimized procedures, enhanced adherence to regulations, and results that are patient-focused. QBD represents a dedication to quality, propelling the pharmaceutical sector toward increased efficacy, reliability, and patient care (Aru *et al.*, 2024).

A 2019 article titled Quality by Design (QbD) and its implementation in Pharma Industry describes Quality by Design (QbD) as a key FDA program in the pharmaceutical manufacturing industry. It emphasizes the incorporation of quality into the process of designing and developing products, instead of depending exclusively on testing the final product. Process robustness is ensured by QbD through risk assessment and control procedures that help identify essential material and process characteristics. By fostering uniformity in commercial manufacturing, this methodical approach improves product quality, efficacy, and safety. The Critical Process Parameters (CPP) and Critical Quality Attributes (CQA) identification, the Quality Target Product Profile (QTPP), and lifecycle management-based continuous improvement are important elements. By facilitating flexible manufacturing changes inside permitted design spaces and supporting regulatory compliance, QbD lowers the number of post-approval submissions and boosts regulator confidence. It includes the development of analytical methods, drug ingredients, and drug products. It encourages a proactive, scientific approach that lowers costs, improves patient safety, and supports ongoing advancements in pharmaceutical manufacturing techniques (Bureau, 2019).

2.3 Global Implementation of QbD in Biopharmaceuticals

QbD is driven by regulatory requirements for high-quality, cost-effective goods and concentrates on strong formulation and clinically applicable criteria. The Quality Target Product Profile (QTPP), process comprehension, scale-up, control tactics, and continuous improvement are important components. Implementing QbD requires the use of tools like Process Analytical Technology (PAT), risk assessment, and Design of Experiments (DoE). By extending these ideas to the creation of analytical methods, Analytical Quality by Design (AQbD) ensures consistent and dependable results through the use of tools like Analytical Target Profile (ATP), Critical Quality Attributes (CQA), and Continuous Method Monitoring (CMM). When Quality by Design (QbD) takes the place of traditional Quality by Testing (QbT), it becomes possible to effectively manage changes to products and processes, which in turn turns regulatory processes into scientific and risk-based evaluations (Sirohiwala *et al.*, 2023).

The target product's profile includes all its attributes, such as composition, physical state, formulation, medical benefits, application site, pharmacokinetics, pharmacodynamics, aerodynamics, toxicology, purity, and sterility, as well as its optimal and suboptimal efficacy states. Creating a manufacturing process necessitates having a thorough awareness of elements including production strategies, objectives, difficulties encountered in the past, and cost-effective ways to fix past errors. Manufacturing expertise is essential for this process because of its large effects and financial ramifications. A novel approach to medicine, Quality by Design (QbD) aims to advance treatments by thorough investigation and comprehension of therapeutic agents and illnesses. By using organized documentation that changes as knowledge and product requirements develop, QbD seeks to enhance process knowledge while adhering to regulatory requirements (Gandhimathi R, 2020) .

Quality by Design (QbD), which emphasizes customer satisfaction through better services, products, and processes, is crucial for contemporary pharmaceutical quality management, according to a review article by Sachin L. Darkunde et al. titled ‘A review on quality by design’ published in 2018, Quality is a top priority for regulatory agencies, and QbD integrates this idea into the whole product lifecycle. Target Product Profile (TPP) and Quality Target Product Profile (QTPP) definitions, identification of critical quality attributes (CQAs), and comprehension of critical material attributes (CMAs) and critical process parameters (CPPs) are all part of the strategy. The 2005 USFDA pilot program demonstrated the use of QbD in NDAs or new drug applications. By enabling method performance criteria registration rather than the method itself, with updates controlled by internal controls, QbD improves both product quality and regulatory flexibility. However it necessitates a large upfront cost as well as cultural changes. Notwithstanding obstacles, QbD emphasizes scientific rigor and risk management in line with the changing pharmaceutical landscape; further research is required to improve methods and overcome adoption barriers (Sachin L. Darkunde, 2020).

Bhise et al.'s Review on " Quality by Design Approach (QBD) for Pharmaceuticals " describes how QbD focuses on establishing critical quality attributes (CQAs) and critical process parameters (CPPs) to guarantee product quality. It is emphasized that risk assessment—which includes risk identification, analysis, and evaluation—is essential for connecting process parameters and material attributes to CQAs. The roles of tools such as the FMEA and Ishikawa diagram in risk assessment are discussed. Process analytical technology (PAT) and design of experiments (DoE) are commended for improving process control and knowledge. A more thorough assessment of potential obstacles, such as the difficulty of integrating QbD into current production processes and the requirement for substantial regulatory communication, would improve the evaluation, nevertheless. Furthermore, even though it emphasizes the theoretical advantages of QbD, more real-world examples and case studies would help to better show its efficacy and implementation. In general, the existing literature offers a strong basis for comprehending QbD; yet, it might benefit from a more comprehensive treatment of these pragmatic issues and obstacles (Bhise *et al.*, 2019).

The integration of Quality by Design (QbD) with Industry 4.0 in pharmaceutical manufacturing represents a cutting-edge approach to improving production efficiency and quality control through digital technologies, according to a study by E.V. Gijo on the Application of tools and techniques of QbD in the Pharmaceutical Process. Continuous process improvement and quick modifications can be made possible by using QbD principles more robustly through the use of data analytics and connected devices. Crucially, though, the integration has issues with compatibility between various digital platforms and data security. To properly manage these complexities, pharmaceutical businesses need to make large investments in both infrastructure and personnel training. Furthermore, the dependence on digital technologies demands strict regulatory compliance and validation, which can be resource- and time-intensive (Gijo, 2021).

Quality by Test (QbT) and Quality by Design (QbD) are two approaches to pharmaceutical quality management that have evolved throughout time. A study by Shrikant M. Mohurle et al. titled “Quality by Design (QbD): An Emerging Trend in Improving Quality & Development of Pharmaceuticals” highlights the proactive and analytical nature of QbD in drug development and production. Encouraging QbD, which is supported by the FDA's emphasis on Design of Experiments (DoE), is a thorough understanding of important material qualities and process factors that guarantee product quality. It encourages production simplification and efficiency, improving product consistency and lowering batch failure rates. The initial cost of technology and the knowledge needed for execution, as well as the difficulty in getting stakeholders to agree on design space and control tactics, are obstacles. Notwithstanding these obstacles, QbD has a lot to offer in terms of guaranteeing medication quality and regulatory compliance, which enhances patient safety and operational dependability in the pharmaceutical sector (Shrikant M. Mohurle, 2019).

The pharmaceutical industry's Quality by Design (QbD) concept stresses integrating quality into products from the development stage, rather than depending exclusively on end-product testing, according to an article titled Quality by Design -A Tool for Pharmaceutical Industry that Has No Near End by Joshi et.al. To guarantee consistent quality, this methodical approach entails creating a strong design space, defining a Quality Target Product Profile (QTPP), and determining Critical Quality Attributes (CQAs). By decreasing waste, errors, and unpredictability while improving process control and knowledge, Quality-Based Design (QbD) has demonstrated benefits above conventional methods. Despite its advantages, QbD has drawbacks, including the requirement for in-depth training and knowledge, technology constraints, and false beliefs about regulatory scrutiny prolonging approvals. To fully realize the promise of QbD and achieve wider acceptance, it will be imperative to improve technology solutions and bridge the gap between industrial practices and regulatory requirements (Joshi *et al.*, 2021).

The article "Quality by Design (QbD) approaches in current pharmaceutical set-up" by Mishra et al. highlights how QbD, which places a strong emphasis on a thorough understanding of formulation and manufacturing processes, has changed pharmaceutical development. In contrast to the conventional one-variable-at-a-time (OVAT) approach, QbD uses the Design of Experiments (DoE) to systematically analyze many variables at once. It is supported by regulatory agencies like as the FDA, EMEA, and ICH. Initial screening can benefit from lowresolution designs like Taguchi, Fractional Factorial Designs (FFDs), and Plackett-Burman Designs (PBDs), but nonlinear responses call for more intricate designs. The application of QbD results in a science-based evaluation of pharmaceutical quality, reducing batch testing through comprehension and management of the process. It provides a strong emphasis on ongoing design space improvement to guarantee high-quality, repeatable pharmaceutical products. QbD adoption has obstacles in spite of its benefits. It can be resource-intensive to require large amounts of baseline data, sophisticated statistical expertise, and close cooperation between industry and regulatory bodies. Additionally, businesses must undergo a cultural transformation in order to make the switch from traditional Quality by Testing (QbT) to QbD (Mishra *et al.*, 2018).

To improve market and operational excellence, Quality by Design, or QbD, became a standard for pharmaceutical manufacturing based on general Quality Management concepts, according to a comprehensive review by Grangeia et al. Complete adoption in commercial manufacturing is still rare, notwithstanding notable accomplishments. Continuous production holds the potential for increased flexibility and resilience, especially in granulation. The analysis highlights areas where QbD application is lacking, such as the independent examination of process parameters (PPs) and formulation attributes (FAs), which may minimize their interactions. It's common to ignore additional contributing elements like batch variability in raw materials and ambient circumstances. A comprehensive knowledge of the process is hampered by the limited integration of PPs across various unit operations. Further areas for methodological improvement are indicated by early inefficient optimization DoEs and single-tool RA methods. To properly utilize QbD in pharmaceutical development, more understanding and integration of these aspects are required. The study's limitations include the possibility of bias in some of the publications and the fact that QbD procedures are changing and might not be adequately represented in the examined literature (Grangeia *et al.*, 2020).

The pharmaceutical sector is gradually adopting Quality by Design (QbD) due to its methodical, scientific approach to drug research and production. The advantages of QbD in process optimization, guaranteeing regulatory compliance, and improving product quality are evaluated in this paper. Ishikawa Diagram, FMEA, and REM for risk assessment, as well as 2-level Full and Fractional Factorial Designs for screening, are commonly used tools in the analysis of sixty research papers. For optimization, Central Composite Design (CCD) is often used. A tendency toward continuous manufacturing, especially in granulation, and the management of raw material variability, as well as Retrospective QbD (rQbD) for historical goods, are being highlighted by emerging trends. Because QbD promotes a deeper understanding of product and process variables and is in line with FDA and ICH recommendations, it has a major impact on regulatory compliance. Nevertheless, there are still issues with completely integrating QbD, especially when it comes to concurrently researching process parameters (PPs) and formulation attributes (FAs). Other shortcomings include inadequate integration among manufacturing processes, which can mask important connections and a comprehensive understanding of the process, and inadequate attention to environmental conditions and raw material variability. Potential biases in the studies chosen for this evaluation and the dynamic nature of QbD practices—which might not be fully captured—are among its limitations. Furthermore, a significant initial knowledge and resource investment is necessary due to the complexity of QbD implementation. Notwithstanding these difficulties, QbD promises to be a significant breakthrough in pharmaceutical manufacturing, offering increased product quality, safety, and economy (Nunavath *et al.*, 2024).

To achieve consistent product quality, Quality by Design (QbD), which focuses on systematic process understanding and control, is crucial to modern pharmaceutical development. To create the Target Product Profile (TPP), Critical Quality Attributes (CQA), and control strategies, it incorporates concepts from ICH recommendations (Q8, Q9, Q10). By lowering variability, enhancing batch-to-batch uniformity, and streamlining manufacturing procedures, QbD increases efficiency. Faster medication development and fewer regulatory obstacles are made possible by its strong risk assessment and management procedures, which promote regulatory compliance. The complexity of integrating QbD across international operations, which necessitates a significant upfront investment in technology and knowledge, is one barrier, though implementation challenges also include changing regulatory demands and variable raw material availability. Unlike these drawbacks, QbD encourages continuous improvement throughout the product lifecycle, lowers costs, and improves product quality, all of which have the potential to yield substantial long-term advantages. QbD is a key component for producing safer, more effective pharmaceutical goods while guaranteeing sustainable production processes, and the pharmaceutical sectors are adopting it at an increasing rate (Khan *et al.*, 2024).

Quality by Design (QbD) is a systematic, scientific strategy that aims to improve product and process understanding and control in order to accomplish set quality targets, according to a review paper by Swain et al. The Target Product Profile (TPP), Quality Target Product Profile (QTPP), and Critical Quality Attributes (CQAs) are among the key components of QbD that are highlighted in this review. In order to guarantee constant product quality, it highlights how important it is to define design spaces for critical material attributes (CMAs) and critical process parameters (CPPs). The essential elements of quality by design (QbD) are covered, including several applications in pharmaceutical operations and risk assessment tools and design of experiments (DoE). A thorough overview and implementation roadmap for QbD in pharmaceutical development are provided by the review. Subsequent research endeavors may delve into the amalgamation of cutting-edge technologies such as artificial intelligence and machine learning to augment process optimization and prediction capacities. Furthermore, expanding the universal application of QbD could involve creating more cost-effective and efficient procedures for smaller pharmaceutical companies (Swain *et al.*, 2019).

The ICH Q8 R2 guidelines describe Quality by Design (QbD) as a methodical, scientific approach to drug development that combines process knowledge and control to meet predetermined quality goals. Critical Quality Attributes (CQAs), Critical Material Attributes (CMAs), and Critical Process Parameters (CPPs) design spaces, and the development of a Quality Target Product Profile (QTPP) are all prioritized in QbD. A key component of this strategy is the design of experiments (DoE), which improves product consistency and regulatory compliance, along with risk assessment tools. The evaluation also emphasizes how important digital control and documentation are to guaranteeing regulatory compliance and traceability. But putting QbD into practice can be resource-intensive, requiring a large initial outlay as well as in-depth understanding. Subsequent research endeavors might look into economic approaches for smaller enterprises and the integration of new technologies such as artificial intelligence and machine learning to boost process optimization and prognostic capacities, thereby expanding the scope and significance of quality by design in pharmaceutical development (Byrne, 2024).

The Quality by Design (QbD) paradigm, which is supported by the FDA, EMA, and ICH, has been adopted by the pharmaceutical industry. This marks a change towards a methodical, scientific, and risk-based approach to drug development, according to a review study by Simoes et al. QbD focuses on expediting R&D, improving manufacturing flexibility, lowering regulatory burdens, and comprehending formulation and manufacturing processes to ensure safety, efficacy, and quality. Even with benefits like lower regulatory monitoring and better product quality, the sector has not fully adopted it. To strengthen QbD's robustness, future research should incorporate sophisticated analytical methods and real-time monitoring. One of the limitations is the first implementation's complexity and resource demands, which call for a significant investment in technology and training. Furthermore, for wider use, industry and regulatory agreement on QbD practices and principles is necessary (Simões *et al.*, 2024).

Quality by Design (QbD) is a systematic approach to pharmaceutical development and manufacturing that attempts to ensure product quality by incorporating full scientific understanding and risk management. This is made apparent by the European Medicines Agency. Quality by Design (QbD) is a globally acknowledged approach that focuses on identifying and managing variability in the production process through statistical, analytical, and risk-management techniques. It makes use of process analytical technology (PAT), contemporary process-analytical chemistry, and multivariate analysis to improve product knowledge and guarantee that medications constantly fulfill predetermined quality criteria. The International Conference on Harmonization (ICH) introduced QbD concepts through recommendations that have been implemented globally. Agencies such as the FDA and EMA have collaborated to encourage consistent application and continual improvement in the pharmaceutical industry (EMA, 2024).

2.4 QbD Implementation in the Indian Biopharmaceutical Industry

Quality by Design, or QbD, is a systematic, risk-based strategy that has transformed quality assurance for pharmaceuticals. In order to ensure product safety, efficacy, and quality while increasing productivity, it places a strong emphasis on integrating quality considerations throughout the development process. The manufacture of products with consistent quality is made possible by QbD through the definition of critical quality attributes (CQAs) and their integration into manufacturing processes. Gained assurance in product quality, effectiveness, and regulatory compliance are some advantages. Although QbD is supported by international regulatory authorities, the Indian pharmaceutical industry is currently adjusting to its implementation. Its long-term advantages are becoming more widely acknowledged, which is why requests for more use and awareness are growing. To promote wider adoption of QbD in India and improve product quality and regulatory compliance globally, proactive steps including training and regulatory support are crucial (Rojhe and Kapoor, 2020).

The biopharmaceutical sector is moving toward gene and cell therapies, which calls for increased manufacturing failure rates, faster market delivery, and better medication quality requirements to maintain global competitiveness. A USP, DBT India, and CII seminar highlighted the need for sophisticated technologies, public-private partnerships, trained labour, and supportive legislation. It is suggested that biotechnology curricula be updated, that academia and industry collaborate more, that R&D funding be increased, that technology transfer be improved, and that regulatory frameworks be revised. The biopharmaceutical sector in India can use these tactics to build on its advantages and take the lead globally (Uppal *et al.*, 2022).

The quality by testing (QbT) strategy, which is the foundation of traditional pharmaceutical development, limits control over material and process variability and necessitates continuous testing. It is also resistant to change. Regulatory bodies support a change to quality by design (QbD), stressing a scientific method to ensure product quality, to overcome these problems. The quality by design (QbD) concepts, which improve comprehension of manufacturing processes and create a design space that preserves quality despite process modifications, are being adopted by the Indian pharmaceutical industry. By implementing QbD at every stage of the process—from design to manufacturing and quality assurance—high-quality medications are ensured, batch failures are decreased, and regulatory confidence is increased. This requires well-defined goals and efficient risk management (Kharb and Rathore, 2022).

Purohit et al.'s study, "Implementation of Quality by Design," offers a thorough analysis of QbD implementation in the pharmaceutical sector, with a particular emphasis on its use in several areas, including biologics, generics, clinical trials, and validation. It highlights QbD as a proactive strategy for guaranteeing product quality through the incorporation of scientific concepts into the procedures involved in medication development and production. The assessment provides light on many viewpoints from around the world, such as the importance of QbD in Asia and India, where implementing it is thought to be essential for improving regulatory compliance and market competitiveness. The paper critically highlights a number of advantages of QbD, such as more regulatory transparency, lower product variability, cost savings, and better-quality assurance. It does, however, also address issues like the early implementation costs and the requirement for thorough training and education for all sector stakeholders. In summary, the study acknowledges the potential of QbD to transform pharmaceutical manufacturing but also recommends continuous modifications and enhancements to these principles to maximize their efficacy in a variety of regulatory frameworks and operational scenarios (Purohit *et al.*, 2019).

The Central Drugs Standard Control Organization (CDSCO) in India has increased its emphasis on Quality by Design (QbD) in response to a global shift towards more severe pharmaceutical quality standards, according to an article by Sanjai Das. Excipients make up more than 90% of a medicine's makeup, and because of their inconsistent quality, they are a major cause of product recalls. For this reason, it is imperative that QbD be implemented early in the drug development process. Testing of the finished product is no longer the focus of regulations; instead, the entire production process—from sourcing ingredients to formulation—is being closely examined. Like the FDA and EMA, CDSCO has stepped up its oversight to make sure that good manufacturing procedures (GMPs) are followed. Significant gaps still exist in excipient regulation, a field that has historically received fewer resources. One of these gaps is the lack of attention paid to the effects of excipient quality on medication stability and patient safety, as seen by the many cases of subpar or counterfeit excipients resulting in fatalities that have occurred worldwide. Regulatory agencies are requiring thorough risk evaluations and improved excipient quality standards in order to close these gaps. Risks can be reduced and product quality can be improved by combining QbD with effective risk management and cutting-edge quality management techniques like Six Sigma and lean manufacturing (Das, 2018).

2.5 Critical Gaps in Studies Related to Quality by Design (QbD)

The essay by A Baldi et.al examines pharmaceutical quality management industrial practices, emphasizing several methodologies such as Total Quality Management, Six Sigma, and Quality by Design (QbD). The significance of regulatory requirements in guaranteeing the safety, effectiveness, and purity of pharmaceutical goods is emphasized. Quality by Design (QbD) is emphasized as a methodical strategy that incorporates quality into the design and development of products, emphasizing that quality ought to be designed in rather than tested out. Important QbD elements are covered, including setting the Target Product Quality Profile, determining Critical Quality Attributes, and managing Critical Process Parameters. The DMAIC process improvement methodology used by Six Sigma is also mentioned in passing in this article. Although it gives a general overview of various techniques to quality management, it doesn't go into detail into the particular tactics, difficulties, or results of implementing QbD in India (Baldi, 2015).

