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Assessment of Quality Control Processes in Genetically Engineered Cell Lines in Ireland: An Impact on Biopharmaceutical Product Consistency

Dissertation submitted in partial fulfilment of the requirements for M. Sc.in Pharmaceutical Business & Technology (QQI)

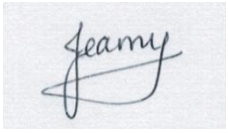
Submitted by,

Jeamy Sera Johnson

May 2025

CANDIDATE DECLARATION

I certify that the dissertation entitled: ***Assessment of Quality Control Processes in Genetically Engineered Cell Lines in Ireland: An Impact on Biopharmaceutical Product Consistency*** submitted for the degree of MSc in Pharmaceutical Business and Technology is the result of my own work and that where reference is made to the work of others, due acknowledgment is given.

Candidate signature: 

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List of Abbreviations

Abbreviation	**Abbreviation Meaning**
ATMPs	Advanced Therapy Medicinal Products
AI	Artificial Intelligence
CHO	Chinese Hamster Ovary cells
CROs	contract research organizations
CAPA	Corrective and Preventive Action
CRISPR-Cas9	Clustered regularly interspaced short palindromic repeats and CRISPR-associated protein 9
CPPs	Critical Process Parameters
CQAs	Critical Quality Attributes
DNA	Deoxyribonucleic acid
ddPCR	Digital Droplet Polymerase Chain Reaction
ELN	Electronic Laboratory Notebook
e-QMS	Electronic Quality Management Systems
EM	Environmental monitoring
ELISA	Enzyme-Linked Immunosorbent Assay
EMA	European Medicines Agency
EU	European Union

FDA	Food and Drug Administration
GMP	Good Manufacturing Practices
HPRA	Health Products Regulatory Authority
HEPA	High Efficiency Particulate Air
HPLC	High-Performance Liquid Chromatography
IPCs	In-Process Controls
ICH	International Conference on Harmonisation
JIT	Just-in-time Inventory Systems
LIMS	Laboratory Information Management System
ML	Machine Learning
MS	Mass Spectrometry
MCB	Master Cell Bank
NIR	Near-Infrared Spectroscopy
NGS	Next-Generation Sequencing
NGS-MAM	Next-Generation Sequencing-Multi-Attribute Method
PCR	Polymerase Chain Reaction
PAT	Process Analytical Technology
QbD	Quality By Design
QC	Quality control
qPCR	Quantitative Polymerase Chain Reaction
RT-PCR	Reverse Transcription PCR
SOPs	Standardized Operating Procedures
WCB	Working Cell Bank

Abstract

Introduction: The growing complexity of biopharmaceutical products derived from genetically engineered cell lines necessitates robust quality control (QC) systems to ensure product consistency, safety, and efficacy. In Ireland, where the biopharmaceutical sector continues to expand, understanding how QC processes are applied and optimized is vital for maintaining regulatory compliance and public trust. This study explores the role of QC in genetically engineered cell line production and its influence on batch consistency, focusing on operational practices, challenges, innovations, and cost-effective strategies.

Methods: A qualitative research approach was employed, guided by an interpretivist paradigm to capture the nuanced experiences of industry professionals. Data was collected through semi-structured interviews with seven QC professionals from various Irish biopharmaceutical firms. Purposive sampling ensured participants held relevant expertise. Thematic analysis was conducted following Braun and Clarke's six-phase method, enabling the identification of patterns and themes that aligned with the study's five objectives.

Results: Six major themes and twenty-three subthemes were identified. Key findings revealed that QC significantly affects product consistency through SOP adherence, potency monitoring, and gene expression validation. Challenges included resource constraints, regulatory fragmentation, and training gaps. Innovative practices such as real-time monitoring, AI integration, and omics-based analysis are emerging as solutions, although barriers like cost and infrastructure remain. Cost-effective strategies such as multi-use systems, shared resources, and outsourcing were highlighted, especially for small-to-medium enterprises. Ethical and societal responsibilities were also seen as integral to modern QC.

Conclusions: The study contributes meaningful insights into how QC is practiced in Ireland's biopharmaceutical sector, confirming that robust, adaptive, and ethically aligned QC systems are essential for consistent and compliant biomanufacturing. It recommends harmonization of standards, investment in training, and broader adoption of innovative and lean QC practices. These findings support policy, operational, and academic improvements in global QC systems.

Keywords: Quality Control, Biopharmaceuticals, Genetically Engineered Cell Lines, Product Consistency, Thematic Analysis, Ireland, Innovation, Regulatory Compliance, Cost-effective Strategies, Ethical Considerations

1. INTRODUCTION

1.1 Overview

This study investigates how Quality Control (QC) processes impact the consistency of biopharmaceutical products derived from genetically engineered cell lines, with a particular focus on practices within Ireland. Genetically engineered cell lines serve as the foundation for modern biopharmaceutical manufacturing, allowing the production of complex therapeutic proteins and biologics. As these products are highly sensitive to changes in production conditions, consistent quality requires robust and adaptable QC systems.

The study is guided by a central research question that explores the influence of QC processes on product consistency, alongside the challenges and potential improvements in these practices. It is structured around five research objectives, including examining current QC processes, identifying challenges, exploring innovative and cost-effective strategies, and recommending industry-wide best practices.

Using a qualitative methodology, insights were gathered from experienced professionals in the Irish biopharmaceutical industry. Their perspectives were thematically analyzed to identify key trends, practices, and gaps in QC implementation.

This chapter introduces the topic, outlines the study's rationale, and sets the context for the chapters that follow. It provides a foundation for understanding the importance of QC in genetically engineered cell lines, not just as a technical requirement, but as a strategic, ethical, and operational pillar in biopharmaceutical production. By linking academic literature with practitioner insights, the study aims to provide actionable recommendations for improving QC processes in a dynamic, innovation-driven industry.

1.2 Study Context

The rapid advancement of genetic engineering has transformed the landscape of biopharmaceutical production, enabling the development of sophisticated therapies, including monoclonal antibodies, recombinant proteins, and gene therapies. Central to this process are genetically engineered cell lines, which serve as the biological factories for producing these complex molecules. These cell lines are genetically modified to express therapeutic genes and are cultivated in controlled environments to produce uniform, high-quality outputs (Capes-Davis, 2018).

However, despite their utility, the use of such cell lines introduces substantial complexity into biomanufacturing. These systems are inherently sensitive to environmental changes, including shifts in temperature, pH, media composition, and handling procedures. Any deviation from optimal conditions can result in variations in gene expression, protein folding, or post-translational modifications—directly impacting the safety, efficacy, and regulatory compliance of the final product (Dai and Shen, 2022).

The reliability of these production systems, therefore, depends heavily on rigorous Quality Control (QC) frameworks that monitor critical quality attributes (CQAs) throughout the production lifecycle. Such frameworks include bioassays, genetic expression profiling (Quantitative Polymerase Chain Reaction - qPCR)/Digital Droplet Polymerase Chain Reaction - ddPCR), and environmental monitoring protocols. Ensuring consistency across multiple batches and across different production scales is a known challenge in this domain (Hyde, 2024; Lamanna *et al.,* 2018).

Within Ireland, the biopharmaceutical sector has grown significantly, housing major global firms and research hubs. This context provides a robust environment for examining QC practices specific to genetically engineered cell lines. Irish facilities are also subject to regulatory standards set by the HPRA, EMA, and FDA, necessitating both compliance and innovation in QC systems. Thus, this research is situated at the intersection of scientific advancement, operational complexity, and regulatory expectation—making it both timely and relevant to industry needs.

1.3 Justification and significance of the study

This research addresses a timely and industry-relevant gap by focusing specifically on Quality Control (QC) in genetically engineered cell line-based biopharmaceutical production. Although extensive literature exists on cell line development and upstream/downstream bioprocessing, fewer studies have explored how QC systems operate within this context and how they influence product consistency and regulatory compliance (Mirasol, 2018; Capes-Davis, 2018).