Analytical Quality by Design, or AQbD, is a systematic methodology that improves pharmaceutical analytical method development and validation. Jayagopal et al.'s study explores this concept. In order to build method operational design regions (MODR) and control techniques, it stresses integrating principles such as Critical Material Attributes (CMA), Quality Target Product Profile (QTPP), Critical Quality Attributes (CQA), and Critical Method Parameters (CMP) through the use of Design of Experiments (DoE). Although AQbD approaches are extensively examined in the paper, it does not directly address how Quality by Design (QbD) might be used to biopharmaceutical manufacturing in India. The knowledge gap is in the strategic application and results of QbD in the Indian biopharmaceutical setting, including the region's particular obstacles, regulatory considerations, and possible advantages. Overcoming this gap might offer information on how to raise the standard and productivity of biopharmaceutical manufacturing in India (Jayagopal, 2017).

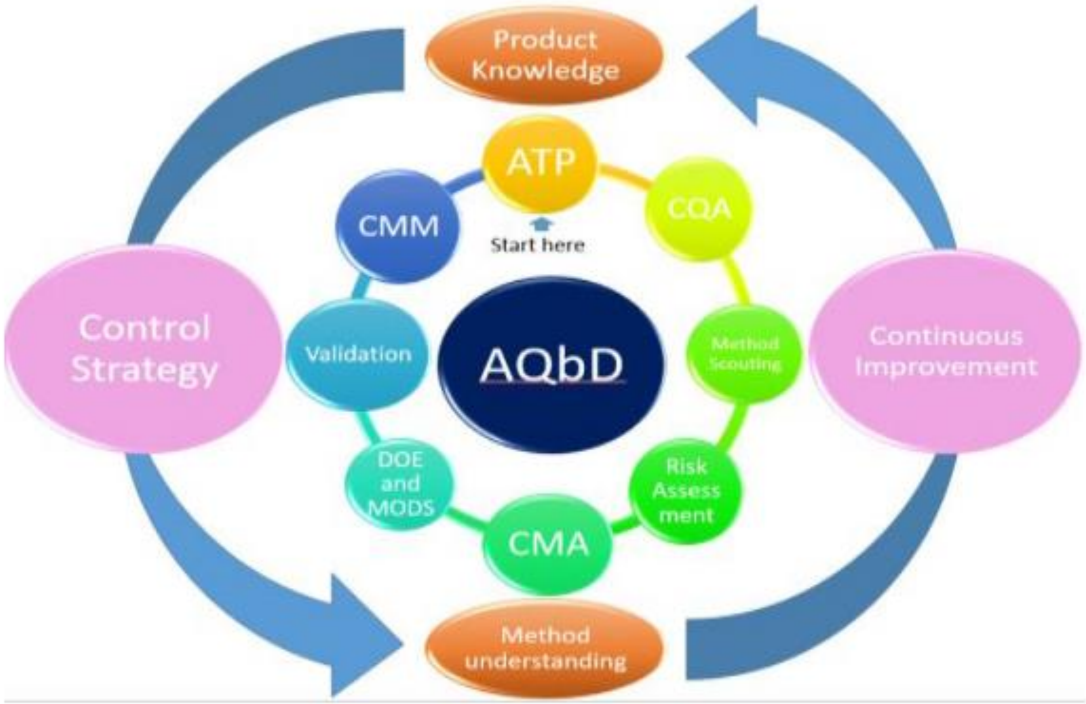

Figure: 4 AQbD Life Cycle(Jayagopal, 2017)

Pharma regulatory agencies stress the need for methodical techniques in the development of new drugs, where Quality by Design (QbD) and Analytical QbD (AQbD) are essential components. Gaps persist despite major progress. Numerous reviews of AQbD's application in separation procedures have been conducted, emphasizing the significance of developing risk-based methods. Comprehensive recommendations, however, are lacking for combining AQbD with cutting-edge analytical technologies that go beyond separation methods, including vibrational spectroscopy. Moreover, the literature currently in publication frequently ignores the real-world difficulties associated with implementing methods in a variety of laboratory settings and the dynamic nature of analytical requirements during the course of a drug's lifespan. Furthermore, in order to verify the Method Operable Design Region (MODR) and guarantee its practical application, more reliable approaches are required. Closing these gaps may result in more adaptable and efficient regulatory strategies, improving pharmaceutical quality control overall (Deidda, 2018).

Pharmaceutical companies can benefit greatly from Quality by Design (QbD), which promotes self-regulated flexibility while guaranteeing high standards and productive production. The ICH Q8 guidelines stress that design, not testing, should be the primary method of incorporating quality into goods. To optimize process parameters and guarantee product quality, QbD requires defining the Target Product Profile (TPP) and determining Critical Quality Attributes (CQA). There are still gaps even though QbD lowers failure costs and permits real-time product release. The existing body of literature frequently falls short of providing detailed instructions for combining QbD with cutting-edge analytical tools and neglects to address real-world implementation issues in a variety of production settings. Additionally, more reliable techniques for verifying and maintaining the design space are required due to the dynamic nature of pharmaceutical procedures. Filling up these gaps would improve QbD's effectiveness and adaptability, which would ultimately improve pharmaceutical quality control and lower variability (Verma, 2015).

In contemporary pharmaceutical development, Quality by Design (QbD) is a strong approach that emphasizes the incorporation of quality into the design of the product and process, as opposed to depending exclusively on testing and inspection. The main features of QbD are emphasized in this review, along with the identification of process factors and quality attributes that are crucial for every unit operation. The QbD framework relies heavily on the ICH Guidelines Q8, Q9, and Q10, which offer frameworks for quality risk management, pharmaceutical development, and quality systems, respectively. The development of dependable processes that regularly produce safe, high-quality medications is made easier by the QbD approach. It also emphasizes the significance of essential quality traits and a quality target product profile. By improving risk assessment and management procedures, QbD provides a great deal of regulatory freedom. The research covered here concentrate on the methods and instruments used in QbD, emphasizing its advantages and potential without addressing the problems that come with it (Powar, 2020).

2.6 Chapter Summary

This chapter explores into Quality by Design (QbD), a revolutionary idea that was first presented by Dr. Joseph M. Juran more than ten years ago. QbD incorporates quality into product design from the beginning instead of depending on post-production measures. Informed by thorough research and development, QbD indicates establishing quality across the product lifecycle and is endorsed by the FDA. It is governed by ICH Q8 (R2), ICH Q9, and ICH Q10. This chapter examines Quality by Design (QbD) principles and approaches, their worldwide application in the biopharmaceutical business, and their particular use in the Indian context. It pays attention to the advantages and difficulties encountered both domestically and internationally. It also points out important gaps in the existing literature, especially with relation to the Indian context, and emphasizes the necessity of additional study to improve QbD's comprehension and application.

CHAPTER THREE

METHODOLOGY

3.1 Introduction

A research method is a systematic approach and series of procedures used to collect, analyze, and interpret data to address a specific research question or hypothesis. These methods encompass the strategies, processes, or techniques employed in data collection and analysis to uncover new insights or enhance understanding of a topic.(Booth, 2024) It includes both the general plan of action and the specific actions taken to guarantee that the study is carried out in an organized and repeatable way. The current research employs a thorough methodology to investigate the application and consequences of Quality by Design (QbD) in the pharmaceutical sector, with a specific emphasis on biopharmaceuticals. To comprehend the guiding concepts, procedures, and legal frameworks for QbD activities, the study starts with a thorough analysis of the body of prior research. The success of QbD in enhancing product quality and compliance will be assessed with the use of statistical techniques and quantitative analysis. This methodology guarantees a comprehensive comprehension of how QbD might improve pharmaceutical manufacturing procedures and its larger impacts on the Indian industry. Each step of the methodology will be thoroughly explained in the parts that follow.

3.2 Research Paradigm

A research paradigm is an organized framework for carrying out studies that includes assumptions and viewpoints that direct theories and methods. It represents how scholars view the advancement of knowledge and establishes an outline for the research process. Important elements of research paradigms consist of:

Ontology: Views regarding the nature of reality, addressing the question of whether there is just one reality or many.

Epistemology: The study of knowledge; centres on the reliability, extent, and techniques of knowledge acquisition.

Research Methodology: The guidelines and procedures (such as data collecting and analysis) for examining the social realm and proving the reliability of created knowledge (helpinproject, 2019) .

A research paradigm is based on the combination of research methodology and research philosophy. Research philosophy encompasses the formulation of research hypotheses, nature, and knowledge as well as the presentation of the study's data type, knowledge of data sources, and theoretical analysis techniques.

3.2.1 Research Philosophy

A key component of business and economics research is research philosophy, which shapes presumptions and ideas about the best ways to collect, evaluate, and apply evidence linked to a phenomenon. It addresses the nature and evolution of knowledge, hence understanding the philosophical foundations of research is crucial for researchers. Recognizing the main research philosophies—interpretivism, positivism, realism, and pragmatism—offers a foundation for choosing the best techniques and approaches for a particular study. Research philosophy is linked to the nature of the investigation, assumptions, and knowledge. This issue needs to be addressed because different researchers may hold different beliefs about the nature of knowledge and truth, and philosophy enables us to understand these beliefs (brm, 2024) .

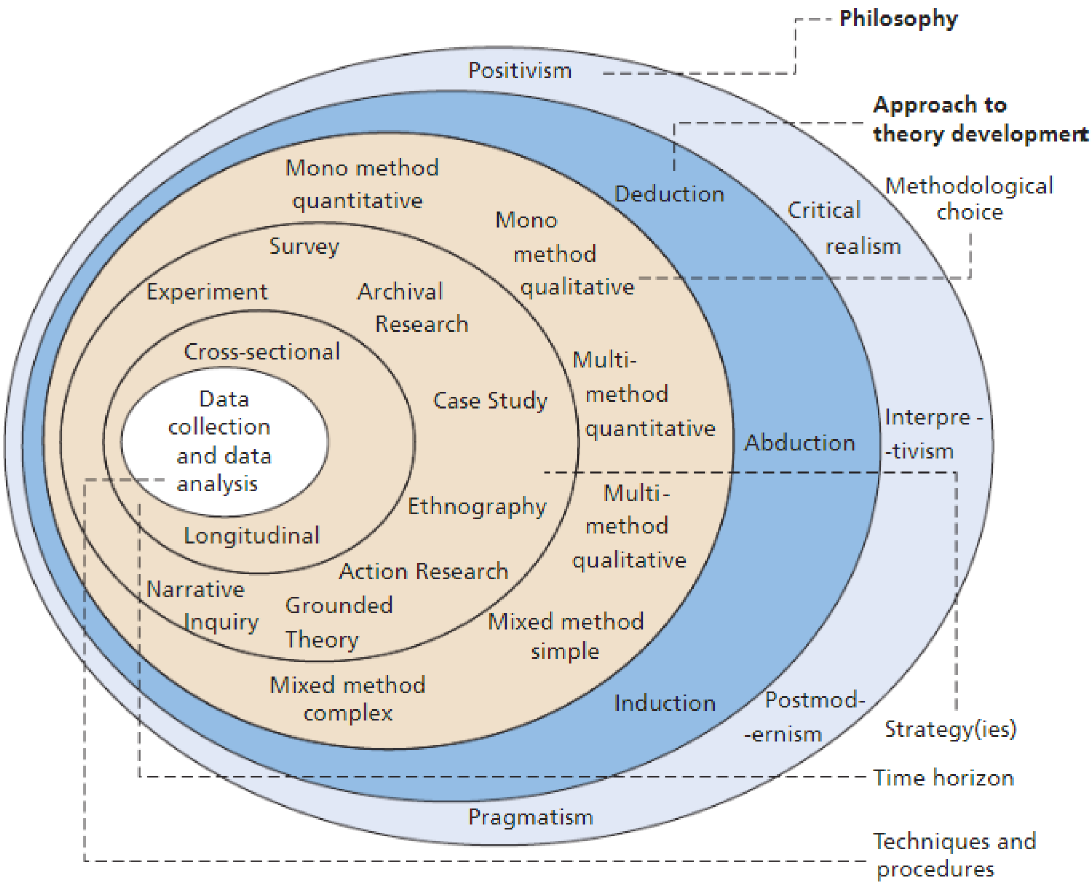

Figure 5: The Research Onion (Saunders *et al.*, 2019)

Every phase of the research process is predicated on presumptions regarding the nature of knowledge and the sources. The author's key presumptions, which form the foundation of the research approach, will be reflected in the research philosophy. In general, there are numerous branches of study philosophy that are connected to various academic fields. Specifically in the context of business studies, there exist four primary research philosophies:

- Pragmatism
- Positivism
- Realism
- Interpretivism

3.2.1.1 Pragmatism

A research philosophy known as pragmatism places a strong emphasis on usefulness and efficiency. Pragmatists think that knowledge comes from experience and that the goal of study should be to find solutions to issues that exist in the actual world. This school of thought frequently uses hybrid methodologies, fusing qualitative and quantitative techniques to provide a more thorough grasp of the subject under study.

3.2.1.2 Positivism

A research philosophy known as positivism places a strong emphasis on objectivity and the application of science to the study of social phenomena. This way of thinking emphasizes organized, quantitative processes, frequently employing statistical techniques for data analysis. According to positivism, only one reality can be quantified and understood, typically through quantitative methods. Positivist research uses statistical information gathered via measurement and observation, as well as a methodical examination of data sources. Researchers gather information, propose theories, and employ statistical evaluations to validate them. Establishing correlations between variables is positivism's primary goal; fundamental causes are not examined.

3.2.1.3 Realism

The research philosophy known as realism places great emphasis on comprehending the fundamental mechanisms and structures that give birth to social phenomena. Realists think that a combination of theoretical reasoning, experimentation, and observation can lead to knowledge. This way of thinking selects techniques based on their applicability, frequently combining qualitative and quantitative methods.

3.2.1.4 Interpretivism (Subjectivism/Constructivism)

A study philosophy known as interpretivism places a strong emphasis on the significance of comprehending the meanings and interpretations that people assign to social phenomena. Interpretivists think that thorough analyses of tiny, qualitative samples can yield knowledge. This school of thought uses qualitative techniques to better comprehend the subject under study, such as ethnography and case studies. It incorporates human interests into the study by using qualitative approaches to investigate these various points of view. In order to examine many points of view and concentrate on providing "why" answers, information is gathered through talks and interviews. Interpretivism recognizes the possibility of prejudice resulting from personal experiences and views (Mauthner, 2020).

In the context of my research topic, "How Can Quality by Design Enhance Biopharmaceutical Manufacturing in India? Exploring Strategies and Outcomes," I employed a positivist research philosophy. This approach aligns with the study's objective to investigate the impacts of Quality by Design (QbD) using systematic, scientific methods.

3.3 Research Approach

An investigation's overall strategy and methodology are included in the research approach. In the end, it guides the research from the initial idea to the final results. It involves the methods and procedures used to collect and evaluate data. The phrase "research approach" in scientific study can have varied meanings for different researchers. It usually refers to techniques for gathering and analyzing data, especially when separating qualitative and quantitative techniques. On the other hand, it is better understood as the study's general plan. Deductive, inductive, and abductive research methodologies are the three main categories into which they belong. There are unique qualities and uses for every strategy.

In a deductive approach, assumptions, theories, and hypotheses are tested for validity. Beginning with a theory, the researcher gathers information to assess its viability. Verifying or disproving the theory is the aim.

Using facts, an inductive approach creates new hypotheses and generalizations. Beginning with research questions, the researcher gathers and analyses data to find answers.

In an abductive approach, "incomplete observations," "surprising facts," or "puzzles" that are stated at the outset of the investigation are explained. Beginning with an observation or phenomenon, the researcher gathers and analyses data in an effort to explain (Grover, 2015).

For a study on "How Can Quality by Design Enhance Biopharmaceutical Manufacturing in India? Exploring Strategies and Outcomes," the researcher adopting a deductive approach involves starting with hypotheses related to the impact of Quality by Design (QbD) and systematically testing these through data collection and analysis.

3.4 Research Design and Strategy

A research design is a strategy employed to carry out a research design, which is a plan to address your research issue. Despite their differences, they are connected by the fact that sound research design makes sure the information gathered adequately answers the study question (DeBose, 2023). This study on "How Can Quality by Design Enhance Biopharmaceutical Manufacturing in India? Exploring Strategies and Outcomes" adopts a descriptive research design.

A descriptive survey is used to provide key information about individuals, including their views, intentions, and attitudes. The purpose of this design is to properly illustrate how Quality by Design (QbD) has affected the Indian pharmaceutical sector. A quantitative approach makes the most sense given the descriptive nature of the investigation. The researcher can gather data from a broad population by using a quantitative technique, which is necessary to get a complete picture of industry procedures and results.

The research strategy includes:

1. Literature Review: Establishing a theoretical foundation and identifying knowledge gaps.
2. Survey Design: Creating a structured survey to gather quantitative data on QbD practices.
3. Data Collection: Administering the survey to a representative sample of biopharmaceutical professionals in India.
4. Data Analysis: Using statistical methods to test hypotheses and validate the theoretical framework.
5. Reporting: Evaluating the effectiveness of QbD and providing recommendations for its implementation in the Indian biopharmaceutical sector.

This structured approach ensures a thorough examination of QbD's impact, contributing to a deeper understanding of its benefits and challenges.

3.5 Research Choice

Choosing the number and types of steps to be utilized in a study is known as research choice, as shown by the "research onion" model. Mono-method, mixed-method, and multi-method techniques are the three main choices.

1. Mono-Method: This refers to collecting and evaluating data using a single method. A study is said to be using a mono-method approach if it uses surveys as its only source of quantitative data. For instance, a researcher looking into customer satisfaction can just gather replies through questionnaires before statistically analyzing the information.
2. Mixed-Method: This strategy provides a thorough study by combining quantitative and qualitative methodologies. It could entail gathering quantitative data through surveys or experiments and qualitative data through focus groups or interviews. The research problem can be comprehended more broadly thanks to the mixed-method approach, which combines specific personal perspectives with numerical data.
3. Multi-method: Refers to the application of several techniques while maintaining a consistent qualitative or quantitative paradigm. For example, a research may use multiple quantitative approaches, such as experiments and surveys, or multiple qualitative approaches, such as focus groups and interviews. By assisting with data triangulation, the multi-method approach improves the validity and accuracy of the conclusions (Saunders *et al.*,2019).

In this study a mono-method approach is employed, utilizing surveys to gather quantitative data from a large participant pool. This approach is suitable for collecting standardized data that can be statistically analysed to evaluate the impact and effectiveness of Quality by Design (QbD) practices in the Indian biopharmaceutical industry.

3.6 Time Horizon

Research is classified into two types according to time frame horizons: cross-sectional and longitudinal. As is typical with most surveys, cross-sectional data consists of observations made at a specific point in time. Conversely, observations for a given variable across protracted time periods—years, quarters, months, or days—make up longitudinal data. Due to deadlines and time restrictions, the majority of academic research takes a cross-sectional method and concentrates on a certain time period. Longitudinal studies, on the other hand, track and measure changes or advancements across time. A cross-sectional technique will be used for this study because it must be finished within a certain time frame (Saunders *et al.*, 2019).

3.7 Study Population and Sampling

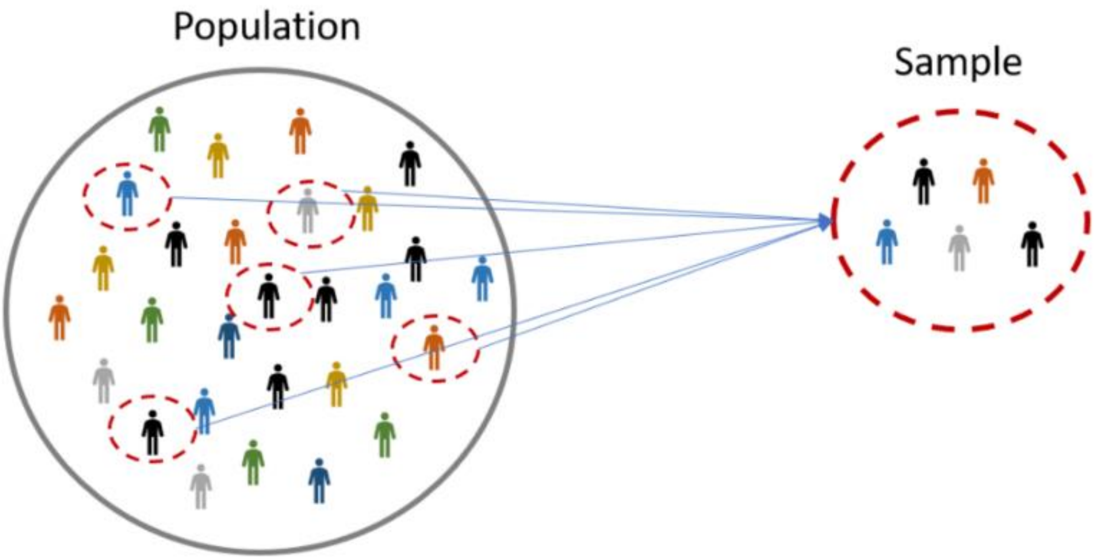

Figure 6: Sample size (Omniconvert, 2023).

To ensure that the survey results fairly represent the intended target group, the research population and sampling technique are essential. The number of completed survey responses that should fairly represent the views or actions of the entire population being studied is referred to as the sample size. The target population in this study is carefully defined to prevent the selection of an excessively big or restricted group. The actual population from which the sample is taken is represented by the sampling frame, which is typically derived from databases or lists that already exist. It is crucial to highlight that due to practical constraints or limited availability of data, this frame may not match the intended population.

The target population's characteristics and the study's goals are taken into consideration while selecting the method of sampling. Because it shows the chance that the true population parameter is inside the error margin, the confidence level is very important. A 95% confidence level, for example, indicates that 95% of the time, the true value would fall within the estimated range if the study were to be repeated. The entire population size is taken into account when calculating the sample size, and modifications are made for smaller populations. For conservative estimations, the sample ratio, also known as the expected outcome proportion, is frequently set at 50% (Martínez-Mesa *et al.*, 2014).

In this study, a sample size of 126 participants was determined to ensure accuracy. The questionnaire for a survey, distributed via email and social media platforms including LinkedIn, included 32 questions divided into 8 different sections. This approach aims to gather reliable data that represents the broader population's views on the topic of "How Can Quality by Design Enhance Biopharmaceutical Manufacturing in India?"

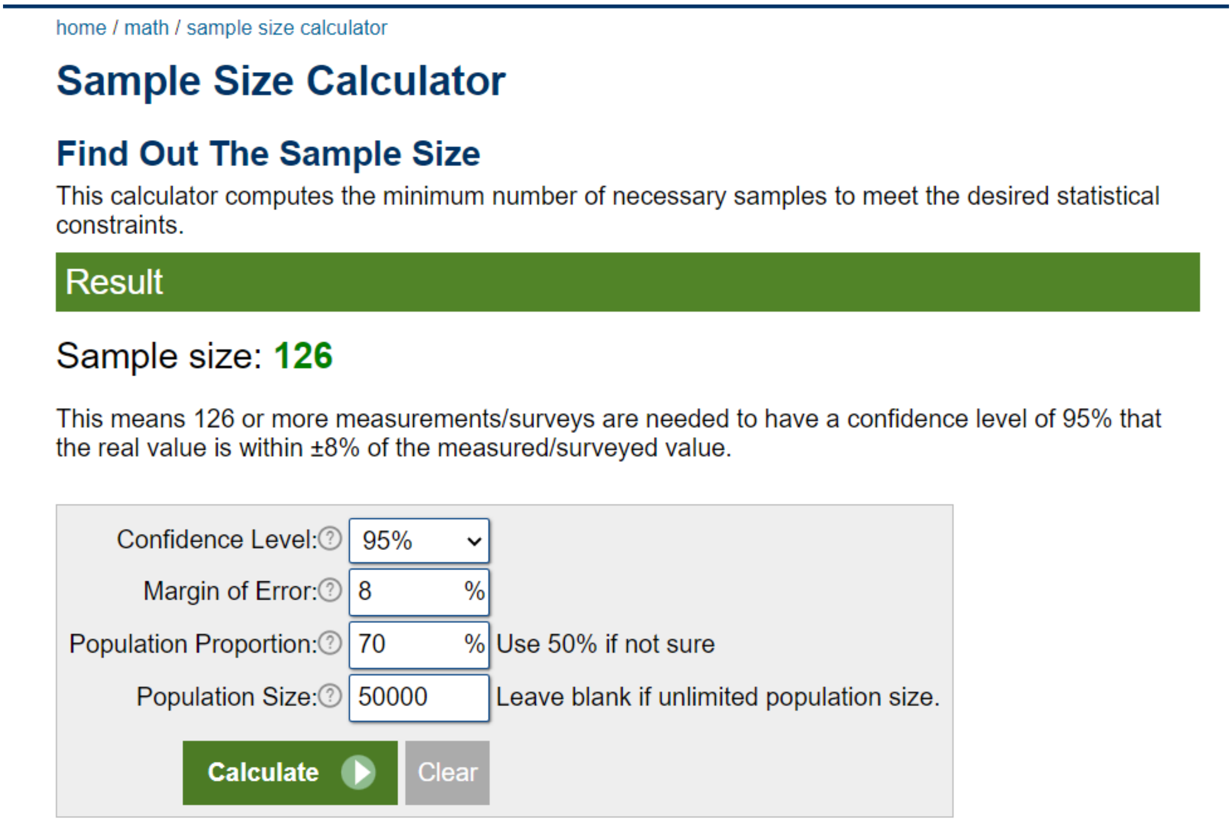

Figure 7: Sample Size Calculation

3.8 Data Collection and Analysis

Data collection is a crucial step in the research process that includes gathering relevant details about the topic being studied. There are several techniques that can be used, such as focus groups, questionnaires, interviews, and observation. The research design and particular study objectives serve as a guidance when choosing a suitable data collection method. A questionnaire has been selected as the main data collecting tool for this study since it is effective in gathering pertinent data from a large number of participants. There will be both closed-ended and open-ended items in the semi-structured questionnaire. This design makes it possible to gather vast information, allowing participants to give thoughtful answers and making it easier to quantify responses for analysis. The questionnaire is an adaptive tool for this study since the open-ended questions will gather qualitative insights and the closed-ended questions will yield measurable data points (Paradis *et al.*, 2016).

Following the collection of data via the questionnaires, descriptive statistics—more particularly, frequencies and percentages—will be used to examine the data. This method will assist in evaluating the accuracy and distribution of the data gathered, giving a comprehensive picture of the opinions and experiences of the respondents. The data will be visually represented with the help of tables and charts, which will facilitate the identification of patterns and trends. The meaning and interpretation of the gathered data are determined by the technique and analytical approach, which are crucial. Meaningful explanations and conclusions about the topic matter will be produced by the research through the application of appropriate descriptive statistics. This methodical approach to data analysis improves the study's overall validity and credibility by ensuring that the conclusions are excellent and reliable. and appropriate for the participants' response.

3.9 Ethical Considerations

In the study "How Can Quality by Design Enhance Biopharmaceutical Manufacturing in India? Exploring Strategies and Outcomes," ethical considerations are crucial. Indian regulatory personnel, process engineers, senior executives, and quality assurance managers selected based on their QbD competence are among the participants. Their choice guarantees relevant and accurate information. Professional networks will be used to approach participants, and electronic informed consent will be obtained, offering voluntary participation and eliminating without penalty. A semi-structured online questionnaire intended for both quantitative replies will be used to gather data.

Data will be kept on secured, password-protected platforms that are only accessible by authorized personnel in order to preserve privacy. In accordance with institutional standards and the GDPR, the data will be kept for five years before being safely deleted. Encrypted data management, compliance with GDPR, and country regulations on privacy all contribute to maintaining confidentiality. By implementing these preventative measures, research ethics requirements adhere to and participants' rights to confidentiality, security, and informed consent are protected.

3.10 Conceptual Framework

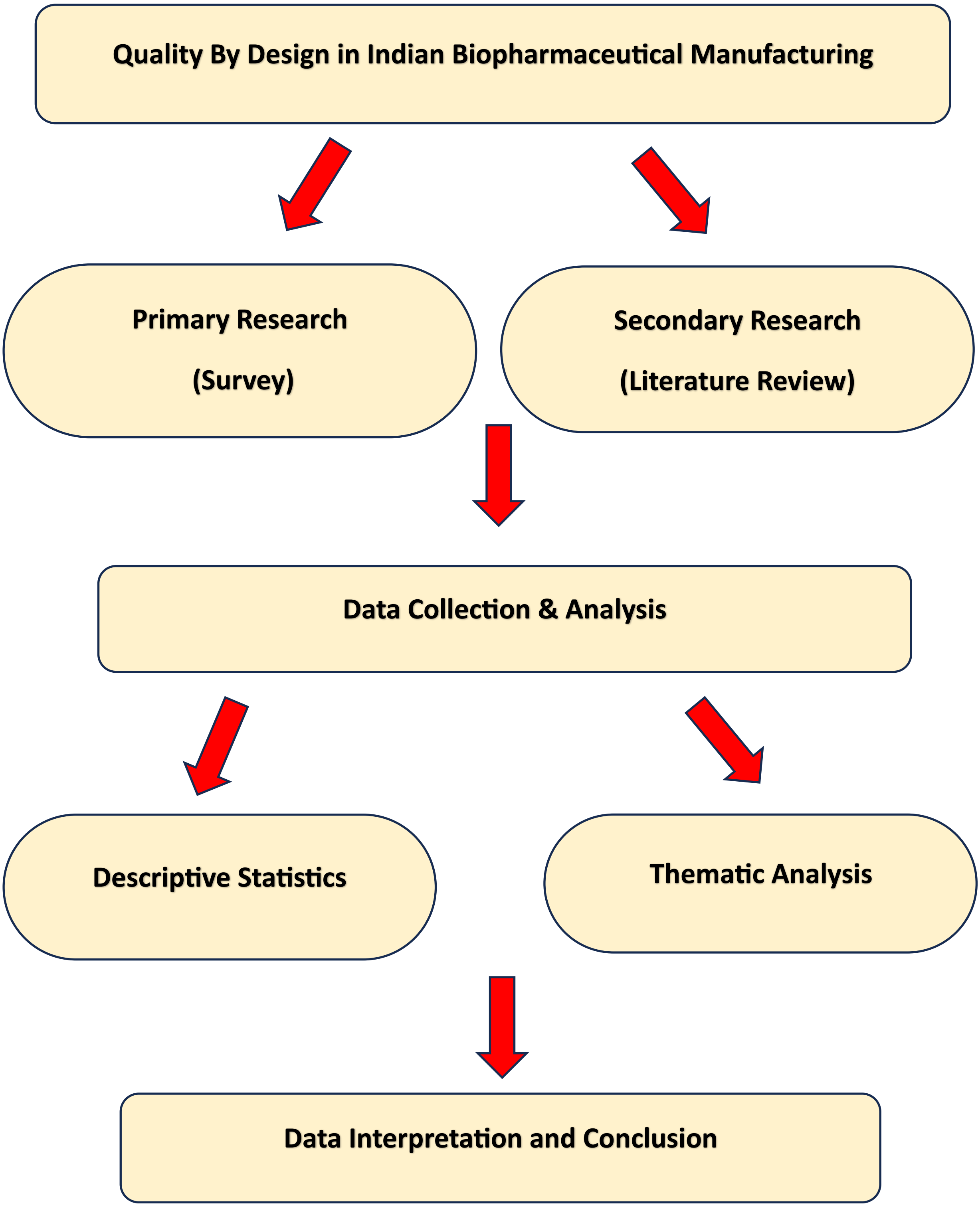

Figure 8: Conceptual framework of the study

CHAPTER FOUR

FINDINGS AND ANALYSIS

4.1 Introduction

This chapter presents the analysis and interpretation of data collected through a survey conducted over two weeks using Google Forms. The survey targeted professionals within the Indian biopharmaceutical industry, focusing on the implementation and impact of Quality by Design (QbD) in manufacturing processes. The survey received a total of 111 responses, providing a robust data set for analysis.

The analysis is structured in two main sections. The first section covers the demographic analysis, which aims to understand the background of the respondents, including their roles, experience, and the organizations they represent. This demographic context is crucial as it provides insight into the perspectives from which the respondents view QbD implementation.

The second section focuses on objective-wise analysis, where the data is examined in relation to the specific objectives of the study. This includes assessing the current level of QbD integration in Indian biopharmaceutical manufacturing, exploring the strategies employed by companies, analyzing the outcomes of QbD adoption, and identifying the challenges faced during implementation.

The findings from these analyses will provide a comprehensive understanding of the effectiveness of QbD in enhancing product quality, regulatory compliance, and operational efficiency in the Indian biopharmaceutical sector.

4.2 Demographic Considerations

4.2.1 The Distribution of Respondents According to Their Respective Roles

Respondents	Frequency	% Frequency
Quality Officer	60	54.1%
Process Engineer	13	11.7%
Senior Management	17	15.3%
Regulatory Compliance Officer	7	6.3%
Others	14	12.6%
Total	111	100.0%

Table 4.2.1: The various roles of the respondent from the survey questionnaire

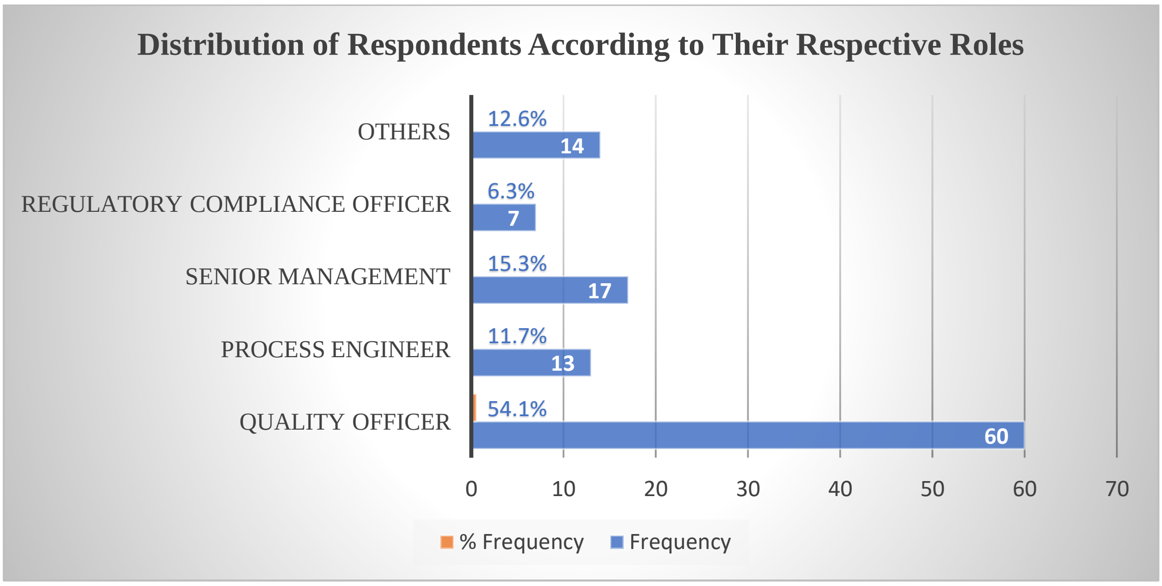

Figure 4.2.1: A clustered bar chart representing the number and percentage of the respondents to each category

The survey's demographic data reveals that a significant portion of the respondents, 54.1%, are Quality Officers. This is the largest group represented, underscoring the critical focus on quality within the sample. The next largest group is Senior Management, comprising 15.3% of respondents, indicating that a substantial portion of the survey participants are involved in high-level decision-making processes. Process Engineers represent 11.7% of the respondents, while Regulatory Compliance Officers make up 6.3%. The remaining 12.6% of respondents fall into the "Others" category, which likely includes a variety of roles not explicitly listed in the survey options. This diverse representation across roles provides a comprehensive view of Quality by

Design (QbD) practices from various functional areas within the biopharmaceutical industry. The strong representation of Quality Officers aligns well with the study's focus on QbD, as these professionals are typically at the forefront of implementing and managing quality frameworks.

4.2.2 Experience in Biopharmaceutical Industry

Experience In Years	No of Participants	% of Experience
Less than 5 years	71	64.0%
5-10 Year	26	23.4%
10-15 year	12	10.8%
More than 15 years	2	1.8%
Total	111	100.0%

Table 4.2.2: Respondents' Experience in the Biopharmaceutical Industry

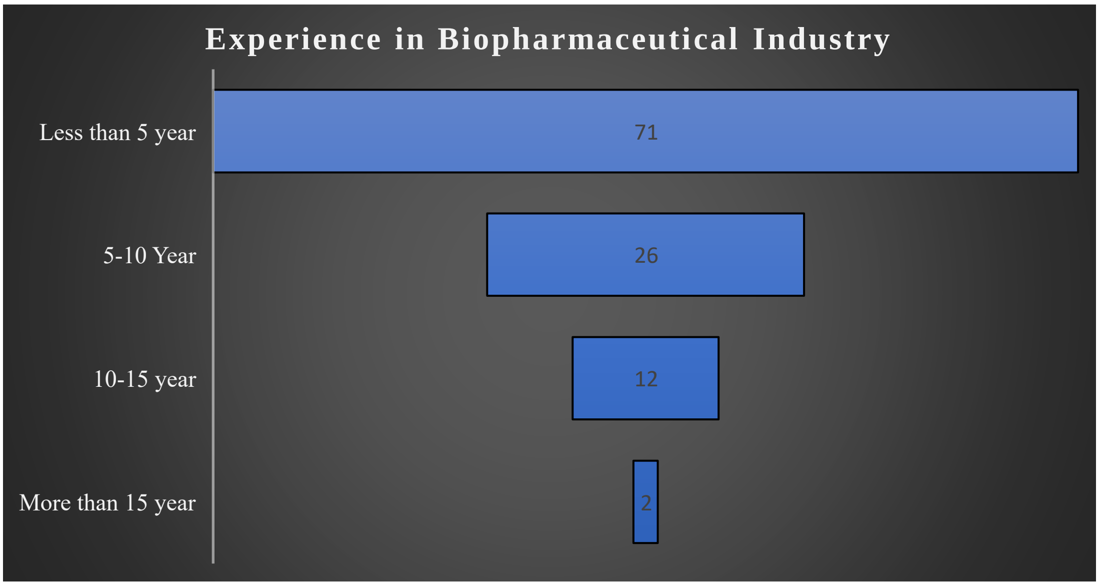

Figure 4.2.2: A funnel chart represents the number of years of experience among the participants

The majority of respondents, 64.0%, have less than 5 years of experience in the biopharmaceutical industry, indicating that the survey primarily captures the perspectives of relatively new entrants or younger professionals in the field. This is followed by 23.4% of respondents who have between 5 and 10 years of experience, providing a balance between fresh perspectives and mid-level industry insight. Only 10.8% of the respondents have 10 to 15 years of experience, and a mere 1.8% have more than 15 years of experience, reflecting a smaller representation of highly seasoned professionals in the sample. This distribution suggests that the implementation of QbD may be more prevalent among newer professionals or that the industry's workforce has seen a significant influx of newer talent, who are potentially more attuned to modern quality management practices.

4.2.3. Size of Organization

Size of Organizations	No: of Participants Worked	Average of Participants worked
Medium(50-200 employees)	54	48.6%
Large(more than 200 employees)	37	33.3%
Small(less than 50 employees)	20	18.0%
Total	111	100.0%

Table 4.2.3 Distribution of Respondents by Size of the Organization

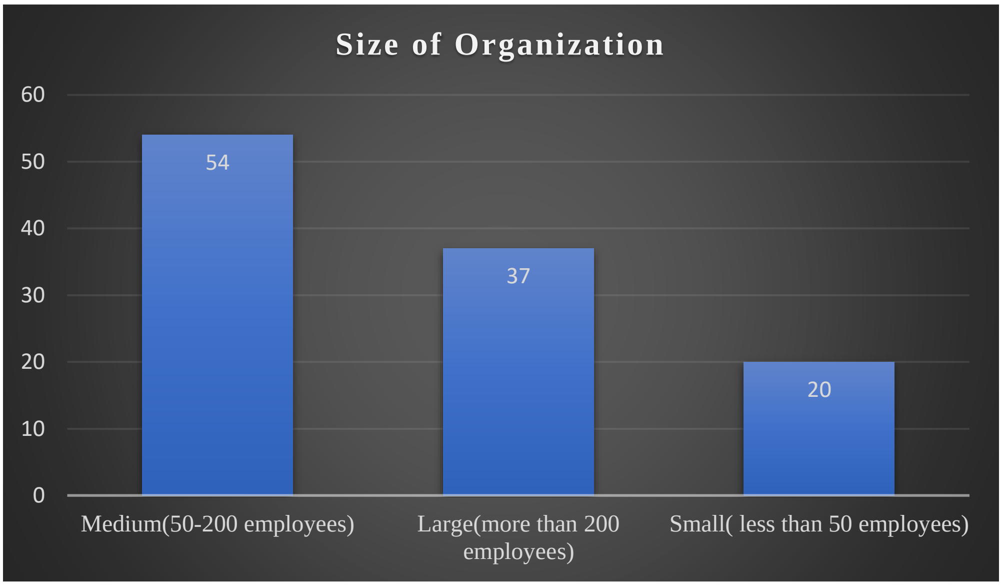

Figure 4.2.3: A clustered column chart represents the number of participants and the average number of participants by organization size.