QC is often perceived as a back-end verification tool; however, in the context of genetically engineered cell lines, it plays a central, proactive role in ensuring product quality from the earliest stages of development. With increasing regulatory scrutiny,

particularly under frameworks like ICH Q8–Q11 and 21 CFR Part 11, biopharmaceutical manufacturers must demonstrate not only the efficacy but also the reproducibility and robustness of their products. This necessitates precise and adaptive QC systems capable of detecting subtle deviations in gene expression, cell viability, and contamination risk (Hyde, 2024; ICH, 2024).

Furthermore, small- to medium-sized enterprises face unique challenges in implementing cost-effective yet compliant QC systems. This research identifies scalable strategies that smaller facilities can adopt without compromising on quality. The study also contributes by uncovering industry professionals' perspectives, which are often underrepresented in academic discourse.

By capturing firsthand accounts from Irish QC professionals, the research bridges the gap between theoretical standards and operational realities. It also supports industry-wide knowledge sharing, contributing to a body of best practices that can be adopted by both emerging and established facilities within and beyond Ireland.

1.4 Aim of the study

The present study aims to examine how quality control (QC) processes influence the consistency of biopharmaceutical products that are derived from genetically engineered cell lines, in Ireland. It investigates the common challenges that are faced during the QC processes so as to identify and come up with possible areas of improvement in the processes. In order to improve the QC processes of genetically engineered cell lines in Ireland and to develop industry-wide best practice recommendations, this study aims to explore the QC processes deeply and to identify innovative approaches that helps in enhancing the quality of biopharmaceuticals.

This research is guided by the following research question:

How do the quality control processes employed in genetically engineered cell lines in Ireland influence the consistency of biopharmaceutical products, and what are the key challenges and potential improvements in these processes?

For a more comprehensive understanding and focus, this research question is broken down using the following research objectives:

1. Evaluating different QC processes and understanding its influence in the product consistency of biopharmaceuticals derived from genetically engineered cell lines.
2. Examining common challenges and areas of improvement in the QC processes.
3. Identifying potential innovative approaches for maintaining product consistency.
4. Identifying cost-effective QC processes that can be implemented, particularly in facilities of smaller production.
5. Developing possible recommendations for industry-wide best practices to improve the QC processes of genetically engineered cell lines.

1.5 Structure of the Study

Chapter 1: Introduction

The first chapter gives an overview of genetically engineered cell lines, the QC processes involved in them and how they influence the consistency of biopharmaceutical products within Ireland. It outlines the research objectives, significance and the research questions that guide the study.

Chapter 2: Literature Review

This chapter gives a review of existing research on genetically engineered cell lines. It explores different methods used in gene therapy, the advancements over the years and the research already conducted into them. It identifies gaps in the literature and establishes a framework against which the findings of primary research can be compared.

Chapter 3: Research Methodology

The chapter outlines how the overall study has been conducted. It discusses the philosophical approach and the research paradigms that has been used detailing the process and logic used to support the primary data collection method. Additionally, this chapter details the target population and also the ethical considerations involved in the study.

Chapter 4: Findings and analysis

In this chapter, the findings that have been obtained with the help of primary data collection methods are analysed thematically. A qualitative methodology of data collection such as interviews were employed in the study. Identification of themes and sub themes from the findings helped in addressing each objective of the study.

Chapter 5: Conclusion and Recommendations

Chapter 5 summarises the key findings from the study and describes the implications. Recommendations are made for industry-wide adoption of best practices to improve the QC processes. The chapter reflects on the limitations of the study outlines future research directions.

1.6 Conclusion

In conclusion, this introductory chapter has outlined the rationale, context, and justification for examining Quality Control (QC) processes in genetically engineered cell line-based biopharmaceutical production. The importance of this research stems from the increasing complexity of biological products and the critical role that QC plays in ensuring product consistency, regulatory compliance, and ultimately, patient safety.

Genetically engineered cell lines, while offering tremendous potential for therapeutic innovation, present unique challenges in maintaining consistent output due to their sensitivity to environmental and procedural variations. This makes QC not merely a technical necessity but a strategic function that spans process design, monitoring, and release. The chapter has also framed the study within the Irish biopharmaceutical context, which provides a rich setting for investigating QC practices due to the presence of leading global firms and stringent regulatory frameworks.

The chapter presented the central research question and five specific objectives, which guide the study's focus on current QC practices, implementation challenges, innovative approaches, cost-effective strategies, and industry-wide recommendations. A qualitative methodology, incorporating thematic analysis of interviews with Irish QC professionals, was selected to explore these objectives in depth.

Ultimately, this study aims to generate practical insights and contribute to improving QC processes across the biopharmaceutical sector. By grounding the research in both industry practice and academic theory, the study seeks to support continuous improvement, encourage knowledge sharing, and inform regulatory and operational strategies that enhance the reliability and sustainability of modern biopharmaceutical manufacturing.

2. LITERATURE REVIEW

2.1 Introduction

The biopharmaceutical industry relies heavily on genetically engineered cell lines to produce complex biological therapeutics and has revolutionized modern medicine. These cell lines are engineered to produce recombinant proteins, monoclonal antibodies, and other biologics that have significantly improved the treatment of various diseases. However, the production of these complex biological products requires stringent quality control (QC) processes to ensure their consistency, safety, and efficacy. This literature review aims to provide a comprehensive assessment of the QC processes in genetically engineered cell lines, particularly within the context of Ireland, and to identify key gaps and opportunities for further research.

2.1.1 The Importance of Quality Control in Biopharmaceuticals

Quality control is a critical aspect of the biopharmaceutical manufacturing process. It involves a series of tests and procedures that are designed to ensure that the final product meets predefined quality standards. Biopharmaceuticals are inherently complex and heterogeneous due to their production in living cells and the various post-translational modifications they undergo. This complexity necessitates rigorous QC measures to ensure product consistency and clinical performance. QC processes involve extensive analysis of critical quality attributes, including protein structure, post-translational modifications, and impurity profiles. They help in monitoring and controlling critical process parameters, minimizing variability in production conditions that could affect product quality. When manufacturing changes are necessary, QC processes guide comparability assessments in order to ensure that product quality and clinical performance remain consistent before and after the change (Lamanna *et al.*, 2018). For genetically engineered cell lines, QC processes are essential to monitor the consistency and stability of the cell lines, the expression of the desired product, and the absence of contaminants.

The European Medicines Agency (EMA) and the U.S. Food and Drug Administration (FDA) have established stringent guidelines to ensure that biopharmaceutical products meet high standards of quality and safety (EMA, 2021; FDA, 2024). In Ireland, the Health Products Regulatory Authority (HPRA) plays a crucial role in overseeing the regulatory compliance of biopharmaceutical products. The HPRA ensures that QC processes are in line with international standards, thereby safeguarding public health (HPRA, 2025). The implementation of robust QC processes is particularly important given the complexity of genetically engineered cell lines and the potential variability in product quality.

Cell lines are established cell cultures with a homogeneous genotype and phenotype. When an appropriate culture media and room are provided, these cultures can reproduce indefinitely (Capes-Davis, 2018). Genetically engineered/modified cell lines are the product of biotechnological methods that modify the genetic material of cell lines. Cell banks are created using genetically engineered cell lines by allowing the cells in the culture to proliferate when controlled conditions are maintained. Cell bank creation is very important to ensure biological product efficacy and its purity. The usage of master cell bank (MCB) and a working cell bank (WCB) helps to get detailed characterization data that is fundamental for assessing a product's biosafety (Mirasol, 2018). Cell lines are typically derived from mammalian cells, such as Chinese hamster ovary (CHO) cells, and are engineered to express recombinant proteins. The use of genetically engineered cell lines offers several advantages, including high yield, scalability, and the ability to produce complex glycoproteins. However, these cell lines also present unique challenges, such as genetic instability, variability in protein expression, and the potential for contamination with adventitious agents. To address these challenges, QC processes must be designed to monitor critical quality attributes (CQAs) of the product, such as purity, potency, and safety.