When examining the size of the organizations represented in the survey, it is evident that nearly half of the respondents (48.6%) work in medium-sized organizations, defined as those with 50 to 200 employees. Large organizations, with more than 200 employees, account for 33.3% of the respondents, while small organizations, with fewer than 50 employees, represent 18.0%. This distribution suggests that QbD practices are being adopted across organizations of varying sizes, with a slightly higher representation from medium-sized companies. The inclusion of responses from both large and small organizations provides valuable insights into how the size of a company might influence the adoption, implementation, and outcomes of QbD practices in the biopharmaceutical industry.

Among the 111 respondents, the most commonly manufactured biopharmaceutical products are Oral Dosage Form (66.7%) and Injectables (48.6%). Topical Dosage Forms are produced by 19.8% of respondents, while 11.7% indicated their companies manufacture other types of biopharmaceutical products. This indicates a strong focus on oral and injectable products, with some diversity in other dosage forms within the industry.

4.2.4 Participants' Experience Under Different Regulatory Categories

Regulatory Bodies	No: of company function (Employees Worked)	Proportion of Participants
FDA	58	26.9%
GMP	75	34.7%
EU	30	13.9%
CDSCO	49	22.7%
Others	4	1.9%
Total	216	100.0%

Table 4.2.4 Distribution of Participants' Experience Across Various Regulatory Categories

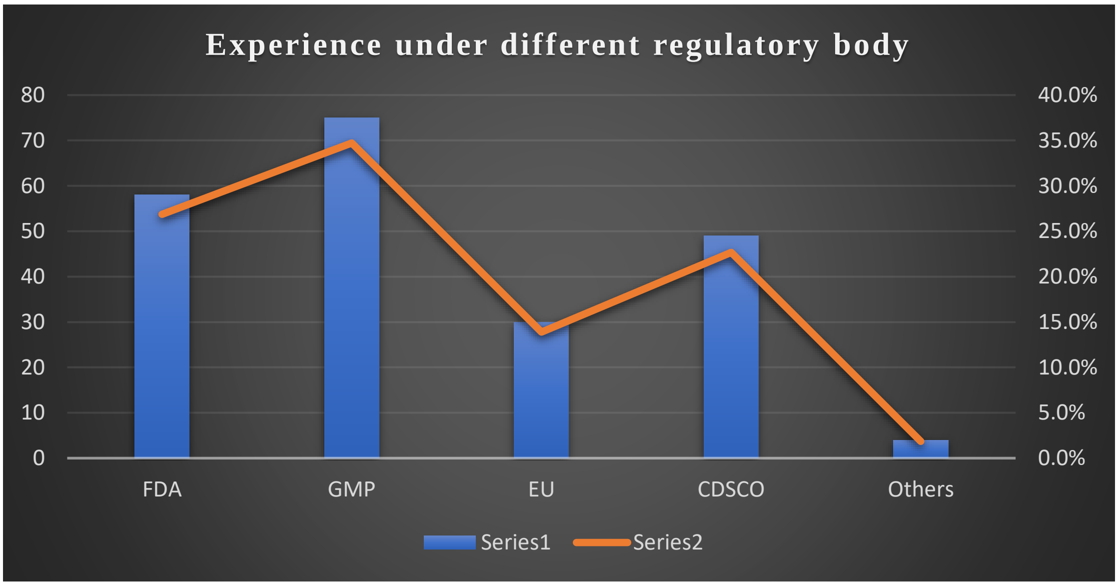

Figure 4.2.4: The clustered column chart indicating the proportion of participants working under each regulatory body

The table and chart illustrate the distribution of participants' experiences across various regulatory bodies, acknowledging that the same respondents might have worked under multiple regulatory frameworks.

- FDA (Food and Drug Administration): 58 experiences (26.9%) are associated with FDA regulations, highlighting its significance, especially for companies involved in global markets.
- GMP (Good Manufacturing Practice): The largest number of experiences, 75 (34.7%), fall under GMP standards, reflecting a widespread emphasis on maintaining high-quality manufacturing practices.
- EU (European Union Regulations): 30 experiences (13.9%) are under EU regulations, indicating that a portion of companies are engaged in the European market.
- CDSCO (Central Drugs Standard Control Organization): 49 experiences (22.7%) are linked to CDSCO, underscoring the importance of local regulatory compliance in India.
- Others: A small number, 4 experiences (1.9%), fall into the "Others" category, representing companies under different or multiple regulatory bodies. (PICS, Malaysia, Singapore)

The data reveals that GMP and FDA are the predominant regulatory frameworks experienced by participants, suggesting a focus on both global market compliance and stringent quality standards. The significant representation of CDSCO reflects the relevance of adhering to local regulatory requirements in India. The EU and other categories, although smaller, indicate specific market engagements or regulatory overlaps among participants.

4.3 Analysis of the objectives gained from the Survey Questionnaire

4.3.1 Analysis of Objective 1: Assessing the current level of familiarity and integration of Quality by Design (QbD) Principles among the respondents.

4.3.1.1 Familiarity with Quality by Design (QbD) Principles

Question asked to the participants: How familiar are you with Quality by Design (QbD) principles?

Familiarity level	No: of participants	Proportion of Familiarity
Familiar	58	52.3%
Very Familiar	33	29.7%
Somewhat Familiar	18	16.2%
Not Familiar	2	1.8%
Total	111	100.0%

Table 4.3.1.1 The comprehension and familiarity of respondents with QbD principles

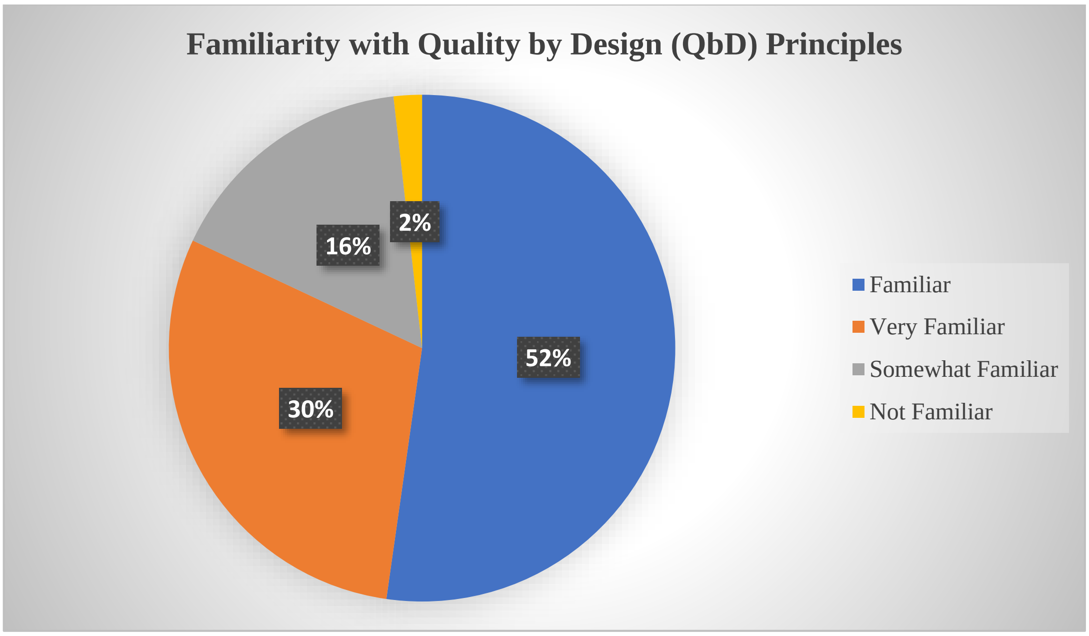

Figure 4.3.1.1 The Pie Chart representing the extent of Participants' Familiarity with QbD Principles

The survey results reveal a high level of familiarity with QbD principles among the participants. A majority, 52.3%, of respondents identified themselves as "Familiar" with QbD, indicating that they have a solid understanding of these principles and likely apply them in their professional roles. Following this, 29.7% of the participants reported being "Very Familiar" with QbD, suggesting that nearly a third of the respondents possess an in-depth knowledge of QbD, possibly gained through extensive experience or specialized training.

Interestingly, 16.2% of the respondents are "Somewhat Familiar" with QbD, which indicates that while they have some awareness of QbD concepts, they may not be fully comfortable with all aspects of its application. This group could benefit from further training or exposure to QbD practices. Only 1.8% of the participants indicated that they are "Not Familiar" with QbD principles, suggesting that the vast majority of respondents have at least some level of understanding of these key quality management concepts. That is the percentage of people who are not even familiar is too small.

4.3.1.2 Extent of QbD Integration

Question asked to the participants: What extent of a QbD integration is there in the production processes of your company?

QbD integration Level	No: of Respondents	Percentage
Completely integrated	43	38.7%
Primarily Integrated	39	35.1%
Partially Integrated	29	26.1%
Total	111	100.0%

Table 4.3.1.2: The varying degrees of integration of QbD principles within organizations.

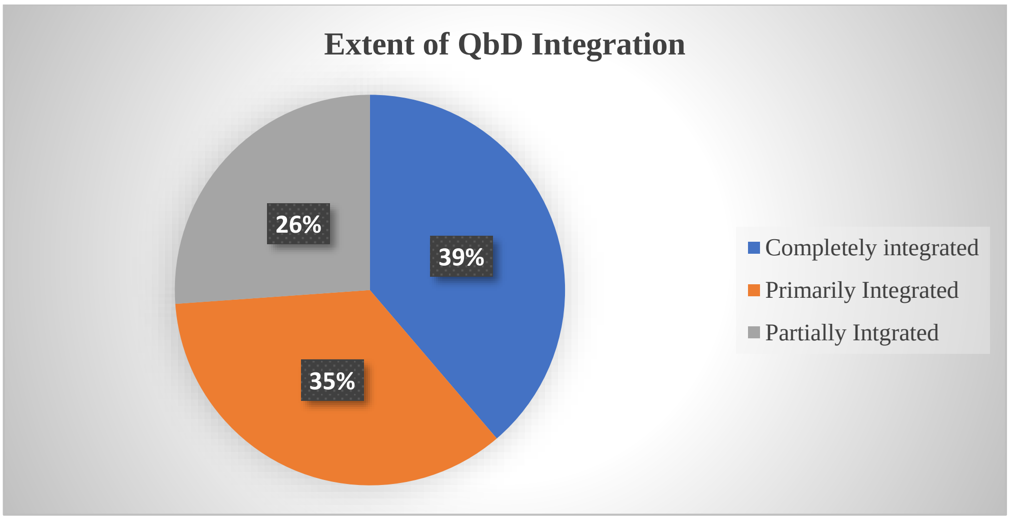

Figure 4.3.1.2 Pie Chart representing the Extent of QbD Integration in Organizations

Regarding the extent to which QbD principles have been integrated into their organizations, the data shows a significant level of adoption. 38.7% of respondents reported that QbD is "Completely Integrated" within their processes, while 35.1% indicated that it is "Primarily Integrated." This demonstrates that the majority of organizations represented in the survey have embedded QbD into their core manufacturing and quality processes. Another 26.1% of respondents noted that QbD is "Partially Integrated," suggesting that while some aspects of QbD are in place, there may still be room for further integration. The overall high level of QbD integration indicates a strong commitment to maintaining quality and regulatory compliance in biopharmaceutical manufacturing.

4.3.1.3 QbD Aspects Implemented by the Company

Question asked to the participants: Which aspects of QbD has your company implemented?

QbD Principles Adopted	Company Response	% of Response
Quality Target Product Profile (QTPP)	57	15.6%
Critical Quality Attributes (CQAs)	78	21.3%
Critical Process Parameters (CPPs)	66	18.0%
Risk Management	72	19.7%
Process Analytical Technology (PAT)	44	12.0%
Continuous Process Verification (CPV)	49	13.4%
Total	366	100.0%

Table 4.3.1.3 Comprehensive Overview of QbD Aspects Implemented by Companies

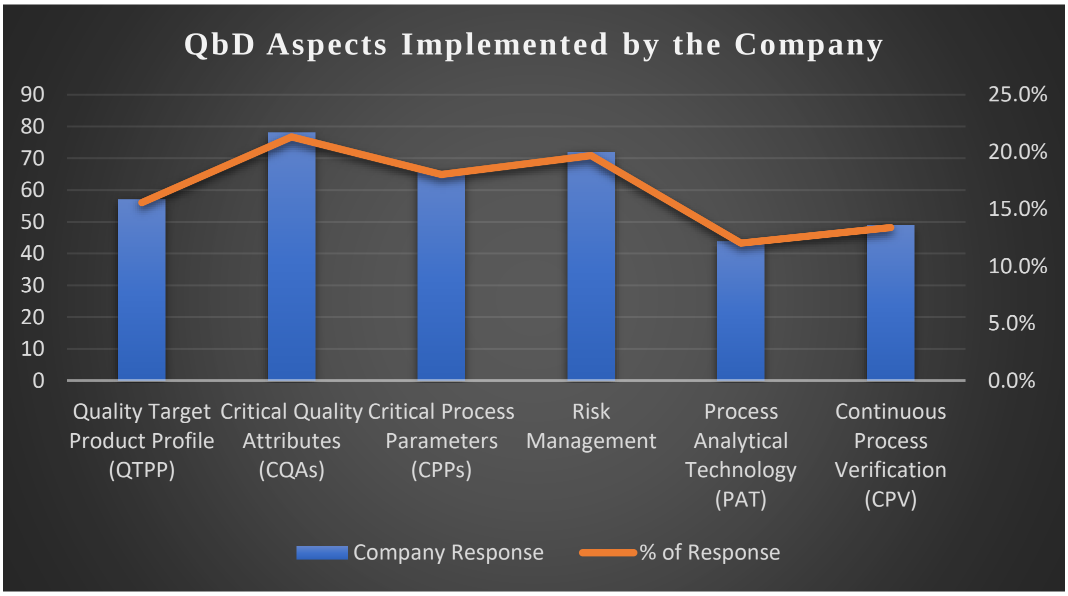

Figure 4.3.1.3 A clustered column chart representing the QbD aspects adopted by the companies

The data reflects the variety of Quality by Design (QbD) principles that companies have adopted. The most commonly implemented aspect is Critical Quality Attributes (CQAs), with 78 responses, representing 21.3% of the total. This indicates that many companies prioritize defining and monitoring CQAs to ensure that their products meet desired quality standards.

Following CQAs, Risk Management is the second most implemented aspect, with 72 responses (19.7%). This suggests a strong focus on identifying and mitigating risks throughout the manufacturing process to maintain consistent product quality and regulatory compliance.

Critical Process Parameters (CPPs) are also widely adopted, with 66 responses (18.0%), indicating that companies emphasize controlling process variables that could impact product quality.

Quality Target Product Profile (QTPP), which received 57 responses (15.6%), highlights the importance of defining the desired product characteristics at the development stage to guide the manufacturing process.

Less frequently implemented are Continuous Process Verification (CPV) and Process Analytical Technology (PAT), with 49 (13.4%) and 44 (12.0%) responses, respectively. These aspects involve ongoing monitoring and control strategies that ensure product quality is maintained throughout the manufacturing process, indicating that while these technologies are recognized, their adoption may still be growing.

4.3.1.4 Duration of QbD Principles Application by the Company

Question asked to the participants: What is the duration of your company's application of QbD principles?

Years of QbD application	No: of the Participants worked there	Average year of QbD implementation
1-3 Years	48	43.2%
Over 5 years	29	26.1%
less than 1 year	19	17.1%
3-5 Years	15	13.5%
Total	111	100.0%

Table 4.3.1.4: Timeframe of QbD Principles Application Across Companies

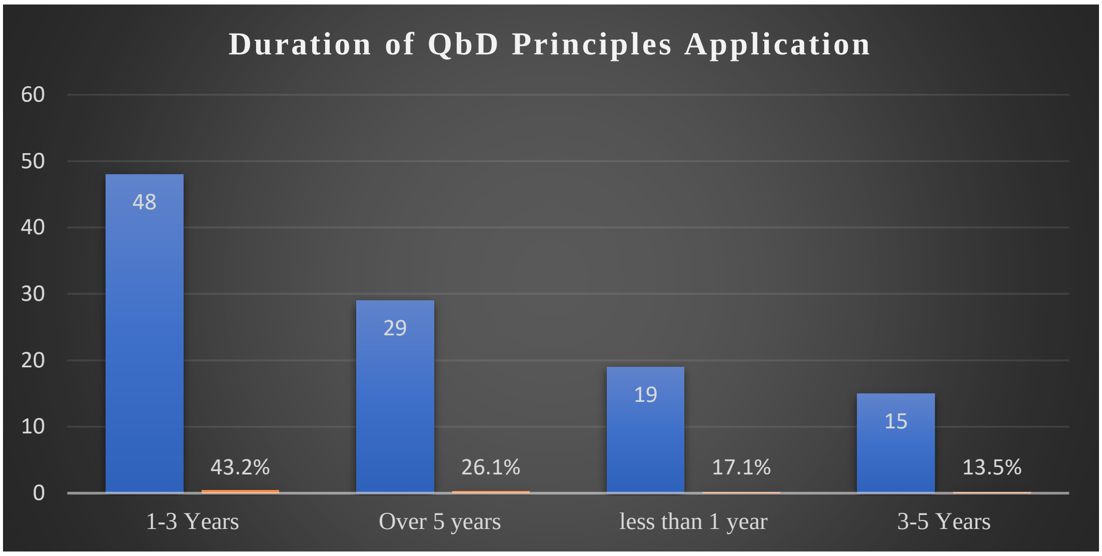

Figure:4.3.1.4 A clustered column chart showing the duration of companies' QbD principles

The data on the duration of QbD principles application reveals that most companies have been applying QbD for 1-3 years, with 48 participants (43.2%) indicating this time frame. This suggests that many companies are in the relatively early stages of QbD implementation, reflecting a growing trend in the adoption of these principles.

A significant number of participants, 29 (26.1%), reported that their companies have been applying QbD for over 5 years. This group likely represents more mature implementations, where QbD principles have been deeply integrated into the company's processes and culture.

On the other hand, 19 participants (17.1%) indicated that their companies have adopted QbD principles for less than 1 year. This highlights the recent uptake of QbD in some organizations, possibly driven by new regulatory requirements or a shift towards more robust quality management practices.

Finally, 15 participants (13.5%) have worked in companies where QbD has been implemented for 3-5 years, representing organizations that are likely transitioning from initial adoption to more entrenched practices.

4.3.2 Analysis of Objective 2: To investigate the specific strategies utilized by Indian biopharmaceutical manufacturers to implement QbD principles

4.3.2.1 Reasons for Implementing QbD Principles in Business

Question asked to the participants: Why did your business choose to implement QbD principles?

Reasons QbD Implementation	Participants Response	Percentage of response
Improve Product Quality	59	53.2%
Regulatory requirements	25	22.5%
Operational efficiency	22	19.8%
Competitive advantage	5	4.5%
Total	111	100.0%

Table 4.3.2.1: Key Motivations for Implementing QbD Principles in Business

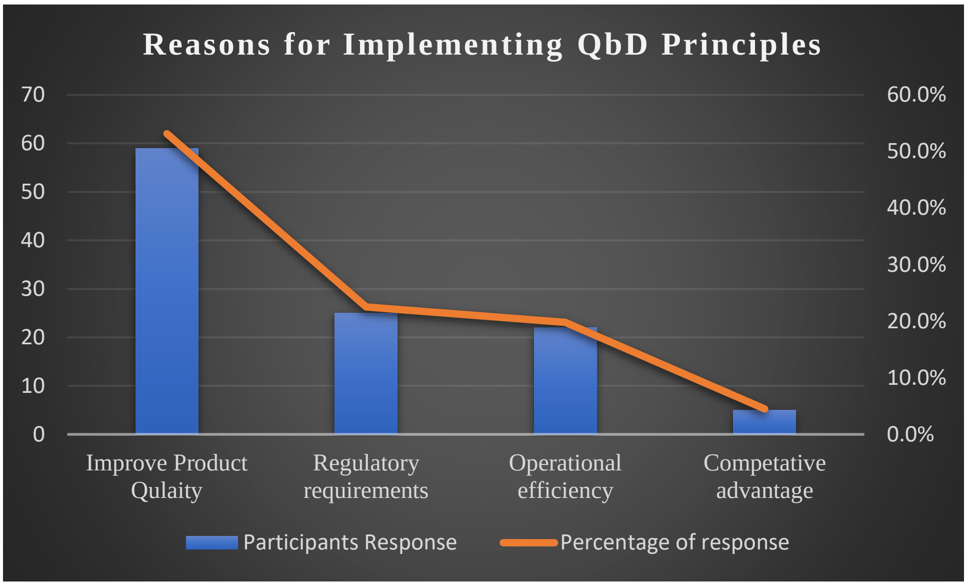

Figure 4.3.2.1: Clustered column chart compares the reason for implementing QbD principles in Indian Biopharma manufactures

The data reveals that the primary motivation for companies to implement Quality by Design (QbD) principles is to improve product quality, with 53.2% of respondents citing this as their main reason. This indicates a strong focus on enhancing the reliability, safety, and effectiveness of biopharmaceutical products through QbD practices.

Regulatory requirements are the second most common reason, mentioned by 22.5% of respondents. This highlights the role of regulatory compliance as a significant driver for QbD adoption, ensuring that products meet stringent industry standards and guidelines.

Operational efficiency is another important factor, with 19.8% of participants identifying it as a key reason for implementing QbD. This suggests that companies recognize the value of QbD in streamlining processes, reducing waste, and improving overall production efficiency.

Finally, competitive advantage is cited by 4.5% of respondents, indicating that a smaller portion of companies view QbD as a strategic tool for differentiating themselves in the marketplace.

4.3.2.2 Specific Strategies Used for QbD Implementation

Question asked to the participants: What specific strategies has your company used to implement QbD?

QbD Implementation Strategy	Number of Responses	Percentage of Total Responses
Training and Development Programs	87	32.3%
Hiring QbD Experts	45	16.7%
Investing in New Technologies	51	19.0%
Collaborating with External Consultants	38	14.1%
Developing Internal QbD Guidelines	48	17.8%
Total	269	100.0%

Table 4.3.2.2: Various methods and strategies that companies employ to successfully implement QbD principles.

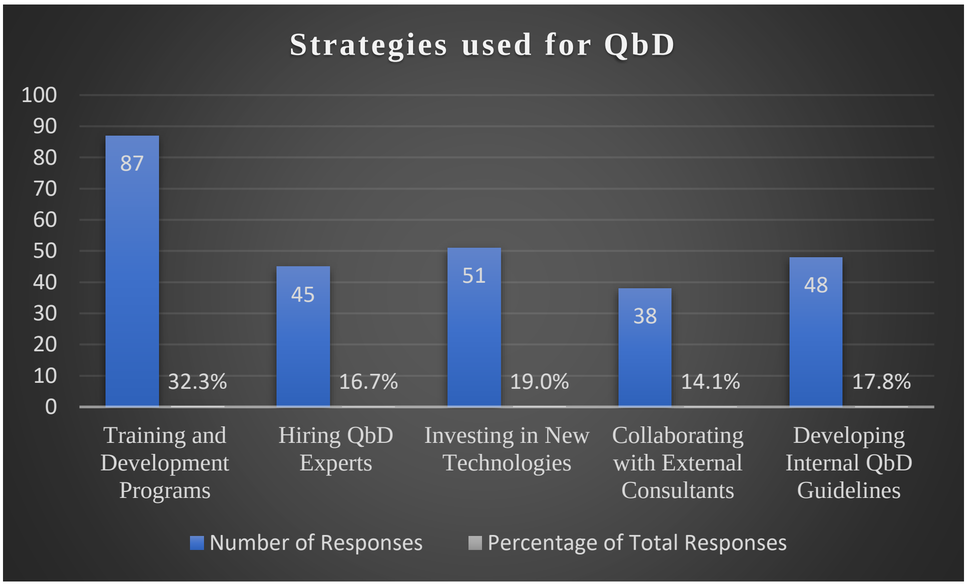

Figure 4.3.2.2: The clustered column chart represents the number and percentage of each QbD strategy implemented.

In terms of the strategies employed to implement QbD, Training and Development Programs are the most widely used, with 32.3% of the responses. This emphasizes the importance of educating and empowering employees to effectively apply QbD principles in their work.

Investing in New Technologies is another key strategy, accounting for 19.0% of the responses. This reflects the need for advanced tools and technologies to support QbD practices, such as process analytical technology (PAT) and continuous process verification (CPV).

Hiring QbD Experts is mentioned by 16.7% of respondents, highlighting the importance of bringing in specialized knowledge and expertise to successfully implement QbD.

Developing Internal QbD Guidelines (17.8%) and Collaborating with External Consultants (14.1%) are also significant strategies, indicating that companies are taking a structured approach to QbD by creating internal frameworks and seeking external expertise to guide their efforts.

4.3.2.3 Effectiveness of QbD Implementation Strategies

Question asked to the participants: How effective have these strategies been in implementing QbD?

Effectiveness Rating	Number of Responses	Percentage of Total Responses
Effectiveness Rating	52	46.8%
Very Effective	50	45.0%
Somewhat effective	9	8.1%

Table 4.3.2.3: The evaluation of how effective the QbD strategies have been in practice.

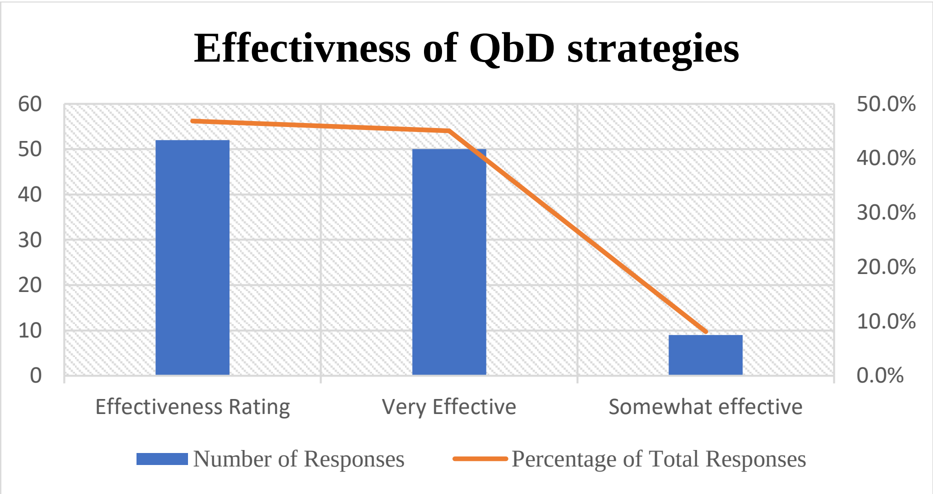

Figure 4.3.2.3: Clustered column chart representing the effectiveness of QbD strategies implemented

The data reveals that the majority of respondents find their QbD implementation strategies to be highly effective. Specifically, 46.8% of the participants rated the effectiveness of their QbD strategies as simply "Effective," while an additional 45.0% considered them "Very Effective." This indicates that nearly all respondents believe that their QbD strategies are working well to achieve the desired outcomes, such as improved product quality, regulatory compliance, and operational efficiency.

Only 8.1% of respondents rated the strategies as "Somewhat Effective," suggesting that there is a small group of participants who see room for improvement in how QbD principles are applied in their organizations. This could point to challenges in implementation, such as inadequate resources, training, or integration with existing processes.

4.3.2.4 Tools and Methods Employed for QbD Implementation

Question asked to the participants: What tools and methods does your business employ to implement QbD?

QbD Tool/Method	Number of Responses	Percentage of Total Responses
Design of Experiments (DoE)	65	23.3%
Risk Assessment Tools	72	25.8%
Process Analytical Technology (PAT)	56	20.1%
Continuous Process Verification (CPV)	59	21.1%
Statistical Process Control (SPC)	27	9.7%
Total	279	100.0%

Table 4.3.2.4: various techniques and tools that companies use to implement QbD principles effectively.

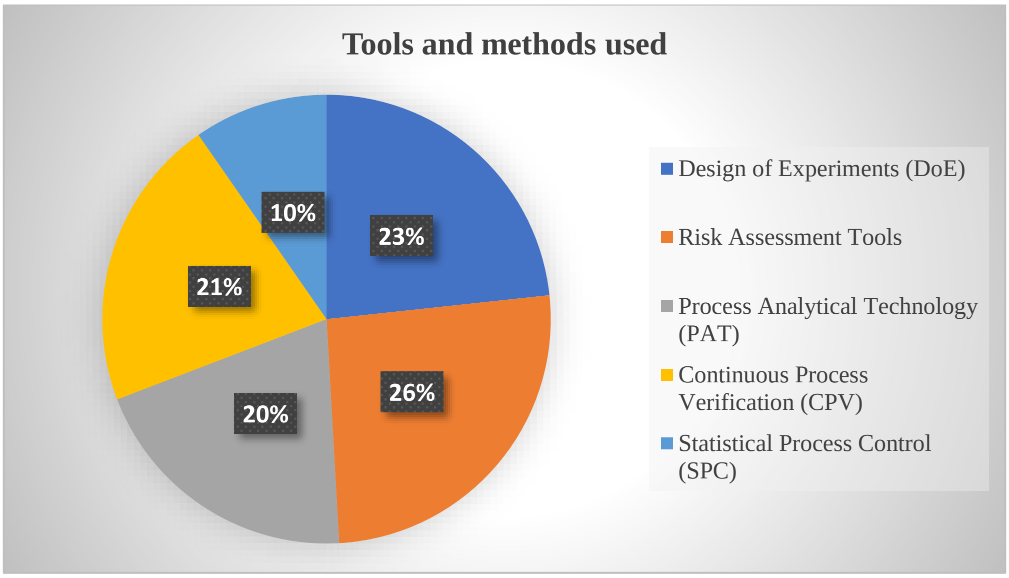

Figure 4.3.2.4: Pie Chart representing the tools and methods used for QbD implementation

The survey also explored the specific tools and methods used to implement QbD principles. The most frequently used tool is Risk Assessment Tools, with 25.8% of responses. This highlights the importance of identifying and managing risks throughout the product development and manufacturing process, which is a cornerstone of QbD.

Design of Experiments (DoE) is another widely used method, accounting for 23.3% of responses. DoE is crucial for systematically investigating the relationships between various factors affecting a process and optimizing them to achieve the best possible outcomes.

Continuous Process Verification (CPV) and Process Analytical Technology (PAT) are also significant tools, with 21.1% and 20.1% of responses, respectively. These methods ensure that processes are continuously monitored and controlled in real-time, helping to maintain consistent product quality and enabling proactive adjustments as needed.

Finally, Statistical Process Control (SPC), which received 9.7% of responses, is a method used to monitor and control a process through the use of statistical techniques, ensuring that the process operates at its full potential.

4.3.3 Analysis of Objective 3: To analyze the outcomes of QbD implementation, focusing on its impact on product quality, regulatory compliance, and operational efficiency in India.

4.3.3.1 Comprehensive Impact of QbD on Various Aspects of the Business Question asked to the participants: What Impact Has QbD Implementation Had on Your

Company's Product Quality, Regulatory Compliance, Operational Effectiveness, and Financial Performance?

Aspect of Impact	Significant Impact	Major Impact	Minor Impact	No Impact	Not Sure
Product Quality	71	31	8	1	N/A
Regulatory Compliance	42	56	12	1	N/A
Operational Effectiveness	68	20	16	7	N/A
Financial Impact	63	N/A	28	15	5

Table 4.3.3.1: Overall impact across different critical aspects of the business.

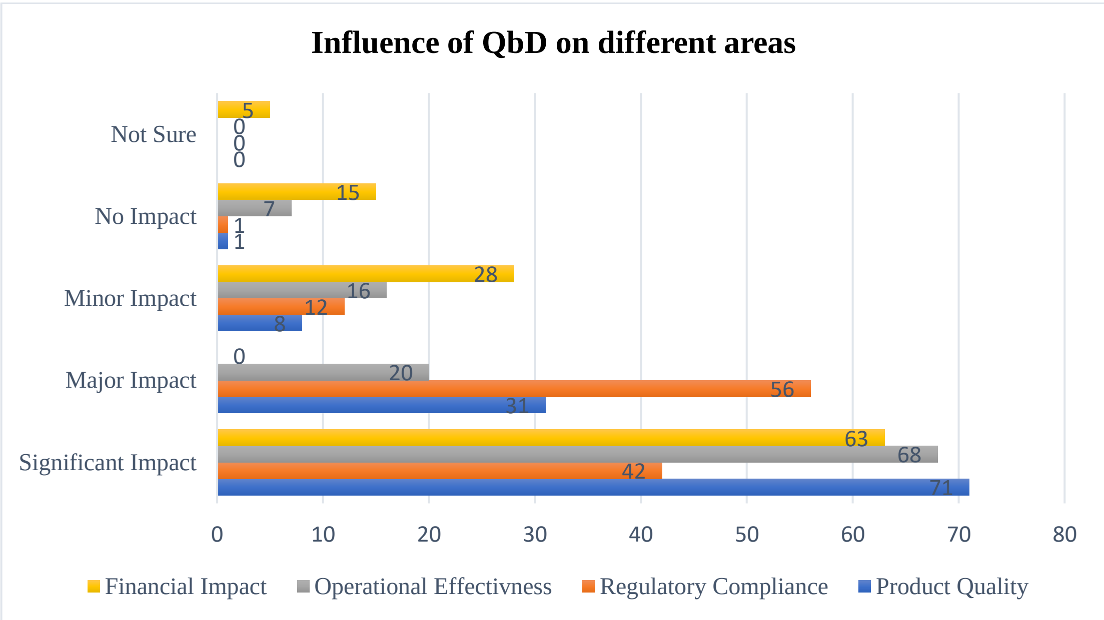

Figure 4.3.3.1: The clustered bar chart represents the broad influence of QbD on key business area

Product Quality: The implementation of QbD has had a profound impact on product quality, with 71 respondents (64.0%) reporting a significant impact and 31 respondents (27.9%) indicating a major impact. This reflects that QbD practices are highly effective in ensuring that products consistently meet the desired quality standards. Only a small number, 8 respondents (7.2%), observed a minor impact, and just 1 respondent (0.9%) felt there was no impact. The absence of "Not Sure" responses in this category suggests strong confidence in the positive influence of QbD on product quality across the board.

Regulatory Compliance: QbD has also substantially influenced regulatory compliance, as evidenced by 42 respondents (37.8%) indicating a significant impact and 56 respondents (50.5%) observing a major impact. This highlights the role of QbD in helping companies align with regulatory requirements more effectively. A smaller group, 12 respondents (10.8%), reported a minor impact, while 1 respondent (0.9%) noted no impact. The consistent reporting of positive impacts across these categories underscores the importance of QbD in maintaining regulatory compliance.

Operational Effectiveness: In terms of operational effectiveness, QbD implementation has led to a significant impact for 68 respondents (61.3%) and a major impact for 20 respondents (18.0%). However, 16 respondents (14.4%) indicated a minor impact, and 7 respondents (6.3%) felt there was no impact on operational effectiveness. This distribution suggests that while QbD is largely successful in improving operational efficiency, there is variability in its effectiveness, potentially due to differences in how fully QbD is integrated into operations.

Financial Impact: The financial impact of QbD shows that 63 respondents (56.8%) experienced a significant impact, which implies that QbD can lead to considerable financial benefits, likely through cost savings and efficiency gains. Meanwhile, 28 respondents (25.2%) observed a minor impact, and 15 respondents (13.5%) reported no impact on financial performance. Additionally, 5 respondents (4.5%) were not sure about the financial impact of QbD. This variation suggests that while many companies benefit financially from QbD, others may not yet see substantial financial returns, possibly due to the initial costs of implementation or the time needed to realize financial gains.

4.3.4 Analysis of objective 4: To identify and examine challenges hindering the adoption of QbD in Indian biopharmaceutical manufacturing, including technical and regulatory barriers.

4.3.4.1 Main Barriers to QbD Implementation in the Business

Question asked to the participants: What are the main barriers your business is facing in putting QbD into practice?

Barrier	Number of Responses	Percentage of Total Responses
Limited Technical Expertise	61	23.4%
High Upfront Investment	58	22.2%
Raw Material Quality Issues	36	13.8%
Supply Chain Management Problems	39	14.9%
Regulatory Barriers	35	13.4%
Resistance to Change	32	12.3%
Total	261	100.0%

Table 4.3.4.1: Primary obstacles that companies face when trying to adopt QbD principles.

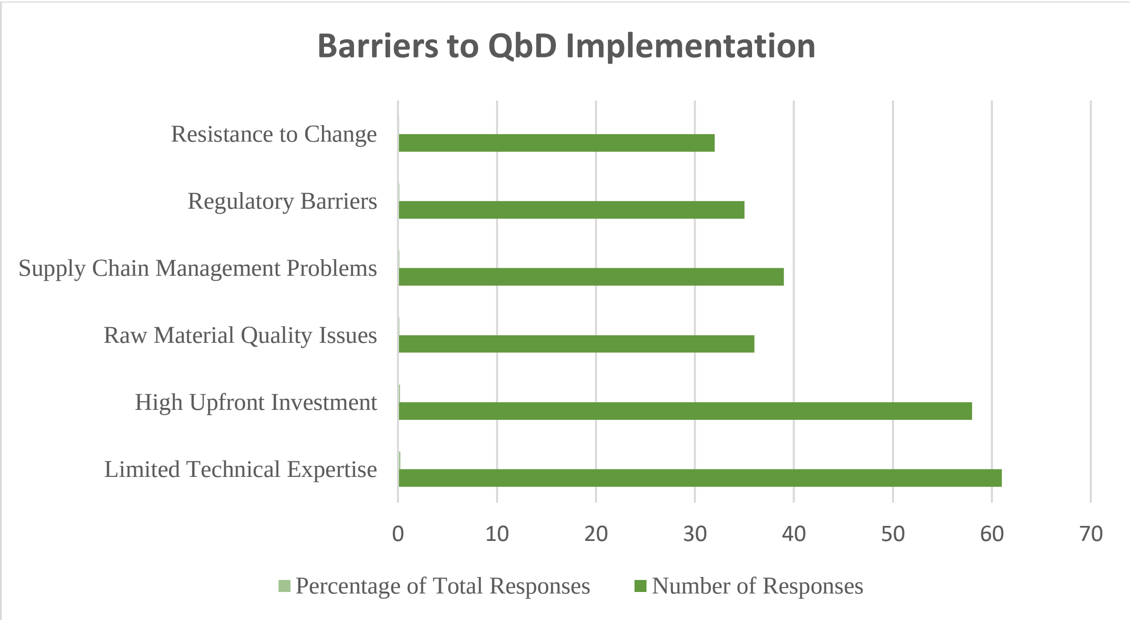

Figure 4.3.4.1: Clustered bar chart representing the barriers to QbD principles

The data identifies several key barriers that companies face when attempting to implement Quality by Design (QbD) principles.

Limited technical expertise emerges as the most significant barrier, with 23.4% of respondents (61) indicating this as a challenge. This suggests that a lack of specialized knowledge or skills required to implement QbD effectively is a major hindrance for many companies. It highlights the need for investment in training and development programs to build the necessary expertise within the organization.

High upfront investment is the second most commonly cited barrier, affecting 22.2% of respondents (58). This reflects the substantial financial resources required to adopt QbD, including investments in new technologies, training, and infrastructure. For many companies, especially smaller ones, these costs can be prohibitive and may delay or prevent the adoption of QbD.

Supply chain management problems were identified by 14.9% of respondents (39) as a barrier to QbD implementation. Effective QbD practices rely heavily on the consistent quality and availability of raw materials, which are often complicated by supply chain issues. Addressing these problems requires improving supplier relationships, quality control processes, and logistics management.

Raw material quality issues were cited by 13.8% of respondents (36) as a significant barrier. The variability in raw material quality can undermine QbD efforts, as the process depends on consistent inputs to ensure high-quality outputs. Companies may need to establish stricter quality control measures and better supplier oversight to mitigate this issue.

Regulatory barriers, mentioned by 13.4% of respondents (35), highlight the challenges companies face in navigating complex and sometimes inconsistent regulatory requirements. These barriers can slow down the implementation of QbD or require additional resources to ensure compliance. Companies might benefit from closer collaboration with regulatory bodies to streamline processes and align with standards more effectively.

Resistance to change was noted by 12.3% of respondents (32) as a barrier. This reflects the cultural and organizational challenges that can arise when introducing new methodologies like QbD. Overcoming resistance requires strong leadership, clear communication about the benefits of QbD, and possibly incremental implementation to allow employees to adapt gradually.