2.2 Influence of QC Processes on Product Consistency

Quality control (QC) processes are fundamental to ensuring the consistency, safety, and efficacy of biopharmaceutical products derived from genetically engineered cell lines. The consistency of these products is critical because even minor variations can impact their therapeutic effectiveness and safety profile. This section will delve into the various aspects of QC processes and their influence on product consistency. Unlike small-molecule drugs, biologics are highly sensitive to changes in manufacturing conditions, which can lead to variability in their structure and function. This variability can affect their pharmacokinetics, immunogenicity, and overall therapeutic efficacy. Therefore, maintaining consistency is crucial for ensuring that these products perform as intended in clinical settings.

2.2.1 Cell Line Quality as Foundation for Product Consistency

The quality of cell lines used in manufacturing directly impacts product consistency. Industry experts now recognize that cell line quality, stability and reproducibility are pressing challenges faced by the industry due to which final product has the ultimate

impact (Hyde, 2024). This perspective represents an important evolution in thinking about quality control in biopharmaceutical manufacturing.

2.2.2 Cell Line Characterization

Modern quality control approaches begin with thorough cell line characterization. This includes identity testing of cells (e.g., short tandem repeat analysis), purity test (the absence of microbial contaminants or adventitious cellular and the potential cross-contamination that can occur with other cell lines), in vitro, in vivo, and polymerase chain reaction (PCR)-based assays (Mirasol, 2018). A comprehensive characterization of cell lines, including growth behaviour, productivity, and unique characteristics, forms the foundation for a successful manufacturing process (Mirasol, 2018). Regulatory agencies have made it mandatory for cell lines to be characterized and tested prior to being used in Phase I clinical trials. This characterization, along with clearance studies has been effective in preventing adverse events related to agent contamination in biopharmaceutical products (Mirasol, 2018).

Clonality of cell lines is also very important. Cloning minimises heterogeneity within cell banks but heterogeneity cannot be prevented during bio-production. This highlights the need for continuous monitoring throughout the entire duration of manufacturing (Mirasol, 2018).

2.2.3 Analytical Techniques

Advanced analytical techniques are at the forefront of QC processes in biopharmaceutical manufacturing. These techniques provide detailed insights into the molecular characteristics of the product, enabling early detection of deviations from predefined quality standards. High-Performance Liquid Chromatography (HPLC) and Mass Spectrometry (MS) are methods that assess purity and identity, detecting subtle changes that could affect product consistency. These methods can detect impurities, degradation products, and other quality attributes that may impact product consistency (O'Flaherty *et al.*, 2020).

Recent advancements in analytical techniques, such as single-cell sequencing and omics technologies, offer new opportunities for monitoring product quality at a molecular level. These techniques can provide detailed insights into the genetic and metabolic profiles of cell lines, thereby enabling more precise QC measures. For example, single-cell

sequencing can identify genetic variations within cell populations that may affect protein expression and quality (Evrony *et al.*, 2021; Dai and Shen, 2022).

2.2.4 Quality by Design (QbD)

The Quality by Design (QbD) approach has transformed quality control in biopharmaceutical manufacturing. Rather than testing quality into products, QbD principles focus on building quality into processes from the outset. Implementing QbD principles in bioprocess development helps in the identification of critical process parameters (CPPs) and how that impacts quality of a product, thereby enabling more consistent and robust processes (Thompson, 2023).

The International Conference on Harmonisation (ICH) Quality Guidelines, particularly the updated ICH Q5A(R2) guideline, provide comprehensive frameworks for quality control processes (ICH, 2024). This version preserves the fundamental concepts of the original Guideline and offers further suggestions for the proven and complementary methods for controlling possible virus contamination of biotechnology products.

2.2.5 Emerging Technologies

Innovative technologies, such as microfluid-based systems, are enhancing QC efficiency. These systems offer miniaturization and automation, enabling standardized testing for complex cell-based products like advanced therapy medicinal products (ATMPs) (Zia *et al.*, 2024). Such advancements reduce variability and improve consistency.

2.2.6 Impact on Product Consistency

Robust QC processes directly influence product consistency by detecting deviations early and ensuring CQAs meet predefined standards. For example, HPLC and MS can identify minor impurities that might compromise therapeutic efficacy, while in-process controls (IPCs) maintain process stability. The EMA's guideline on bioanalytical method validation outlines requirements for accuracy, precision, specificity, and robustness, ensuring reliable QC outcomes (EMA, 2022). Compliance with these standards is crucial in Ireland, where the HPRA enforces EMA regulations. The integration of regulatory guidelines and new technologies strengthens outcomes, making QC a cornerstone of biopharmaceutical quality.

2.3 Common Challenges and Areas for Improvement

Several challenges persist in the implementation and optimization of QC processes in the production of biopharmaceuticals derived from genetically engineered cell lines. This section will explore the common challenges faced in QC processes and identify areas for improvement.

2.3.1 Cell Line Complexity and Stability

Biopharmaceuticals, such as monoclonal antibodies, have intricate structures with post-translational modifications, making it difficult to maintain consistency. One of the primary challenges in QC processes is the inherent complexity of genetically engineered cell lines. These cell lines are typically derived from mammalian cells, such as Chinese hamster ovary (CHO) cells, which are engineered to express recombinant proteins. The genetic modifications and the dynamic nature of cell cultures can lead to variability in protein expression, genetic instability, and the presence of adventitious agents (Li *et al.*, 2022).

Genetic Instability: Maintaining genetic stability in engineered cell lines remains challenging. Cell line stability testing requires robust protocols that assess multiple parameters throughout a cell's lifespan. Genetic instability can result in changes to the cell line's genetic makeup over time, potentially affecting the expression of the desired protein. This instability can be due to the integration of multiple copies of the transgene, chromosomal rearrangements, or epigenetic modifications (Gemble *et al.*, 2022).

2.3.2 Method Validation

The use of advanced analytical techniques is essential for monitoring the quality of biopharmaceutical products. However, the validation and implementation of these techniques can be challenging. The validation of analytical methods is a complex process that involves demonstrating the method's suitability for its intended purpose. This includes assessing the method's specificity, linearity, range, accuracy, precision, and robustness (5). Ensuring that these methods are validated and consistently applied across different facilities can be challenging.

Standardizing analytical methods across different facilities remains challenging despite technological advancements. Variations in equipment, reagents, and operator techniques can lead to inconsistent results, complicating product quality assessment. For complex biologics, detecting subtle quality variations requires sophisticated analytical techniques

and expertise. Implementing these techniques consistently across different manufacturing sites demands significant resources and standardized protocols (EMA, 2022).

2.3.3 Cell Banking System Challenges

Developing effective cell banking systems poses considerable obstacles. Industry guidelines prescribe a two-tiered approach that includes a master cell bank from which a working cell bank is created to provide a continuous supply of cells for production. This approach allows for the inclusion of extensive characterization data, which is critical in determining the biosafety of the product. However, employing these systems necessitates meticulous attention to cryopreservation, storage, and transportation. Experts believe that research and development efforts to identify and select an optimal freeze medium for individual banks, in addition to attempts to create the ideal controlled freezing process, is worthwhile taking the time and will ultimately go a long way toward promoting stability of a cell over a period of time when stored in the freezer (Mirasol, 2018) .

2.3.4 Regulatory Compliance and Scalability

Biomanufacturing is subject to stringent regulatory scrutiny. Compliance with regulations governing manufacturing processes, quality control measures, and Good Manufacturing Practices (GMP) is critical for ensuring the safety of new drugs, vaccines, and therapies during preclinical and clinical trials, as well as commercial biologic manufacturing (Eder, 2024).

The scaling up of biomanufacturing processes to accommodate increased demand while preserving product quality involves considerable hurdles. Scalability must be balanced with process efficiency, resource allocation, and cost effectiveness, which necessitates careful planning and investment in infrastructure and technology (Eder, 2024).

2.3.5 Areas for Improvement

Improvements include adopting automation and real-time monitoring to enhance efficiency and reduce variability (Zia et al., 2024). Also, continuous bioprocessing represents a significant advancement in maintaining product consistency by reducing risk of variability batch-to-batch. By maintaining steady-state production rather than batch processing, manufacturers achieve more consistent product quality. Furthermore, implementing single-use technologies have also revolutionized biopharmaceutical manufacturing by contributing significantly to product consistency while offering operational advantages. They reduce contamination risk, simplifies the cleaning process

and also reduces costs that are associated with sterilization and cleaning (Thompson, 2023.