4.3.4.2: Technical Challenges Experienced in Using QbD

Question asked to the participant: What are the main barriers your business is facing in putting QbD into practice

Technical Challenge	Number of Responses	Percentage of Total Responses
Lack of Skilled Personnel	46	24.3%
Insufficient Training	48	25.4%
Inadequate Technology	55	29.1%
Complexity of QbD Principles	40	21.2%
Total	189	100.0%

Table 4.3.4.2: Key Technical Obstacles in Implementing QbD in Indian Manufactures

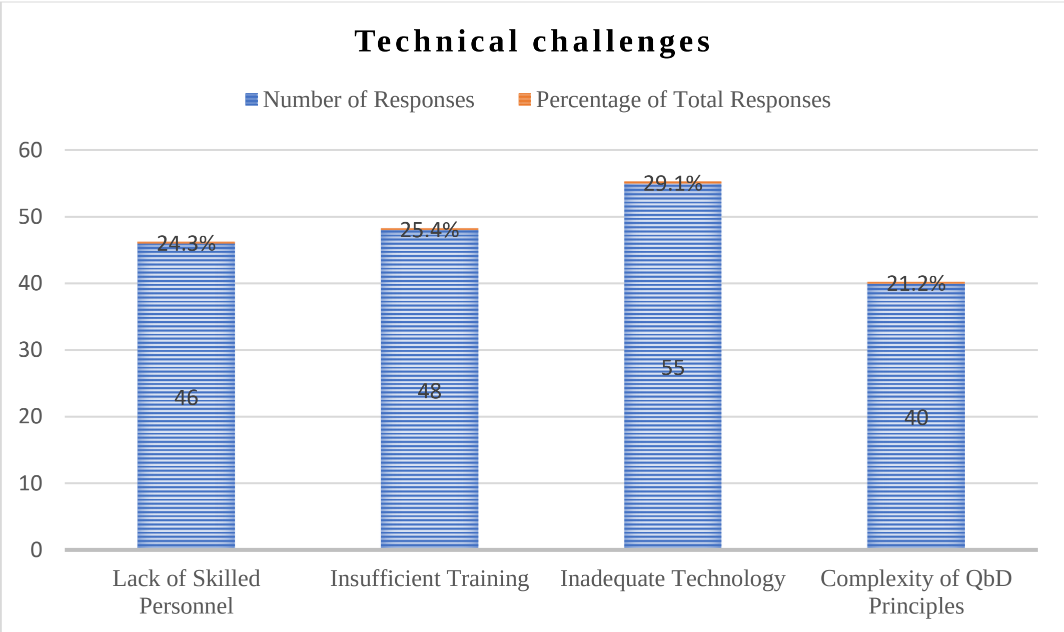

Figure 4.3.4.2: Stacked column chart indicating the response towards the technical challenges

The data indicates several significant technical challenges that companies encounter when implementing QbD.

Inadequate technology is the most frequently cited technical challenge, affecting 29.1% of respondents. This suggests that companies may lack the advanced tools and systems necessary to fully implement QbD. Upgrading technological infrastructure and investing in state-of-the-art equipment may be crucial steps in overcoming this barrier.

Insufficient training is highlighted by 25.4% of respondents as a key issue. This points to the need for more comprehensive training programs that equip employees with the necessary skills and knowledge to apply QbD principles effectively.

A lack of skilled personnel is noted by 24.3% of respondents. This aligns with the need for training but also indicates a broader issue of attracting and retaining individuals with the expertise required to implement QbD.

The complexity of QbD principles is recognized as a challenge by 21.2% of respondents. This complexity may deter companies from fully embracing QbD or lead to partial implementations that do not realize the full benefits of the methodology. Simplifying QbD processes or providing clearer guidance could help mitigate this challenge.

4.3.4.3: Regulatory Challenges in Implementing QbD

Question asked to the participants: What regulatory challenges does your business encounter while implementing QbD?

Regulatory Challenge	Number of Responses	Percentage of Total Responses
Lack of Clear Guidelines	55	35.0%
Inconsistent Regulations	48	30.6%
Long Approval Times	54	34.4%
Total	157	100.0%

Table 4.3.4.3: Primary Regulatory Hurdles in QbD Implementation

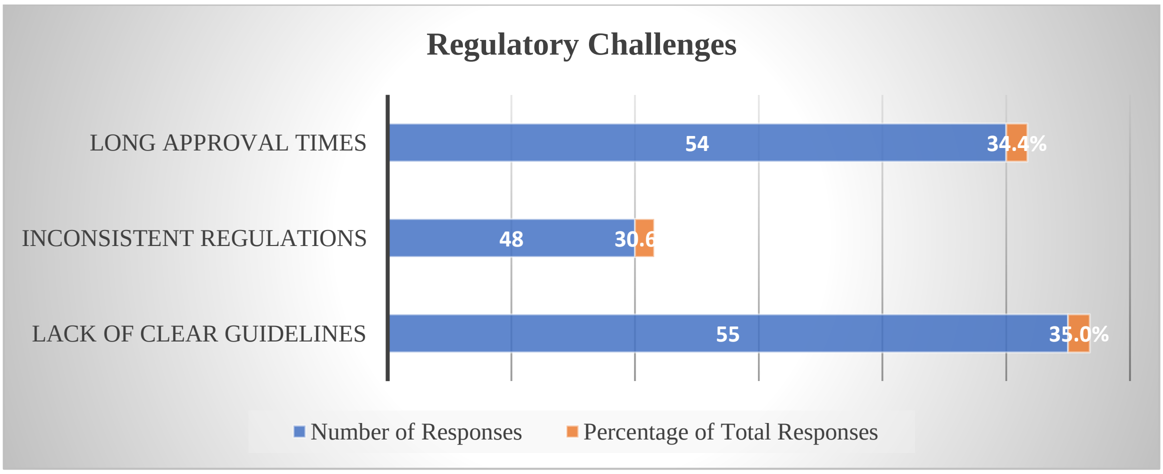

Figure 4.3.4.3: Stacked bar chart representing the extent of regulatory challenges in implementing QbD

The data also reveals key regulatory challenges that hinder the implementation of QbD:

A lack of clear guidelines is the most significant regulatory challenge, affecting 35.0% of respondents. This suggests that unclear or ambiguous regulations make it difficult for companies to align their QbD practices with regulatory expectations. Enhanced communication and clearer regulations from authorities could help address this issue.

Long approval times are cited by 34.4% of respondents as a major challenge. Delays in regulatory approval can hinder the timely implementation of QbD and slow down product development cycles. Streamlining approval processes could significantly benefit companies in this regard.

Inconsistent regulations are noted by 30.6% of respondents as a barrier. Variability in regulations across regions or regulatory bodies can complicate the QbD implementation process, making it harder for companies to maintain compliance. Harmonizing regulations across different jurisdictions could alleviate this challenge.

4.3.4.4: Analysis of Barriers and Regulatory Support in QbD Implementation

Question asked to the participants: To what extent do these barriers affect your company's efforts to implement QbD, and how important is regulatory support in facilitating QbD implementation?

The first chart indicates the degree to which various barriers affect companies' efforts to implement Quality by Design (QbD). The results show that a significant portion of respondents, 46.8%, feel that these barriers have a "Significant" impact on their QbD implementation efforts. Meanwhile, 28.8% of respondents believe the barriers are "Somewhat significant," and 21.6% view them as "Very significant." Only a small fraction, 2.7%, consider these barriers to be "Not significant." This distribution highlights that most companies experience considerable challenges that substantially hinder their ability to fully implement QbD practices.

The second chart underscores the critical role of regulatory support in facilitating QbD implementation. An overwhelming majority, 62.2%, of respondents rate regulatory support as "Very important" for successful QbD adoption, with an additional 31.5% deeming it "Important." A minor proportion, 4.5%, considers it "Somewhat important," and only 1.8% views it as "Not important." This data clearly emphasizes that strong regulatory backing is essential for overcoming barriers and effectively integrating QbD into biopharmaceutical manufacturing processes.

4.3.4.5: Assistance Needed to Resolve QbD Implementation Issues

Question asked to the participants: What kind of assistance would be most useful in resolving implementation-related issues with QbD?

Type of Assistance	Number of Responses	Percentage of Total Responses
Technical Training Programs	71	26.5%
Financial Incentives	60	22.4%
Regulatory Guidance	65	24.3%
Industry Collaborations	34	12.7%
Access to Expert Consultants	38	14.2%
Total	268	100.0%

Table 4.3.4.5: Support Required to Overcome QbD Implementation Challenges

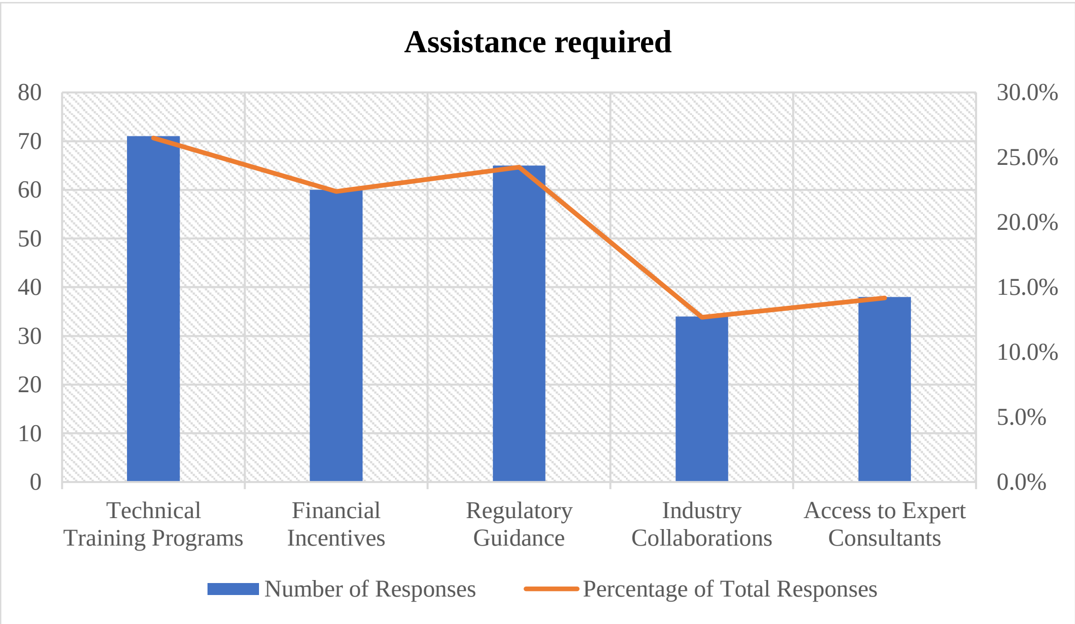

Figure 4.3.4.5: Clustered column chart representing responses towards the type of assistance required to overcome the challenges.

To overcome the barriers, companies have identified several types of assistance that would be beneficial:

The most requested form of assistance is technical training programs, with 26.5% of respondents indicating this need. This underscores the importance of equipping staff with the knowledge and skills required to implement and maintain QbD practices effectively.

Regulatory guidance is needed by 24.3% of respondents, highlighting the importance of clear and consistent advice from regulatory bodies to help companies navigate the complexities of QbD implementation.

Financial incentives are seen as critical by 22.4% of respondents. Given the high upfront investment costs associated with QbD, financial support could significantly reduce the burden on companies and encourage wider adoption.

Access to expert consultants is noted by 14.2% of respondents as an important type of assistance. Expert consultants can provide tailored advice and guidance, helping companies to overcome specific challenges in their QbD implementation efforts.

Industry collaborations are highlighted by 12.7% of respondents as a beneficial form of assistance. Collaboration with other companies or industry groups could facilitate the sharing of best practices and resources, making it easier to implement QbD effectively.

4.3.5 Analysis of Objective 5: To provide recommendations to address identified barriers and enhance the effective implementation of QbD in Indian biopharmaceutical manufacturing.

4.3.5.1 Recommended Changes to Improve QbD Adoption in the Biopharmaceutical Sector in India

Question asked to the participants: What changes would you recommend making to improve QbD adoption in the biopharmaceutical sector in India?

Recommended Change	Number of Responses	Percentage of Total Responses
Increased Awareness and Education	75	26.3%
Better Regulatory Frameworks	75	26.3%
More Industry Collaboration	47	16.5%
Improved Access to Technology	56	19.6%
Government Support	32	11.2%
Total	285	100.0%

Table 4.3.5.1: Key Recommendations to Enhance QbD Adoption in the Indian Biopharmaceutical Sector

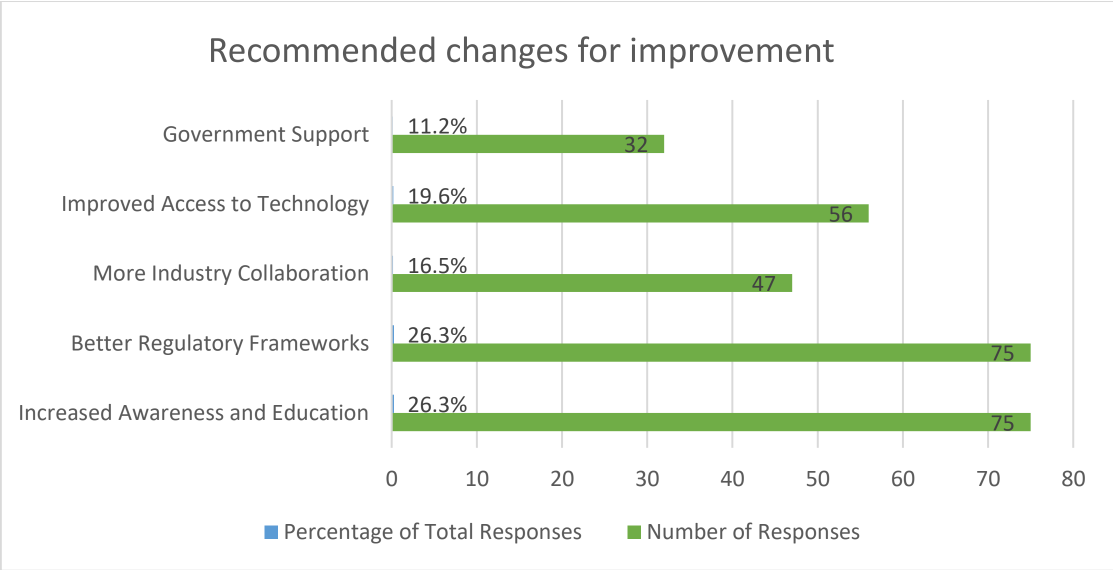

Figure 4.3.5.1: Clustered bar chart representing the changes recommended by the respondents

The most commonly recommended changes to enhance QbD adoption are Increased Awareness and Education and Better Regulatory Frameworks, each supported by 26.3% (75 responses) of the participants. These recommendations highlight the need for broader educational initiatives and improved regulatory systems to facilitate QbD integration. Improved Access to Technology is also a significant recommendation, with 19.6% (56 responses) of respondents advocating for it. More Industry Collaboration is seen as important by 16.5% (47 responses), indicating that working together across the industry could help overcome challenges. Lastly, Government Support is recommended by 11.2% (32 responses), underscoring the role of government initiatives in promoting QbD adoption.

4.3.5.2 Expectations for QbD Development in the Indian Biopharmaceutical Sector

Question asked to the participant: In what way do you think QbD will develop in the Indian biopharmaceutical sector?

Expectation Level	Number of Responses	Percentage of Total Responses
Very Optimistic	52	46.8%
Optimistic	50	45.0%
Neutral	8	7.2%
Negative	1	0.9%

Table 4.3.5.2: Projected Expectations for QbD Development in India's Biopharmaceutical Sector

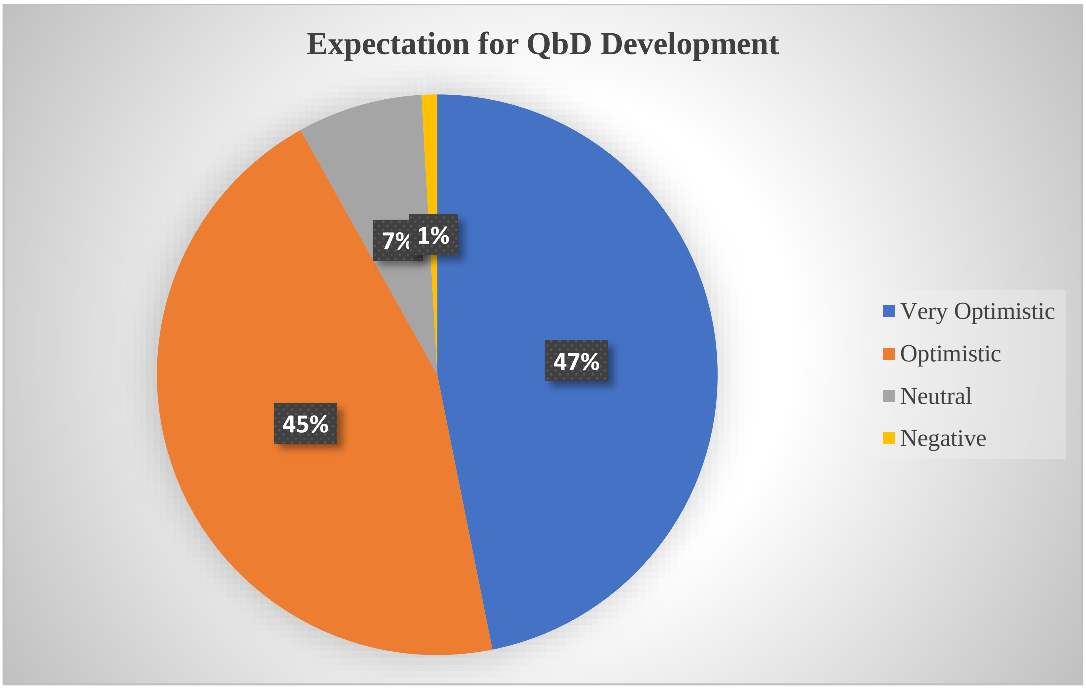

Figure 4.3.5.2: Pie chart indicating the expectation level of the participant about the future of QbD in India

The expectations for the future development of QbD in India are highly positive. 46.8% (52 responses) of participants are Very Optimistic, and 45.0% (50 responses) are Optimistic about the future of QbD in the Indian biopharmaceutical sector. A small percentage is Neutral (7.2% or 8 responses), while only 0.9% (1 response) is Negative. This overwhelmingly positive outlook suggests that most stakeholders believe in the potential for significant growth and development in QbD practices within the industry.

4.3.5.3: Possible Advantages for India with Increased QbD Adoption

Question asked to the participant: What possible advantages do you see for India as a result of more QbD adoption?

Possible Advantage	Number of Responses	Percentage of Total Responses
Improved Product Quality	82	27.33%
Enhanced Regulatory Compliance	66	22.00%
Greater Operational Efficiency	64	21.33%
Increased Global Competitiveness	54	18.00%
Reduced Production Costs	34	11.33%
Total	300	100.00%

Table 4.3.5.3: Potential Benefits of Increased QbD Adoption for India

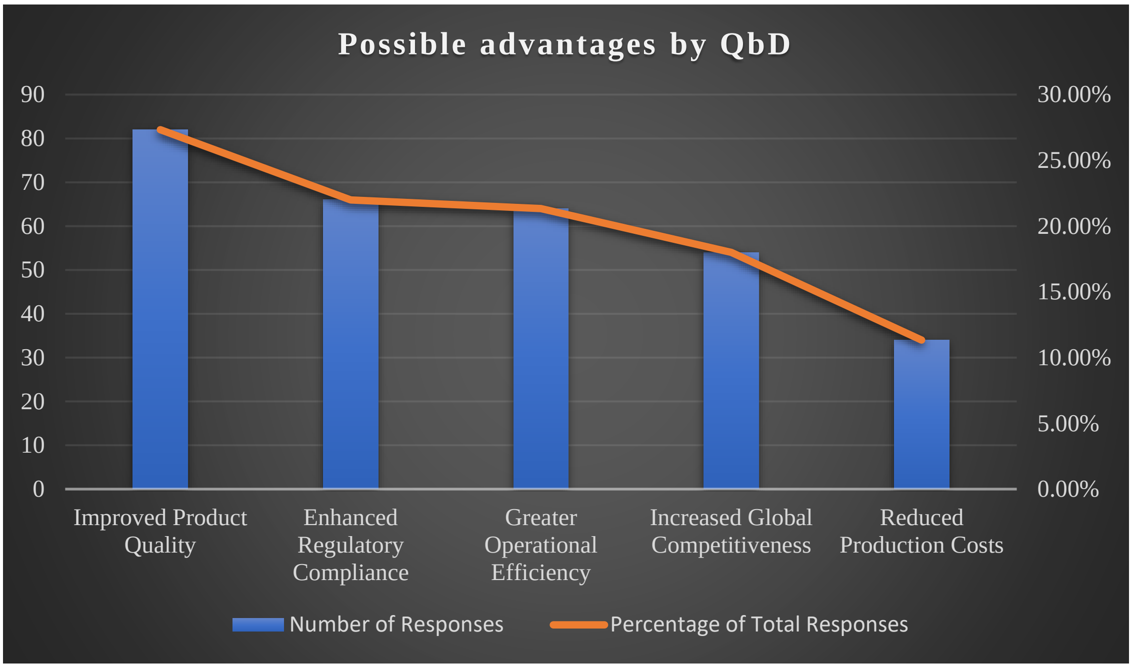

Figure 4.3.5.3: Clustered column chart representing the possible advantages of the QbD adoption

The most recognized advantage of increased QbD adoption in India is Improved Product Quality, with 27.33% (82 responses) indicating this benefit. Enhanced Regulatory Compliance is identified by 22.00% (66 responses), suggesting that QbD can help Indian companies better meet regulatory requirements. Greater Operational Efficiency is noted by 21.33% (64 responses), reflecting the belief that QbD can streamline processes and reduce inefficiencies. Increased Global Competitiveness is considered a major advantage by 18.00% (54 responses), highlighting the potential for QbD to help Indian firms compete more effectively on a global scale. Lastly, Reduced Production Costs are cited by 11.33% (34 responses), pointing to the financial benefits that could result from more efficient manufacturing processes.

4.3.5.4: Analysis of Possible Adverse Impacts of Increased QbD Adoption

Question asked to the participant: What possible adverse impacts do you think a rise in QbD adoption could lead to?

Possible Adverse Impact	Number of Responses	Percentage of Total Responses
High Implementation Costs	62	29.7%
Technical Complexity	60	28.7%
Resistance to Change	50	23.9%
Regulatory Hurdles	37	17.7%
Total	209	100.0%

Table 4.3.5.4: Comprehensive Analysis of the Potential Adverse Impacts Resulting from Increased QbD Adoption

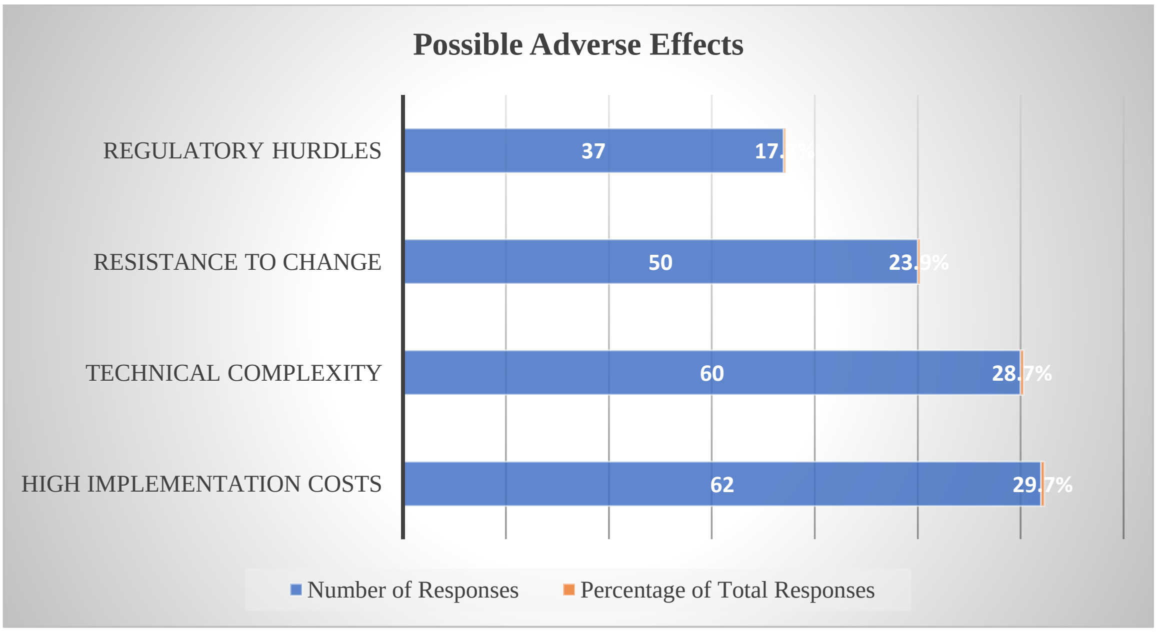

Figure 4.3.5.4: Stacked bar chart representing the possible adverse effect that can be caused by the implementation of QbD

4.3.5.5: Overall Satisfaction with QbD Implementation and Recommendations for Adoption by Biopharmaceutical Manufacturers.

Question asked for the participant: What is your overall satisfaction with your company's current QbD implementation, and would you recommend other biopharmaceutical manufacturers in India to adopt QbD principles?

Aspect	Category	Number of Responses	Percentage of Total Responses	Total
Satisfaction with Current QbD Implementation	Very Satisfied	59	53.2%	100.0%
	Satisfied	32	28.8%	
	Neutral	19	17.1%	
	Dissatisfied	1	0.9%	
Recommendation for QbD Adoption	Definitely	68	61.3%	100.0%
	Probably	33	29.7%	
	Not Sure	7	6.3%	
	Probably Not	3	2.7%	
	Definitely No	_	_	

Table 4.3.5.5: Comprehensive Overview of Overall Satisfaction with QbD Implementation and Recommendations for Its Adoption Among Biopharmaceutical Manufacturers

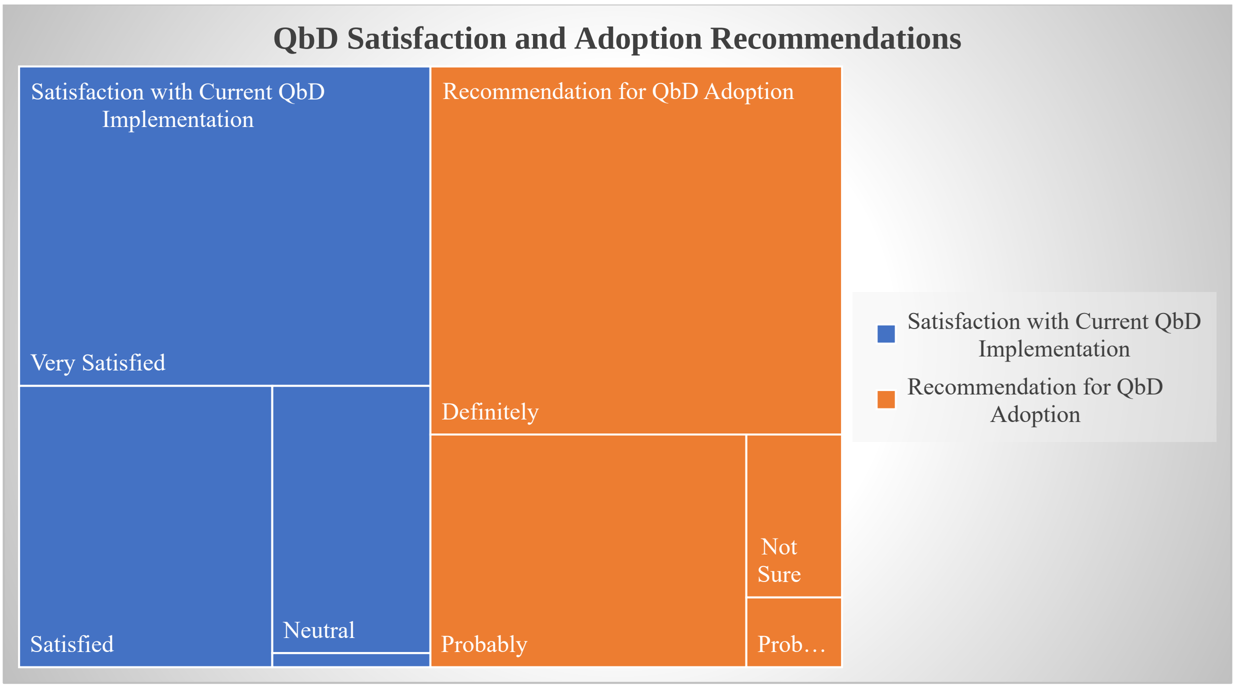

Figure 4.3.5.5: Tree map represents the satisfaction with current QbD implementation and recommendation for QbD adoption

4.3.5.6: Key Insights and Recommendations from Respondents on QbD Implementation in the Indian Biopharmaceutical Industry

Question asked to the participants: Please provide any additional comments or suggestions regarding QbD implementation in the Indian biopharmaceutical industry

The additional comments and suggestions provided by respondents regarding QbD implementation in the Indian biopharmaceutical industry reveal several key themes and recommendations. A significant number of respondents expressed positive feedback on the benefits of QbD, particularly in enhancing product quality, operational efficiency, and regulatory compliance. One comment highlighted the comprehensive benefits of QbD, noting that it "enhances product quality, operational efficiency, regulatory compliance, and global acceptance." This viewpoint was reinforced by other respondents who recognized QbD's effectiveness in maintaining high production standards, with one stating simply that "QbD helps to improve product quality."

In addition to its impact on quality and efficiency, some respondents emphasized the importance of integrating QbD principles early in the development process, particularly during R&D. For instance, one respondent mentioned, "QbD shall be there from the initial R&D stage onwards," suggesting that early adoption of QbD can lead to more robust outcomes. Another comment suggested that making QbD a regulatory requirement in India could significantly enhance pharmaceutical manufacturing practices, reflecting the need for stronger regulatory frameworks: "Regulation rule to be implemented in India which becomes more effective for pharmaceutical manufacturing by QbD."

The role of QbD in problem-solving and ensuring patient safety was also noted, with comments such as "QbD is really helpful in problem solving" and "The quality by design principles help in delivering pharmaceuticals having good product quality and patient safety." These remarks underscore the belief that QbD not only meets regulatory demands but also provides tangible benefits for patient outcomes.

Several respondents recommended increasing awareness and providing more training on QbD principles within the biopharmaceutical sector. Comments like "Give awareness and training regarding QbD among the employees in the Biopharmaceutical sector" and "Every industry should provide training assistance and guidance to their employees" indicate a perceived gap in knowledge and skills that needs to be addressed. These suggestions imply that while QbD's benefits are recognized, its full potential can only be realized through adequate training and education.

There were also strong endorsements for the broader adoption of QbD principles, with some respondents urging all biopharmaceutical manufacturers to adopt these practices to improve product quality and safety. For example, one respondent noted, "I recommend all biopharmaceutical manufacturers should adopt QbD principles to improve product quality and patient safety," reflecting a widespread belief in the positive impact of QbD. This was supported by another comment stating, "I definitely recommend it to the Indian biopharmaceutical industry."

However, not all feedback was entirely positive. Some respondents expressed concerns about the current state of regulatory standards in India. For instance, one comment noted, "India is very backward in Regulatory standards and compliance," suggesting a perceived need for improvement in regulatory enforcement and standards within the country. This aligns with the broader theme of needing stronger regulatory frameworks and better implementation of QbD practices.

4.4 Data Interpretation

Objective 1: To evaluate the current level of Quality by Design (QbD) integration within Indian biopharmaceutical manufacturing processes.

The study found that QbD is in its initial stages of integration within the Indian biopharmaceutical sector. While a majority of companies have started implementing QbD principles, the level of integration varies significantly. Only 38.7% of respondents indicated complete integration, with the remaining companies either primarily or partially integrating QbD. This highlights the need for more comprehensive efforts to fully embed QbD into all manufacturing processes. The early stage of QbD adoption in India suggests that while the industry recognizes its potential benefits, there is still considerable work to be done to achieve widespread and effective implementation.

Objective 2: To investigate specific strategies utilized by Indian biopharmaceutical manufacturers to implement QbD principles.

The research identified several key strategies employed by Indian biopharmaceutical companies to implement QbD, including the focus on CQAs, QTPPs, and DoE. These strategies are essential for ensuring that products meet the desired quality standards and for complying with regulatory requirements. However, the effectiveness of these strategies is often limited by the challenges that companies face in implementing them fully. These challenges include high costs, the complexity of aligning QbD with existing regulatory frameworks, and the need for advanced technology and expertise. Companies that have successfully implemented these strategies have reported positive outcomes, but there is a clear need for further development and support to ensure that these strategies can be effectively adopted across the industry.

Objective 3: To analyze the outcomes of QbD implementation, focusing on its impact on product quality, regulatory compliance, and operational efficiency in India.

The outcomes of QbD implementation in India are generally positive, with reported improvements in product quality, regulatory compliance, and operational efficiency. Companies that have fully integrated QbD report better outcomes compared to those with only partial integration, highlighting the importance of full-scale adoption for achieving the best results. However, the partial adoption of QbD by many companies means that these benefits are not uniformly experienced across the industry. The variability in QbD implementation also suggests that the industry is still in the process of understanding and optimizing these practices and that there is significant potential for further improvements in outcomes as QbD becomes more widely adopted.

Objective 4: To identify and examine challenges hindering the adoption of QbD in Indian biopharmaceutical manufacturing, including technical and regulatory barriers.

The study identified several key challenges that hinder the adoption of QbD in India, including the complexity of aligning QbD with existing regulatory frameworks, the high initial costs associated with its implementation, and the need for advanced technology and specialized expertise. These challenges are particularly pronounced in smaller companies, which may lack the resources to overcome them. The regulatory environment in India, while supportive of QbD in principle, still presents significant barriers to its widespread adoption, particularly in terms of the alignment with international standards and the availability of clear, consistent guidance for companies. Addressing these challenges will be critical to ensuring that QbD can be effectively adopted across the Indian biopharmaceutical industry.

Objective 5: To provide recommendations to address identified barriers and enhance the effective implementation of QbD in Indian biopharmaceutical manufacturing.

Based on the findings, several recommendations have been proposed to address the identified barriers and enhance the effective implementation of QbD in India. These recommendations include the need for comprehensive training programs, increased investment in technology, and stronger regulatory support to facilitate the widespread adoption of QbD. In particular, there is a need for greater collaboration between industry, academia, and regulatory bodies to develop and implement effective training programs that can equip professionals with the skills and knowledge needed to successfully implement QbD. Additionally, the provision of financial incentives and support for smaller companies could help to alleviate some of the financial barriers to QbD adoption.

4.5 Chapter Summary

This chapter provided a comprehensive thematic analysis of Quality by Design (QbD) implementation within the Indian biopharmaceutical sector, based on survey data collected from industry professionals. The analysis was structured around five key objectives: understanding the extent of QbD integration, identifying the strategies and tools employed for QbD implementation, assessing the impact of QbD on various business aspects, evaluating the barriers to QbD adoption, and gathering insights and recommendations from industry participants.

Key findings highlighted that while the integration of QbD has significantly improved product quality, regulatory compliance, and operational effectiveness, challenges such as limited technical expertise, high implementation costs, and regulatory hurdles remain prevalent. The chapter also underscored the importance of regulatory support and the need for increased awareness and training to facilitate broader adoption of QbD principles across the industry.

The insights gathered from respondents provided valuable recommendations for enhancing QbD implementation, including the need for better regulatory frameworks, industry collaboration, and technical training programs. Overall, the chapter emphasized the critical role of QbD in advancing the Indian biopharmaceutical industry towards global standards of quality and safety, while also highlighting the areas that require focused attention for further improvement.

CHAPTER FIVE

CONCLUSION AND FUTURE RECOMMENDATIONS

5.1 Summary Findings from Primary Research

The primary research conducted in this study provided crucial insights into the current state of Quality by Design (QbD) implementation within the Indian biopharmaceutical industry. The survey, which gathered responses from 111 industry professionals, revealed that while there is a growing recognition of the importance of QbD, the level of integration across the industry is varied and often incomplete.

A key finding from the survey is that 38.7% of respondents reported complete integration of QbD principles into their manufacturing processes, indicating a solid foundation for QbD adoption in a segment of the industry. However, a significant portion,35.1%, reported primary integration and 26.1% reported only partial integration. This suggests that while many companies are beginning to adopt QbD, they are still in the early stages of this process, with full-scale implementation yet to be realized. The reasons for this partial integration are multifaceted. For some companies, particularly smaller firms, the high initial costs associated with QbD adoption, including investments in new technologies and infrastructure, present a significant barrier. Additionally, the complexity of aligning QbD with existing regulatory frameworks and the need for specialized expertise further complicate the implementation process. This has resulted in a situation where only a fraction of the industry has fully embraced QbD, while others are still navigating the challenges associated with its adoption.

Despite these challenges, companies that have fully integrated QbD report significant improvements in product quality, regulatory compliance, and operational efficiency. For instance, respondents indicated that QbD has led to more consistent product quality, reduced variability in manufacturing processes, and better alignment with regulatory requirements. These benefits are particularly important in the highly regulated biopharmaceutical industry, where compliance with stringent quality standards is essential for market access and patient safety. However, the benefits of QbD are not uniformly experienced across the industry. Companies that have only partially integrated QbD report fewer improvements, highlighting the importance of full-scale adoption for realizing the full potential of QbD. This finding underscores the need for continued efforts to promote comprehensive QbD adoption across the industry, ensuring that all companies can benefit from the enhanced quality, compliance, and efficiency that QbD offers.

The research also highlighted the role of younger professionals in driving QbD adoption within the industry. Respondents with less than five years of experience were more likely to report familiarity with QbD principles and active involvement in QbD implementation efforts. This is likely due to the increased emphasis on QbD in recent educational and training programs. However, this generational divide also points to a potential knowledge gap among more seasoned professionals, who may not have had the same level of exposure to QbD during their formative years in the industry. Addressing this gap through ongoing training and professional development will be crucial for ensuring that all professionals, regardless of their experience level, are equipped with the knowledge and skills needed to effectively implement QbD.

5.2 Summary Findings from Secondary Research

The secondary research, conducted through an extensive literature review, provided additional context and insights into the global landscape of QbD implementation, highlighting best practices, challenges, and opportunities that are relevant to the Indian context.

The literature review revealed that in developed markets such as the United States and Europe, QbD has been widely adopted and integrated into the pharmaceutical manufacturing process. Regulatory bodies like the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have established clear guidelines and frameworks that support QbD adoption, leading to significant advancements in product quality, operational efficiency, and regulatory compliance. These regions have benefited from a strong regulatory environment that promotes innovation while ensuring that products meet the highest quality standards.

In contrast, the literature indicates that developing markets, including India, face several unique challenges in adopting QbD. These challenges include limited access to advanced technologies, inadequate infrastructure, and a regulatory environment that is not fully aligned with international standards. The literature suggests that these challenges must be addressed through targeted investments, capacity-building initiatives, and regulatory reforms to facilitate the wider adoption of QbD in these regions.

One of the consistent themes in the literature is the critical importance of training and education in driving successful QbD implementation. Case studies from developed markets demonstrate that companies that invest in comprehensive training programs for their employees are more likely to achieve successful QbD implementation. These programs not only equip employees with the technical skills needed to implement QbD but also foster a culture of quality and continuous improvement. The literature emphasizes that training should be an ongoing process, with regular updates to ensure that employees are aware of the latest developments in QbD practices and technologies. This finding aligns with the primary research, which also identified a need for ongoing training and professional development in the Indian context. The generational divide in QbD knowledge identified in the primary research highlights the importance of targeted training programs that address the specific needs of both newer and more experienced professionals. The literature highlights the critical role of advanced technologies, such as Process Analytical Technology (PAT) and real-time data analytics, in supporting QbD implementation. These technologies enable companies to monitor and control critical quality attributes in real-time, ensuring consistent product quality and compliance with regulatory standards. The adoption of these technologies is essential for the successful implementation of QbD, as they provide the tools needed to effectively manage complex manufacturing processes and ensure that products meet the desired quality standards.

However, the literature also points out that the successful integration of these technologies requires significant investment and support from regulatory bodies. In regions where regulatory agencies have provided clear guidelines and support for QbD, companies have been more successful in adopting these technologies and realizing the benefits of QbD. The literature suggests that similar regulatory support is needed in developing markets like India to overcome the existing barriers to QbD adoption.

The literature review identifies several challenges in the Indian regulatory environment hindering the adoption of QbD, such as unclear guidelines, inconsistent requirements across regions, and lengthy approval times for new products. These challenges create uncertainty and can slow down adoption, particularly for smaller firms that lack the resources to navigate these complexities. Addressing these issues by aligning regulations with international standards, providing clearer guidance, and streamlining approval processes is essential. A more supportive regulatory framework would facilitate wider QbD adoption and help India's biopharmaceutical industry compete more effectively on the global stage.

5.3 Limitations of the Study

This study provides valuable insights into the current state of Quality by Design (QbD) implementation in the Indian biopharmaceutical industry; however, several limitations should be acknowledged. The study achieved a response rate of 88.1%, with 111 responses out of 126 participants. Although this is a relatively high response rate, the study may still be subject to response bias, as the opinions and experiences of non-respondents might differ from those who participated, potentially skewing the findings. Additionally, the geographic focus on the Indian biopharmaceutical industry limits the generalizability of the findings to other countries or regions with different regulatory environments, technological advancements, and market dynamics. The reliance on self-reported data gathered through surveys, introduces potential biases such as social desirability bias and recall bias, which could affect the accuracy of the findings.