By addressing such challenges and leveraging new technologies, the biopharmaceutical industry can enhance QC processes and ensure the consistency, safety, and efficacy of life-saving therapies. Future innovations and collaborations between industry stakeholders, regulatory bodies, and academic institutions can be crucial in driving continuous improvement and maintaining high standards of product quality.

2.4 Innovative Approaches for Maintaining Product Consistency

Maintaining product consistency in the production of biopharmaceuticals derived from genetically engineered cell lines is a critical challenge. Traditional quality control (QC) processes, while essential, may not be sufficient to address the complexities and variability inherent in these advanced manufacturing systems. Therefore, innovative approaches are necessary to enhance the precision, efficiency, and reliability of QC processes. This section will explore various innovative approaches, including advanced analytical techniques, digital tools, artificial intelligence (AI), and other emerging technologies that can help maintain product consistency.

2.4.1 Advanced Cell Line Engineering Technologies

Gene editing tools, such as CRISPR-Cas9 (clustered regularly interspaced short palindromic repeats and CRISPR-associated protein 9), have transformed cell line development. They enable the creation of more efficient cell lines for biopharmaceutical manufacturing and, when combined with synthetic biology methodologies, are anticipated to greatly improve the capabilities of bioprocessing systems (Zhang *et al.*, 2021). This precise engineering enables more regulated protein expression and product quality.

2.4.2 Next-Generation Sequencing (NGS)

Next-generation sequencing (NGS) is a complex technique that allows for comprehensive genomic analysis of cell lines. From host cell line creation to master cell bank cloning, NGS provides molecular insights at the sequencing level, enabling for continuous monitoring of genetic stability during the entire process. It enables complete genome sequencing, identifying even the smallest genetic changes that may have an impact on biologic production. Unlike previous approaches, which rely on both in vivo

and in vitro experiments and sometimes need longer timelines with reduced sensitivity, NGS enables speedy and precise cell line characterisation while satisfying stringent regulatory standards (Armiento, 2024; Armiento, 2025).

2.4.3 Next-Generation Sequencing-Multi-Attribute Method (NGS-MAM)

Next-generation sequencing -Multi-Attribute Method (NGS-MAM) is anticipated to play an increasingly important role in biopharmaceutical quality control in the next years, including cell line characterisation. MAM is developed to discover, analyze, and track many Critical Quality Attributes (CQAs) in a single sample. Implementing MAM can lead to improved understanding of Chinese Hamster Ovary (CHO) cell lines during manufacture, as well as continuous monitoring of genetic and phenotypic stability. It has the potential to replace established methods for monitoring genomic stability and finding previously difficult-to-identify modifications. The application of the NGS-MAM approach can result in much fewer resource needs, up to a fivefold reduction in time limitations, and cheaper costs, all while providing high-quality data and decision support (Armiento, 2025).

2.4.4 Continuous Manufacturing and Real-time Monitoring

Continuous bioprocessing represents a paradigm shift from traditional batch manufacturing. It allows for real-time monitoring of critical quality attributes (CQAs) and the implementation of in-process controls (IPCs) to ensure consistent product quality. This approach can also reduce the risk of contamination and improve overall process efficiency. The transition to continuous manufacturing requires significant investment in equipment and process development (Steiner, 2018; Thompson, 2023). Additionally, regulatory approval for continuous manufacturing processes can be complex and time-consuming.

Process Analytical Technology (PAT) enables real-time monitoring and control of critical process parameters. It is a framework for designing, analyzing, and controlling manufacturing processes through the use of advanced analytical techniques and real-time data. PAT aims to ensure consistent product quality by monitoring and controlling critical process parameters (CPPs) and CQAs. PAT tools, such as near-infrared spectroscopy (NIR) and Raman spectroscopy, can provide real-time data on process parameters and product quality. This information can be used to make timely adjustments and ensure

consistent product quality. The implementation of PAT requires significant investment in analytical equipment and personnel training. Additionally, the integration of PAT data into existing QC systems can be challenging and requires sophisticated data management tools (Dahlgren *et al.*, 2020; Thompson, 2023).

Innovative approaches, including advanced analytical techniques, digital tools, AI, and emerging technologies, offer promising opportunities for maintaining product consistency in the production of biopharmaceuticals derived from genetically engineered cell lines. Automated systems helps in sample preparation and analysis reducing human error and improving data integrity, ensuring consistent results. Techniques like microfluid-based systems offer miniaturization and multi-analysis capabilities, standardizing QC for complex products (Zia *et al.*, 2024). These approaches enhance the precision, efficiency, and reliability of QC processes, ensuring consistent product quality and safety. However, the implementation of these innovations requires significant investment in infrastructure, personnel training, and regulatory compliance.

2.5 Cost-Effective QC Processes for Smaller Production Facilities

Smaller production facilities in the biopharmaceutical industry often face unique challenges due to limited resources, financial constraints, and the need to maintain high standards of product quality and consistency. Implementing robust quality control (QC) processes is essential, but traditional QC methods can be expensive and resource-intensive. Therefore, developing cost-effective QC processes is crucial for these facilities to ensure product consistency without compromising on quality or safety. This section will explore various cost-effective QC strategies, their applications, and the potential benefits for smaller production facilities.

2.5.1 Cost-Effective QC Strategies

Smaller production facilities, often referred to as small and medium-sized enterprises, face several challenges in implementing QC processes. They often have limited financial resources, making it difficult to invest in expensive analytical equipment and advanced technologies. Access to highly trained personnel with expertise in advanced QC techniques is limited. Meeting regulatory requirements when resources are limited is complex and costly, requiring significant investment in time and resources. They also may not have the economies of scale to justify large investments in QC infrastructure.

The implementation of cost-effective QC strategies can help in overcoming these challenges.

Electronic Quality Management Systems (e-QMS): An e-QMS streamlines documentation and compliance, reducing administrative costs and enabling scalability (Gamlen and Clapperton, 2010).

Single-use Technologies for Smaller Operations: Single-use technologies offer particular advantages for smaller facilities. They reduce both capital and operational expenses by eliminating complex cleaning validation requirements (Thompson, 2023).

Smaller production facilities can benefit from collaborative networks and shared resources to enhance their QC capabilities. This can include partnerships with academic institutions, research organizations, and others to share knowledge, resources, and expertise. Collaborative networks can provide access to advanced analytical equipment, training programs, and expert advice. By sharing resources and knowledge, facilities can enhance their QC processes without the need for significant investment. The main benefits of collaborative networks include access to advanced technologies, reduced costs, and enhanced knowledge sharing. By working together, smaller facilities can achieve greater efficiency and improve their QC capabilities (Callahan, 2023; Larghero and Textoris, 2024). Additionally, strategic outsourcing of specialized testing to contract research organizations or academic institutions enables smaller facilities to access advanced analytical capabilities without investing in expensive equipment and expertise. This approach allows for comprehensive quality control while minimizing capital expenditures (Playter, 2023).

Multiplexed Immunoassays: Multiplexed immunoassays offer a cost-effective alternative to traditional analytical techniques such as high-performance liquid chromatography (HPLC) and mass spectrometry (MS). These assays can simultaneously measure multiple analytes in a single sample, reducing the need for multiple tests and the associated costs. Multiplexed immunoassays can be used to monitor critical quality attributes (CQAs) such as protein concentration, purity, and post-translational modifications. By measuring multiple parameters in a single test, these assays can provide comprehensive data on product quality without the need for multiple analytical instruments (Ahsan, 2021). The main benefits of multiplexed immunoassays include reduced costs, faster turnaround times, and the ability to perform multiple tests

simultaneously. This makes them particularly suitable for smaller production facilities with limited resources.

Lean Manufacturing Principles: Lean manufacturing principles aim to minimize waste and optimize efficiency in production processes. These principles can be applied to QC processes to reduce costs and improve productivity. Lean manufacturing principles can be applied to QC processes by streamlining workflows, reducing unnecessary steps, and optimizing the use of resources. This includes the implementation of just-in-time (JIT) inventory systems, continuous improvement methodologies, and the elimination of non-value-added activities. The main benefits of lean manufacturing principles include reduced costs, improved efficiency, and enhanced product quality. By minimizing waste and optimizing processes, facilities can achieve greater productivity and cost savings (Ghelani, 2021; Robertsone and Markova, 2023).

Digital Tools Implementation: Digital tools and software solutions can help smaller production facilities optimize their QC processes and reduce costs. These tools can provide real-time data analysis, automated reporting, and enhanced process control. Digital tools can be used to automate routine QC tasks, such as data entry and analysis, reducing the need for manual intervention and minimizing errors. These tools can also provide real-time monitoring and alerts, enabling timely corrective actions. The main benefits of digital tools include improved efficiency, reduced costs, and enhanced data management. By automating routine tasks and providing real-time data analysis, facilities can achieve greater productivity and cost savings (Brooks, 2024; Narayanan *et al.*, 2024; Mirasol, 2025).

2.6 Recommendations for Industry-Wide Best Practices

Developing and implementing industry-wide best practices for quality control (QC) processes in genetically engineered cell lines are essential for ensuring consistent, safe, and effective biopharmaceutical products. Best practices provide a framework for standardizing QC processes, optimizing resource use, and maintaining regulatory compliance. This section will explore detailed recommendations for industry-wide best practices.

2.6.1 Standardization and Harmonization of Protocols

Standardizing QC protocols across different facilities is crucial for ensuring consistent product quality. Standardization involves the development and implementation of

uniform methods, procedures, and reference standards for QC processes. This reduces variability and ensures that all facilities adhere to the same quality standards. Implementation of standardized protocols for cell line development and characterization ensures consistency across different manufacturing facilities. Conducting sterility and contamination tests helps to make sure that cell growth over the generations is continuous. Standardized protocols have to cover all aspects of QC, including analytical techniques, in-process controls, release testing, and stability testing. The use of standardized operating procedures (SOPs) and validated analytical methods is essential for maintaining consistency. Standardization ensures that QC processes are consistent and reliable, reducing the risk of variability and improving product quality. It also facilitates regulatory compliance and enhances the efficiency of QC operations. Harmonizing QC protocols requires collaboration between industry stakeholders, regulatory bodies, and academic institutions to develop and disseminate best practices. It can be achieved through the development of international reference standards, the implementation of harmonized analytical techniques, and the use of centralized databases for QC data (Ahmed, 2024; AmpleLogic, 2024; Tricht, 2025).

The use of an electronic laboratory notebook (ELN) and the laboratory information management system (LIMS) helps to maintain standardization in both inter and intra-departments of biopharma companies . ELN assures procedural execution, automates manual procedures, collects data of instruments , and performs computations, limit and calibration checks, as well as inventory checks and updates. These built-in controls in ELNs ensure that standard operating procedures are followed throughout analysis and that the obtained data is authentic by protecting data intergrity. Employing an advanced LIMS solution standardizes data collecting and storage operations, reducing data handling errors. Pharmaceutical organizations can use an integrated LIMS to connect several facilities to a single, cloud-based platform, allowing for easier, real-time data access and sharing across whole laboratory networks (Machina and Wild, 2013; Weiser, 2020; Tricht, 2025).

2.6.2 Training of Personnel

Addressing the skills gap in the biopharmaceutical industry is essential for maintaining high standards of quality control. Investing in training and education for QC personnel is essential for ensuring that they have the skills and knowledge to implement cost-effective QC processes. This includes training in the use of advanced analytical techniques, risk-

based QC strategies, and digital tools. Training programs are to be designed to cover the latest advancements in QC techniques, regulatory requirements, and best practices. This can include workshops, seminars, and online courses to ensure that personnel are up-to-date with the latest developments. Training and education enhance the efficiency and precision of QC processes, ensuring that personnel are well-trained and knowledgeable. This also ensures that QC processes remain up-to-date with evolving regulatory requirements and technological advancements (Haigney, 2024; Pluta, 2024; Tricht, 2025).

2.6.3 Regulatory Compliance

Ensuring regulatory compliance is a critical aspect of QC processes. Regulatory bodies such as the EMA and FDA provide guidelines for the development and implementation of QC processes, emphasizing the importance of standardized protocols and reference standards. Regulatory compliance involves the implementation of standardized protocols, the use of validated analytical techniques, and the maintenance of accurate records. Facilities must ensure that their QC processes are regularly reviewed and updated to meet evolving regulatory requirements. Regulatory compliance ensures that QC processes are consistent and reliable, reducing the risk of variability and improving product quality. It also facilitates global regulatory compliance and enhances the efficiency of QC operations (5; 2).

Developing and implementing industry-wide best practices for QC processes in genetically engineered cell lines is essential for ensuring consistent, safe, and effective biopharmaceutical products. Best practices provide a framework for standardizing QC processes, optimizing resource use, and maintaining regulatory compliance. By adopting these best practices, the biopharmaceutical industry can enhance QC processes and ensure the consistency, safety, and efficacy of life-saving therapies.

2.7 Research Gap Analysis

Quality control processes for genetically engineered cell lines remain fundamental to ensuring biopharmaceutical product consistency, particularly in Ireland's growing biopharma sector. Recent advances in cell line engineering, analytical technologies, and manufacturing approaches offer promising solutions to longstanding challenges. However, significant gaps persist in standardization, cost-effective implementation, and workforce development. This analysis highlights areas where further investigation would contribute significantly to the field.

While the literature review mentions various analytical techniques such as HPLC, mass spectrometry, and next-generation sequencing, there appears to be insufficient standardization across the industry. Studies are needed to establish which analytical approaches provide the most reliable indicators of product quality and consistency across different manufacturing settings. There is limited research on how different quality parameters interact and influence each other. Understanding these relationships could lead to more effective control strategies.

While modern technologies show promise, further study is needed to determine how to adopt sophisticated quality control procedures at a low cost, especially for smaller production plants.

The current literature demonstrates a lack of consensus on standardizing quality control techniques across different types of genetically modified cell lines, providing an opportunity for comparative investigations.

2.8 Conceptual Framework

This section presents a comprehensive conceptual framework derived from the literature review on quality control (QC) processes in genetically engineered cell lines. The framework illustrates the interconnected elements that influence product consistency in biopharmaceutical manufacturing and highlights the relationships between various QC components.

The framework synthesizes the key themes from the literature review, emphasizing how cell line quality forms the foundation for product consistency while highlighting the importance of analytical techniques, regulatory compliance, and advanced technologies. It also acknowledges the challenges faced by smaller production facilities and the need for cost-effective quality control strategies. By highlighting both established practices and emerging approaches, the framework serves as a guide that helps to enhance QC processes and address existing challenges.