Furthermore, there may have been variability in respondents' interpretations of key terms used in the survey, such as "complete integration" and "partial integration," leading to inconsistencies in the data. The study's focus on younger professionals as key drivers of QbD adoption may have inadvertently overlooked the perspectives and challenges faced by more seasoned professionals, suggesting a need for more balanced representation in future research. Additionally, the cross-sectional design of the study provides a snapshot of QbD implementation at a single point in time, which limits the ability to track changes and the evolution of QbD practices over time. The study's emphasis on quantitative data collection also limited the exploration of qualitative insights, which could have provided richer, more refined perspectives on the challenges and successes of QbD implementation.

Moreover, the industry-specific focus on biopharmaceuticals may limit the applicability of the findings to other sectors, as the specific regulatory, technological, and operational challenges faced by biopharmaceutical companies might differ from those in other industries. Finally, the study was conducted within certain resource constraints, including time, budget, and access to proprietary data, which may have affected the scope of the research and the depth of analysis. These limitations should be taken into account when interpreting the results, and they highlight areas for future research to build on and expand the understanding of QbD implementation in India and beyond.

5.4 Future Recommendations

Based on the findings from both primary and secondary research, several recommendations are proposed to enhance the effective implementation of QbD in the Indian biopharmaceutical industry:

It is recommended that comprehensive training programs be developed and made widely accessible to professionals at all levels within the industry. These programs should cover both the fundamentals of QbD and the practical challenges associated with its implementation. Special attention should be given to bridging the knowledge gap between younger and more experienced professionals to ensure that all employees are equipped with the necessary skills to implement QbD effectively. Training programs should also include modules on the latest developments in QbD practices and technologies, as well as on how to overcome common challenges in implementation. This will ensure that employees are not only familiar with the principles of QbD but also confident in their ability to apply these principles in real-world settings. Moreover, training should be an ongoing process, with opportunities for employees to continuously update their skills and knowledge as QbD practices evolve. Companies should invest in advanced technologies, such as Process Analytical Technology (PAT) and real-time data analytics tools, to support the full integration of QbD. These technologies are critical for monitoring and controlling critical quality attributes, ensuring consistent product quality, and enhancing operational efficiency. In addition, companies should explore the potential of emerging technologies, such as artificial intelligence (AI) and machine learning, to further optimize QbD processes and improve decision-making.

Investing in these technologies will require significant financial resources, but the potential benefits in terms of improved product quality, reduced variability, and increased regulatory compliance make it a worthwhile investment. Companies should also consider collaborating with technology providers, academic institutions, and research organizations to gain access to the latest innovations and expertise in QbD technologies. Regulatory bodies, particularly the Central Drugs Standard Control Organization (CDSCO), should provide clearer guidelines and support to facilitate the adoption of QbD. This could include the development of case studies, workshops, and consultations with industry stakeholders. Aligning Indian regulations more closely with international standards, such as those set by the FDA and EMA, would also help Indian companies better understand and meet global expectations. Regulatory agencies should also consider providing more proactive support to smaller companies, including through the provision of tailored guidance and the development of streamlined approval processes for QbD-based products. By creating a more supportive regulatory environment, India can help its biopharmaceutical industry better compete on the global stage and ensure that its products meet the highest quality standards. It is recommended that government and industry associations offer financial incentives, such as grants or tax breaks, to encourage Small and Medium Enterprises (SMEs).

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APPENDICES

Appendix I -Ethical Form

Innopharma education

GRIFFITH COLLEGE

Ethics Application & Declaration Form

DISSERTATION TITLE: How Can Quality by Design Enhance Biopharmaceutical Manufacturing in India? Exploring Strategies and Outcomes

RESEARCHER'S NAME: MERIN CHEERAMKULATH JOSE

PROGRAMME OF STUDY: MSC Pharmaceutical Business and Technology

SUPERVISOR'S NAME: Dr. Favour Okosun
DECLARATION:

The information in this application form is accurate to the best of my knowledge. I undertake to abide by the principles outlined by Innopharma/Griffith College ethics policy in my research dissertation. I confirm that I have completed a full ethics assessment for my research dissertation as per the college guidelines. I will not begin my primary research until such approval from my supervisor and/or ethics Committee has been obtained.

I pledge to carry out my research according to the Innopharma/Griffith College academic integrity standards. Any results presented in my dissertation will be from my own, original research, I will reference and/or acknowledge any material or sources used in its preparation and I will not plagiarise the work of anyone else.

For Student:

[illegible] 05/07/24

STUDENT SIGNATURE: DATE:05/07/2024

The research contained within this research dissertation proposal has been approved.

For Supervisor:

Ethics Committee Approval Required: Yes ☑ No ☐

SUPERVISOR SIGNATURE: Favour Okosun

DATE: 06/Jul/2024

For Ethics Committee (if required):		
Ethics Committee Approval Given:	Yes ☐	No ☐
ETHICS COMMITTEE MEMBER SIGNATURE:		
DATE:		

NOTE: Supervisors are responsible for ensuring their students fill in this form correctly and that all ethical areas have been considered.

SECTION 1: DESCRIPTION OF RESEARCH STUDY

1.1 Purpose and research objectives: With an emphasis on techniques and results to improve medication efficacy and safety, this study explores the application of Quality by Design (QbD) in India's biopharmaceutical industry. Encouraging the integration of quality into processes from the initial stages, QbD centers on ICH recommendations Q8, Q9, and Q10 and is supported by regulatory agencies such as the EMA. The research will appraise how QbD is now integrated, explore particular implementation approaches, and analyze how they affect product quality, legal compliance, and operational effectiveness. It will also pinpoint regulatory and technological barriers and offer suggestions to improve QbD adoption in India.

The significance of this study is in its ability to direct authorities and Indian biopharmaceutical companies toward better manufacturing procedures, guaranteeing the development of high-quality, safe, and effective biopharmaceuticals that satisfy global standards. The study intends to encourage continued innovation and competitiveness in the global market by addressing these goals.

1.2 Research Methodology: An online survey aimed at gathering primary data for this research on Quality by Design (QbD) in biopharmaceutical manufacturing in India will be conducted among a sample of professionals in the biopharmaceutical industry. The survey will be conducted on the following topics: quality assurance managers, process engineers, senior management, and regulatory staff from Indian biopharmaceutical companies. The survey will be conducted on an online platform (e.g., Google Forms, SurveyMonkey). The sample size will be between 50 and 75 respondents. The survey will be open for a period of six to eight weeks.

To ensure adequate response rates, the survey will be sent via email along with the survey URL and follow-up reminder emails. Obtaining approval from the appropriate institutional review board (IRB), guaranteeing privacy and confidentiality, and notifying subjects of their rights and the objective of the study are all examples of ethical considerations. To find underlying components or dimensions in the survey data, data analysis will include descriptive statistics (standard deviations, averages, percentages, and frequencies), inferential statistics (correlation analysis, ANOVA, and t-tests), and exploratory factor analysis.

SECTION 2: POSSIBLE ETHICAL ISSUES

Answer 'yes' or 'no' to the following questions.

SUBJECT MATTER

Does the research proposal involve:

Research into specific company activities that would be deemed sensitive or confidential

No

Research into politically and/or racially/ethnically and/or commercially sensitive areas No
Sensitive, personal, professional or corporate issues No

RESEARCH PROCEDURES

Does the research proposal involve:

Research that might damage the reputation of companies or participants No
Research that may negatively affect the reputation of Griffith College/Innopharma No
Use of personal records without consent No
Use of company data without consent No
The offer of any inducements to participate No
Audio or visual recording without consent No
Using a language other than English No

PARTICIPANTS

Does the research proposal involve

People who are not competent and/or fluent in English No
Does your research group include any of the following vulnerable groups No
(Adults with psychological impairments; Adults with learning difficulties; Adults under the protection/control /influence of others (e.g. in care/prison); Relatives of ill people (e.g. parents of sick children); Hospital or GP participants recruited in a medical facility; persons under the age of 18)

If you have answered NO to ALL questions, please go straight to Section 4.

If you have answered YES to ANY question in SECTION 2, you must fill in SECTION 3.

SECTION 3: STEPS TAKEN TO AVOID ETHICAL ISSUES

[Only fill in this section if you answered YES to ANY of the questions in Section 3. For example, if you answered yes to including participants who are not fluent in English, you might put forward a plan that offers your survey in two languages to take this into account. Another example could be a study where the researcher wants to include information about the care received by children with a long-term condition but it would not be ethical to approach the children directly but it might be acceptable to instead ask parents questions about their child's care. If these plans are acceptable to your supervisor, you may not need to apply for ethical approval from the Ethics Committee].

3.1. If your ethics relates to ***Subject Matter***, outline your action plan to work around any sensitive issues.
3.2. If your ethics relates to ***Research Procedures***, outline your action plan to deal with possible ethical issues in your research procedures.
3.3. If your ethics relates to ***Participants***, outline how you will protect vulnerable persons or those that do not have English as their first language.

SECTION 4: ABOUT YOUR PARTICIPANTS

4.1. Outline your participant profile and why you have chosen them for this study: The study's participant profile consists of Indian regulatory department staff, process engineers, senior executives from biopharmaceutical businesses, and quality assurance managers. The selection of this broad group was based on their direct experience with and knowledge of quality control, regulatory compliance, and biopharmaceutical manufacturing processes. Their observations are useful in assessing the state of QbD integration at the moment, identifying the particular strategies being used, and defining the benefits and challenges associated with QbD adoption in the Indian biopharmaceutical sector. A thorough understanding of the practical and regulatory issues of QbD is ensured by their professional expertise.

4.2 How do you plan to gain access to/contact/approach your participant(s): A focused method will be used to obtain access to study participants. First, a list of Indian biopharmaceutical businesses will be compiled. Professional networks like LinkedIn and personal connections will be used to gather contact information for relevant staff members, including regulatory department staff, process engineers, senior managers, and quality assurance managers. There will be an initial message outlining the goals, significance, and specifics of participation in the study, along with the survey's URL. Reminders later on will guarantee adequate response rates. With ethical permission from the appropriate institutional review board (IRB), we shall respect ethical principles including informed consent, confidentiality, and privacy.

SECTION 5: INFORMATION, CONSENT AND CONFIDENTIALITY

5.1 Participant Information Letter (PIL) for participants

Dear Participants,

I am Merin Cheeramkulath Jose, currently pursuing a Master's in Pharmaceutical Business and Technology at Griffith College, Dublin. As part of my coursework, I am conducting a research study titled "How Can Quality by Design Enhance Biopharmaceutical Manufacturing in India? Exploring Strategies and Outcomes." Your participation is vital to understanding the implementation of Quality by Design (QbD) in the Indian biopharmaceutical industry. This study aims to identify strategies, assess outcomes, and highlight challenges related to QbD adoption, ultimately providing recommendations to enhance manufacturing practices.

Participation involves completing an online survey, which will take approximately 15-20 minutes. Your insights on QbD implementation are crucial, and all responses will be kept confidential and anonymous. Your data will be securely stored and used solely for research purposes. There are no significant risks associated with participation, and your input could significantly impact biopharmaceutical manufacturing practices in India.

You have the right to withdraw from the study at any time without penalty. For any questions or concerns about the study, please contact me at [merincjose@gmail.com]. Rest assured; all data collected will be handled in compliance with the current General Data Protection Regulations (GDPR).

Thank you for considering participation. Your contribution will help advance understanding and improvements in biopharmaceutical manufacturing practices in India.

Sincerely,

Merin Cheeramkulath Jose

Please confirm below that your information letter covers:

Description of the research topic and method	Yes
Details of what participation will involve	Yes
Rights to anonymity	Yes
Confidentiality	Yes
Rights to withdraw from the research	Yes
The contact details of the researcher and supervisor (if necessary)	Yes

5.2 Informed Consent Form (ICF) for Participants

I understand the purpose of this study and voluntarily agree to participate in this research survey. I acknowledge that my responses will be used for the research titled "How Can Quality by Design Enhance Biopharmaceutical Manufacturing in India? Exploring Strategies and Outcomes."

No: my research study involves an online survey only and/or does not require signed consent

SECTION 6: STORAGE OF DATA

[Please ensure that you are abiding by GDPR and the national Data protection laws https://www.hrb.ie/funding/gdpr-guidance-for-researchers/gdpr-and-health-research/).

The student is responsible for storage of data and this will be handed over to the college in an electronic format as part of the thesis submission i.e. primary data and completed ICFs where applicable will be added to the primary data folder on moodle. The rationale is to keep data ***as long as it is still useful*** *and there is an intention to use it further* ***for research*** *so if this is not the case then this can be stipulated here and a shorter retention period given.]*

6.1. How will you store the research data and for how long? How will you manage data protection issues?

Under Griffith College, the study data will be electronically kept on password-protected, secure platforms. In accordance with college policy and GDPR compliance, the data will be kept for five years after the study's conclusion. This retention time ensures that the data is still accessible for any additional investigation or confirmation that may be required.
All information gathered will be private and encrypted to maintain confidentiality in order to handle data protection issues. Only authorized personnel will be able to access the data. Without informed authorization, the data will not be shared with any parties and will only be used for research. The data will be safely erased to stop any unwanted access or use after the retention term.
We guarantee the safety and security of all participant data during the research process by following by GDPR and national privacy laws.

SECTION 7: NON-DISCLOSURE AGREEMENT & STUDENT CONSENT

7.1 Non-Disclosure Agreement (NDA)

Will the final dissertation contain any information pertaining to any source that would warrant the use of a Non-Disclosure Agreement (NDA) e.g. industry-based research? No

7.2 Student consent

If a Non-Disclosure Agreement (NDA) is not required, does the Student consent to allow their completed dissertation to be held/published by Innopharma/Griffith College? Yes

SECTION 8: RECORDING AND RETENTION OF DISSERTATION VIVA

8.1 Viva Recording

The Dissertation viva will be recorded. This recording may be used to facilitate assessment by Innopharma staff, a third reader if necessary and/or if requested by the external examiner for the Programme. The recording will be held in line with current GDPR guidelines and will not be made publicly available.

SECTION 9: DOCUMENT CHECKLIST

NOTE: Applicants must attach the following documents in electronic format to the appendix.

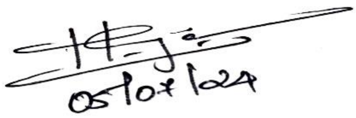
Which documents are added to the appendix? Please tick N/A if not applicable:

9.1 Participant Information Letter (PIL) for Participant	Yes
9.2 Informed Consent Form (ICF) for participant	N/A
9.3 Questions/survey for interviewees/focus groups etc *(can be in draft form)*	Yes
9.4 Any other documents e.g. Non-Disclosure Agreement	N/A

I confirm that this application is complete and all required documents are included in the appendix.

For Student:

STUDENT SIGNATURE: Merin Cheeramkulath Jose



DATE:05/07/24

Appendix II – Survey Questionnaire

Survey Questionnaire: Quality by Design in Biopharmaceutical Manufacturing in India

Section 1: Demographic Information

- **What is your current or previous role in your organization?**
    - Quality Assurance Manager
    - Process Engineer
    - Senior Management
    - Regulatory Compliance Officer
    - Other (please specify)
- **How many years of experience do you have in the biopharmaceutical industry?**
    - Less than 5 years
    - 5-10 years
    - 10-15 years
    - More than 15 years
- **What type of biopharmaceutical products does your company manufacture?**
    - Injectables
    - Oral Dosage forms
    - Topical Dosage form
    - Others
- **What is the size of your organization?**
    - Small (less than 50 employees)
    - Medium (50-200 employees)
    - Large (more than 200 employees)

Section 2: Current Level of QbD Integration

- **Which regulatory category does your company belong to?**
    - FDA (Food and Drug Administration)
    - GMP (Good Manufacturing Practice)
    - EU (European Union regulations)
    - CDSCO (Central Drugs Standard Control Organization)
    - Other (please specify)
- **How familiar are you with Quality by Design (QbD) principles?**
    - Not familiar
    - Somewhat familiar
    - Familiar
    - Very familiar
- What extent of a QbD integration is there in the production processes of your company?
    - Not at all integrated
    - Partially integrated
    - Primarily integrated
    - Completely integrated
- **Which aspects of QbD has your company implemented? (Select all that apply)**
    - Quality Target Product Profile (QTPP)
    - Critical Quality Attributes (CQAs)

- Critical Process Parameters (CPPs)
- Risk Management
- Process Analytical Technology (PAT)
- Continuous Process Verification (CPV)

- **What is the duration of your company's application of QbD principles?**
  - Less than 1 year
  - 1-3 years
  - 3-5 years
  - Over 5 years

Section 3: Strategies for Implementing QbD

- **Why did your business choose to implement QbD principles?**
  - Regulatory requirements
  - Desire to improve product quality
  - Operational efficiency
  - Competitive advantage
  - Other (please specify)

- **What specific strategies has your company used to implement QbD? (Select all that apply)**
  - Training and development programs
  - Hiring QbD experts
  - Investing in new technologies
  - Collaborating with external consultants
  - Developing internal QbD guidelines

- **How effective have these strategies been in implementing QbD?**
  - Not effective
  - Somewhat effective
  - Effective
  - Very effective

- **What tools and methods does your business employ to implement QbD? (Check all that relate.)**
  - Design of Experiments (DoE)
  - Risk Assessment Tools
  - Process Analytical Technology (PAT)
  - Continuous Process Verification (CPV)
  - Statistical Process Control (SPC)

Section 4: Outcomes of QbD Implementation

- **What impact has QbD implementation had on your company's product quality?**

- No improvement
- Minor improvement
- Significant improvement
- Major improvement

- **What effects has QbD had on your company's regulatory compliance?**

  - No impact
  - Minor impact
  - Significant impact
  - Major impact

- **What impact has QbD had on operational effectiveness?**

  - No improvement
  - Minor improvement
  - Significant improvement
  - Major improvement

- **Has the use of QbD resulted in any financial impacts on the company?**

  - No
  - Yes, minor impacts
  - Yes, significant impacts
  - Not sure

Section 5: Challenges in QbD Implementation

- **What are the main barriers your business is facing in putting QbD into practice? (Check all that relate.)**
  - Limited technical expertise
  - High upfront investment
  - Raw material quality issues
  - Supply chain management problems
  - Regulatory barriers
  - Resistance to change
- **To what extent do these barriers affect your company's efforts to implement QbD?**
  - Not significant
  - Somewhat significant
  - Significant
  - Very significant
- **What technical challenges does your company experience while using QbD?**

  - Lack of skilled personnel

- Insufficient training
- Inadequate technology
- Complexity of QbD principles

- **What regulatory challenges does your business encounter while implementing QbD?**
  - Lack of clear guidelines
  - Inconsistent regulations
  - Long approval times

Section 6: Recommendations for Enhancing QbD Implementation

- **What kind of assistance would be most useful in resolving implementation-related issues with QbD? (Check all that apply.)**
  - Technical training programs
  - Financial incentives
  - Regulatory guidance
  - Industry collaborations
  - Access to expert consultants
- **How important is regulatory support in facilitating QbD implementation?**
  - Not important
  - Somewhat important
  - Important
  - Very important
- **What role should the government play in promoting QbD adoption? (Select all that apply)**
  - Providing funding for training and development
  - Offering tax incentives
  - Streamlining regulatory processes
  - Facilitating public-private partnerships
- **What changes would you recommend making to improve QbD adoption in the biopharmaceutical sector in India?**
  - Increased awareness and education
  - Better regulatory frameworks
  - More industry collaboration
  - Improved access to technology

Section 7: Future Prospects and General Feedback

- **In what way do you think QbD will develop in the Indian biopharmaceutical sector?**
  - Very optimistic
  - Optimistic
  - Neutral
  - Negative
- **What possible advantages do you see for India as a result of more QbD adoption? (Check all that apply.)**
  - Improved product quality
  - Enhanced regulatory compliance
  - Greater operational efficiency
  - Increased global competitiveness

- Reduced production costs
- **What possible adverse impacts do you think a rise in QbD adoption could lead to? (Check all that relate.)**
  - High implementation costs
  - Technical complexity
  - Resistance to change
  - Regulatory hurdles

- **What is your overall satisfaction with your company's current QbD implementation?**

  - Very dissatisfied
  - Dissatisfied
  - Neutral
  - Satisfied
  - Very satisfied

- **Would you recommend other biopharmaceutical manufacturers in India to adopt QbD principles?**

  - Definitely not
  - Probably not
  - Not sure
  - Probably
  - Definitely
- **Please provide any additional comments or suggestions regarding QbD implementation in the Indian biopharmaceutical industry**

Thank You for the participation