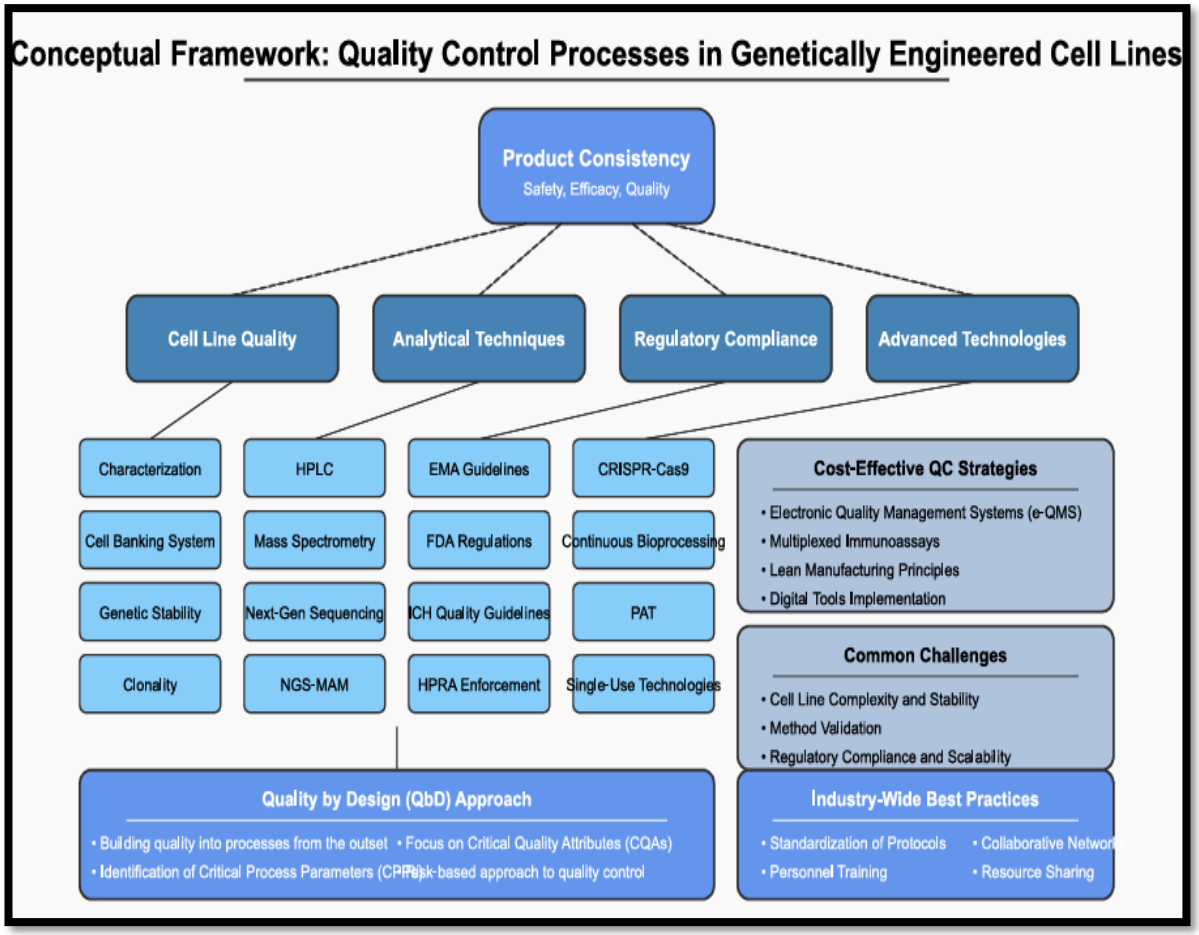


Figure 1: Conceptual framework

2. 9 Conclusion

In conclusion, this chapter provides a comprehensive literature review on the assessment of quality control processes in genetically engineered cell lines, focusing on their impact on biopharmaceutical product consistency. It includes detailed sections on the various aspects of QC processes, including the influence of QC on product consistency, common challenges, innovative approaches, cost-effective solutions, and recommendations for industry-wide best practices. This chapter helped to reinforce the topic's importance by demonstrating the seriousness of the issue at hand, which is the need to assess quality control (QC) processes in genetically engineered cell lines to ensure the consistency, safety, and efficacy of biopharmaceutical products. The concepts generated from this chapter aided in the advancement of the research in terms of data collecting and analysis, and the techniques utilized are addressed in the subsequent chapters.

3. RESEARCH METHODOLOGY

3.1 Chapter Overview

This chapter outlines the methodological framework adopted for the study, detailing the approach used to explore the impact of Quality Control (QC) processes on the consistency of biopharmaceutical products derived from genetically engineered cell lines. Given the exploratory nature of the research and its aim to uncover in-depth insights from industry professionals, a qualitative research methodology was deemed most appropriate. This choice allowed for a deeper understanding of real-world QC practices, implementation challenges, and strategic improvements through the subjective experiences and reflections of practitioners in the field.

The chapter begins by explaining the rationale for selecting a qualitative approach and proceeds to describe the research design, including sampling strategies, participant recruitment, and data collection methods. A semi-structured interview format was used, enabling the researcher to probe specific themes while allowing participants the freedom to express their insights and experiences. This approach ensured consistency across interviews while maintaining the flexibility necessary for rich, nuanced data.

Further sections of the chapter detail how participants were selected using purposive sampling, targeting individuals with direct experience in QC operations within Irish biopharmaceutical facilities. Ethical considerations, including informed consent, anonymity, and data confidentiality, are discussed to demonstrate adherence to institutional research standards.

Finally, the data analysis strategy, specifically thematic analysis, is introduced. This technique allowed for the identification of recurring patterns and emergent themes from the interview transcripts, which were then mapped back to the study's research objectives. The methodology outlined in this chapter ensures that the findings are grounded in authentic, experience-based perspectives and meet the standards of academic rigor and ethical integrity.

3.2 Research Design Overview

The research employed a qualitative, exploratory design to investigate how QC processes influence product consistency in genetically engineered cell line-based biopharmaceutical production. This design was chosen due to its suitability in capturing the complex, context-specific experiences of professionals working in highly regulated and technically

demanding environments. The goal was to generate a nuanced understanding of both the operational challenges and innovative strategies within Quality Control (QC) systems.

Research Approach and Justification: Qualitative research is especially effective in exploring topics where rich, descriptive insights are needed. In this case, examining QC through the lens of industry practitioners offered an opportunity to access tacit knowledge and first-hand reflections that cannot be easily quantified. A positivist or purely quantitative approach would not have sufficiently captured the subjective, ethical, and procedural nuances central to this research.

Sampling Strategy: A purposive sampling method was employed to ensure that participants were selected based on their experience, role, and relevance to the study's objectives. Participants included QC analysts, scientists, and supervisors working in Ireland-based biopharmaceutical companies. This approach ensured that all contributors had meaningful, informed perspectives on genetically engineered cell line QC processes. The diversity in job roles and facility types enriched the thematic findings, enhancing transferability of the results.

Data Collection Method: Semi-structured interviews were conducted to collect qualitative data. This format provided a consistent set of core questions while allowing for flexibility to explore unexpected but relevant insights. Interviews were conducted virtually, recorded with consent, and later transcribed verbatim for analysis. The use of open-ended questions encouraged participants to elaborate on specific experiences, which proved essential in uncovering deep operational insights and revealing industry challenges and best practices.

Ethical Considerations: Ethical integrity was prioritized throughout the research process. Informed consent was obtained from all participants, and data was anonymized to protect confidentiality. Participants were briefed on the purpose of the research, their right to withdraw at any time, and how the data would be used and stored. Approval was obtained from the relevant institutional ethics review board prior to data collection.

Data Analysis: The collected data was analyzed using thematic analysis, following Braun and Clarke's 2006 methodology. This involved familiarization with the data, initial coding, theme identification, theme review, definition, and final write-up. Thematic analysis was selected due to its systematic yet flexible approach to identifying patterns across large qualitative datasets.

In summary, the research design combined methodological rigor with contextual flexibility, enabling the study to capture real-world insights into QC processes. The design supported a rich, reflective exploration of both the technical and human dimensions of quality management in the biopharmaceutical sector.

3.3 Research Methodology

The research strategy for this study on quality control processes in genetically engineered cell lines adopted an interpretivist philosophy. The interpretivist paradigm acknowledges that research is affected by human perspectives and experiences, making it ideal for understanding the complex dynamics of quality control implementation and challenges. Since quality control processes involve human judgment, decision-making, and varied organizational contexts, this philosophical stance enabled a deeper understanding of how different facilities approach and maintain product consistency. This philosophy aligns with the qualitative nature of the study and hence allowed an in-depth exploration of how QC processes influence biopharmaceutical product consistency, the challenges faced, and potential innovations. Additionally, a more flexible and open-ended investigation helped to uncover unexpected insights and adapt the research process with the emergence of new information.

The research employed an inductive research approach which is supported by the interpretivist paradigm. Here, data was collected from industry experts to generate theories and develop insights about the quality control processes. This approach allowed the emergence of patterns and themes from the experts' experiences rather than testing any predetermined hypotheses. This is particularly important in a field where regulatory standards, technological advancements, and quality control practices have always evolved dynamically.

Qualitative approach: A qualitative research design, focussing on semi-structured interviews of experts from Ireland was employed for this research due to the need for a detailed understanding of how quality control processes are implemented and managed. Unlike quantitative methods, which focus on numerical data and statistical analysis, qualitative research provides richer insights into procedural effectiveness, challenges, and improvements. Hence, in-depth interviews of participants enabled them to discuss their experiences in their own words, leading to a greater understanding of the factors influencing quality control in genetically engineered cell lines. This aligned with the

study's objective to explore industry practices, challenges, and areas for enhancement rather than merely measuring predefined variables.

3.4 Research Participants

The interviewees for this research comprised of seven professionals having experience in the Irish biopharmaceutical industry. They held roles like Senior QC Analyst, Associate Research Scientist, Senior Analyst, Analytical Scientist, Technical training specialist, Senior technical QC and Scientist II. This research topic and research objectives revolves around understanding the QC processes and how it influences biopharmaceutical product consistency. The data for this study can only be provided by subject matter experts and those who have knowledge and experience in the field of interest. Hence, the participants were selected carefully through personal connections and LinkedIn. They were chosen from multiple organizations in Ireland to avoid bias and to have a uniform representation of QC processes within Ireland.

From the interviews, I aimed to understand the nuances associated with the QC processes of genetically engineered cell lines. While there were similar patterns identified from these interviews, using thematic analysis, the perspectives varied with each participant's respective work and the experiences they have encountered. Hence intricate details were arrived at and helped to better understand the QC processes. As they have varying experiences throughout the years, there was a better chance of arriving at practical recommendations and ideas. After identifying the participants, data collection was initiated step-by-step.

3.5 Data Collection strategies

First and foremost, participants who had knowledge and experience of genetically engineered cell lines or biopharmaceuticals derived from genetically engineered cell lines were identified through my professional network with the help of LinkedIn and also through my personal connections. A number of potential participants were shortlisted and initially contacted through LinkedIn and WhatsApp. They were given the basic details about the research to ascertain their interest in participating in the research. After initial contact, the individuals who showed interest in the research were provided with further information via email, which included an official request for taking part in the research study along with Participant Information Letter (Appendix B), Informed Consent form (Appendix C), and the interview questionnaire (Appendix D). The appendix D consists

of two sets of questionnaires that were asked to people. The first set of questionnaires focuses on the QC processes of genetically engineered cell lines while the second set of questionnaires is about the QC processes of biopharmaceutical products. The answers obtained from both the questionnaires were analysed together.

Participants who accepted the request were asked to return the signed consent form, following which the day and time of interview were set up to accommodate the participant's schedule, and a meeting was scheduled on the Zoom video/audio conferencing platform. Because all the participants are industry experts in the Irish biopharmaceutical sector, all interviews were scheduled and conducted in accordance with their own preferences and schedules.

The questionnaires for the interviews were derived from each research objective proposed to be achieved in this study. All the questions were structured to gather specific details regarding the possible impact of QC processes of genetically engineered cell lines and how that influences the product consistency of biopharmaceuticals derived from genetically engineered cell lines, from the interviewee's perspective. After completion of the interview, the recordings were transcribed using Microsoft 365, MS word, followed by thematic analysis to identify patterns in the transcripts. The themes and sub themes identified initially were used to guide thematic analysis which was then reviewed and strengthened based on the findings from the interviews.

3.6 Data Analysis strategy

As previously indicated, thematic coding was used to guide data analysis. The initial themes and sub themes were established using the conceptual framework derived from the literature research. This was followed by going through each transcript numerous times to identify refined themes and sub-themes pertinent to the objectives. Based on the reviewed transcripts, the themes and subthemes that were developed linked back to the study objectives, thereby keeping the research grounded in the theoretical foundation of the study and preventing any deviation from the proposed goals. The thematic analysis methodology provided deeper insight into the topic .

3.7 Research Ethics

All of the actions taken in this dissertation were in accordance with fundamental research ethics. All participants were informed of the goal of the study and how the questions asked were important in reaching each of the study objectives. Participants received relevant

details of the interview via the Patient Information Letter (PIL), which was provided prior to the interview. Any clarification requests were promptly addressed via email.

All participants were advised of their rights and the steps that will be taken to secure their identities and avoid confidentiality breaches. None of the participants were requested to divulge any information unrelated to the study's aims. We did not acquire any information that violated the policies of the participants' individual organizations. Participants have the right to withdraw from the study within two weeks of finishing the interview. Once the participant's request for withdrawal is communicated, all acquired data and information on the participant will be erased from storage and no longer be used in the study.

The whole data collecting procedure, from initial contact with the participant to final interview, was tailored to the participant's personal schedule and convenience. Participants were given sufficient time to review the Participant Information Letter and Informed Consent Form, and additional clarifications were provided upon request. Signed consent forms were collected from all participants before scheduling the interview. During the interview, the recording began only with the participants' agreement, and the length of the interview was not so long that it inconvenienced the participants, and it was ensured that the participants were comfortable throughout.

The research methodology and the step-by-step approach to research conduct, enabled the researcher to achieve the significant and deep insights from the industry experts which are relevant to the research objectives and this will be explained in the next chapter ‘Findings and Analysis’.

3.8 Data storage and protection

All data obtained as part of this research are retained in compliance with data protection laws and the General Data Protection Regulation (GDPR). The audio/video interview recordings are saved on the researcher's password-protected personal computer, accessible only to the researcher and also available to their supervisor. Additional copies of the recording are kept in safe cloud storage as a backup. The researcher has saved the interview transcripts in MS Word for data analysis, stored in the password protected personal computer with a backup in cloud storage. A copy of the interview transcripts will be securely preserved for two years after the study is completed.

The raw data, including the signed consent form and audio/video recordings, will be retained in Moodle's secure allocated folders until the test results are announced. The data given to the college for evaluation or future publishing will not contain any personal identifiers of the participants, and there will be no danger of breach in confidentiality.

4. FINDINGS AND ANALYSIS

4.1 Overview

This chapter comprises information about the data collected and the findings obtained from the data. This chapter presents the findings from the thematic analysis of the interview transcripts in a stepwise approach, focusing on the quality control (QC) processes in genetically engineered cell lines and their impact on the consistency of biopharmaceutical products. The analysis aims to address the research objectives by identifying key concepts and recurring themes from the interviews.

4.1.1 Participant Details

The request to take part in interviews were sent out to more than fifty people who are working in the Irish biopharmaceutical industry. Only a total of seven people agreed to participate in the interview as part of the research study. The interviewees held roles in the biopharmaceutical sector like Senior QC Analyst, Associate Research Scientist, Senior Analyst, Analytical Scientist, Technical training specialist, Senior technical QC and Scientist II. All the interviewees were experts in the field having varying experiences and were able to provide multiple facets of data on the same question. Anonymised participant information has been summarised in the table below (Table 1).

Interviewee Number	Job title	Years of experience
1	Senior QC Analyst	5
2	Associate Research Scientist	6
3	Senior Analyst	4
4	Analytical Scientist	5
5	Technical training specialist	6
6	Senior technical QC	6
7	Scientist II	4

Table 1: Participant Summary

4.1.2 Thematic Analysis Procedure

The thematic analysis was conducted to identify key concepts and recurring themes from the interview transcripts. The analysis was guided by the research objectives, which focus on evaluating QC processes, examining challenges, identifying innovative approaches, and developing recommendations for industry-wide best practices.

After the interviews were transcribed, they were read multiple times and then the relevant themes were identified and highlighted. Six major themes that were relevant to the objectives were identified and under these themes twenty-three sub themes were identified. Each of the themes and sub themes were then explained with the help of quotes found in the transcripts belonging to interviewees. Categorizing the subthemes helped to get a deeper understanding of the themes which directly relates back to the objectives.

The thematic analysis followed the Braun and Clarke's 2006 methodology: familiarization with data, theme identification, reviewing themes, defining/naming themes, and final reporting (Naeem *et al.*, 2023).

The themes and sub themes relating to the various research objectives and the interviewees who responded accordingly has been summarised in the below table (Table 2).

Theme	**Sub-theme**	**Research Objective**	**Interviewees Mentioned**
Impact of QC on Product Consistency	Standard Operating Procedures (SOPs) and Documentation	Objective 1	Interviewee 1, 3, 6
	Product Potency Monitoring		Interviewee 2, 6, 5
	Gene Expression Validation		Interviewee 3, 2, 6, 7
	Contamination Detection and Mitigation		Interviewee 2, 4, 5, 6
	Environmental Monitoring and Contamination Control		Interviewee 2, 7
Challenges in QC Implementation	Technical and Operational Challenges	Objective 2	Interviewee 1, 2, 4, 5
	Regulatory Compliance and Data Integrity		Interviewee 1, 2, 4, 5, 6
	Resource Constraints and Financial Limitations		Interviewee 1, 3, 6, 7
	Review Systems		Interviewee 1, 6, 4
	Training Gaps		Interviewee 1,3,5
Innovative Approaches	Advanced Analytical Techniques	Objective 3	Interviewee 2, 5,6,7
	AI and Machine Learning		Interviewee 2,4,3,6
	Real-time Monitoring and Process Automation	Objective 1 & 3	Interviewee 2, 4, 6, 7
Cost-Effectiveness	Multi-Purpose Equipment and Reagents	Objective 4	Interviewee 2, 5, 6

	Training and Standardization		Interviewee 1, 3, 7
	Shared Resources and Collaborative Networks		Interviewee 2, 4, 7
	Outsourcing and Lean QC Strategies		Interviewee 1,5,6
Industry-Wide Recommendations and Future Directions	Standardization and Harmonization	Objective 5	Interviewee 1, 2, 5
	Continuous Improvement and Innovation		Interviewee 3, 7, 6
	Collaboration and Knowledge Sharing		Interviewee 4, 5, 6, 7
Ethical, Regulatory, and Societal Considerations in QC	Ethical Responsibility in QC	Objective 2 & 5	Interviewee 2,3,5
	Regulatory Oversight and Compliance	Objective 2 & 1	Interviewee 1, 2, 4
	Societal Impact and Public Trust	Objective 4 & 5	Interviewee 5,6,7

Table 2: Themes and sub themes

4.2 Findings and Analysis

The results and analysis chapter delves deeper into the ideas given by the experts and demonstrates how the themes tie back to the objectives. The analysis is carried out in relation to each theme and sub-theme in the table above, as well as the appropriate transcript quotes that are relevant to the themes.

4.2.1 Impact of QC on Product Consistency

The biopharmaceutical industry, particularly in the realm of genetically engineered cell lines, is fundamentally dependent on robust Quality Control (QC) systems to guarantee the safety, efficacy, and consistency of therapeutic products. Unlike small-molecule drugs, biopharmaceuticals are highly sensitive to environmental and procedural variations due to their complex structure and biologic origin. Therefore, rigorous QC processes are essential to ensure that each batch meets stringent quality attributes, such as potency, purity, and gene expression fidelity (Lamanna et al., 2018; Capes-Davis, 2018). Product consistency is not only a marker of manufacturing quality but also a critical component in maintaining patient trust and therapeutic reliability.

In Ireland, QC practices are closely regulated by the Health Products Regulatory Authority (HPRA), which aligns with global bodies such as the FDA and EMA.

Regulatory compliance is integral to maintaining consistency, especially in a high-stakes environment where deviations may jeopardize patient outcomes and market approval (HPRA, 2024). QC activities span a range of functions from environmental monitoring and documentation practices to advanced analytical methods, all aimed at minimizing batch-to-batch variability (Hyde, 2024).

Interview insights confirm the indispensable role of QC in real-world manufacturing. One analyst highlighted, "*We have to check as a QC personal whether it is out of trend… and if it is out of trend, then there is investigation*" (Interviewee 1). Such vigilance is vital to ensure that even minor deviations are caught early, safeguarding both product integrity and public health. In effect, QC serves as both a gatekeeper and a continuous improvement mechanism—upholding consistency while adapting to evolving scientific and regulatory standards (O'Flaherty et al., 2020).

4.2.1.1 Standard Operating Procedures (SOPs) and Documentation

Clear and enforceable Standard Operating Procedures (SOPs) are foundational to consistent quality outcomes in biopharmaceutical manufacturing. These documents guide every step of QC testing—from sample handling and storage to analytical procedures and data reporting. Interviewee 1 emphasized the need for precision in documentation: *"…the SOP should be written more clearly, so that it can be understood and implemented very nicely…"* Such clarity reduces human error and standardizes responses to potential deviations.

Interviewees described rigorous documentation as both a compliance necessity and an operational safeguard. Interviewee 6 noted, *"Without proper documentation, audits can fail even if the testing is perfect."* Interviewee 3 explained that, *"Documentation also helps us detect if there's a pattern in deviation across multiple batches."* From a regulatory perspective, adherence to written SOPs aligns with Good Manufacturing Practices (GMP) outlined by the FDA and EMA. Deviations from SOPs trigger immediate investigation and Corrective and Preventive Action (CAPA) protocols, underscoring their critical role in regulatory compliance and audit preparedness (FDA, 2023; HPRA, 2024). Literature further supports the view that well-documented procedures are central to quality assurance and reproducibility (Hyde, 2024).

In smaller facilities where resources may be stretched, consistent SOP implementation becomes even more crucial, ensuring that every technician, regardless of experience level,

performs tasks to the same standard. This consistency is pivotal in maintaining data integrity and traceability—both of which are heavily scrutinized during regulatory inspections (Gamlen and Clapperton, 2010).

4.2.1.2 Product Potency Monitoring

Product potency, defined as the biological activity of a drug, must be tightly controlled to ensure therapeutic efficacy. This is particularly critical in biologics where minor alterations in protein structure or activity can lead to significant clinical effects. Interviewee 2 explained, *"…we ensure that the cells exhibit the same biological activity every single time…"* indicating the use of parallelism studies and validated bioassays to verify performance consistency across batches.

Interviewee 6 added, *"Potency assays must match up with our reference cell lines. If not, the batch is scrapped."*

Potency is typically assessed using cell-based assays, enzyme-linked immunosorbent assay (ELISA), or reporter gene assays, all of which must be validated for sensitivity, specificity, and linearity (Evrony et al., 2021). These techniques help establish batch comparability and provide evidence for regulatory filings. According to Lamanna et al. (2018), potency testing is a cornerstone of biopharmaceutical QC due to its direct link to clinical performance. According to Interviewee 5, *"We faced a case where the reference standard drifted over time—without robust potency monitoring, we would've released a subpar batch."*

Failing potency standards often prompts a root cause analysis, and if necessary, batch rejection. This layer of scrutiny protects patients and helps uphold public confidence in biopharmaceutical therapies. In essence, potency monitoring acts as a safeguard, ensuring that every product reaching the market performs as intended.

4.2.1.3 Gene Expression Validation

Ensuring that genetically engineered cell lines express the intended product accurately and consistently is a fundamental part of QC. Techniques such as Quantitative Polymerase Chain Reaction (qPCR), Digital Droplet Polymerase Chain Reaction (ddPCR), and reverse transcription PCR (RT-PCR) are widely employed to validate gene expression levels. Interviewee 2 described, *"…we have a lot of gene expression studies and then we have a lot of PCR studies where we determine the titre value of the particular viruses that have been integrated into the cells…"*

Interviewee 3 noted, *"Expression levels can drop without visible contamination—it's gene silencing, and PCR is the only way to detect it."*

Literature highlights the value of these methods in maintaining product consistency. Dai and Shen (2022) argue that the sensitivity of qPCR and ddPCR allows for precise quantification, enabling early detection of expression drift. Mirasol (2018) further notes that these molecular techniques support the verification of both product integrity and genetic stability, especially when used longitudinally across cell passages. This multi-point monitoring is consistent with what Interviewee 6 added that, *"We run gene expression checks at different stages—post-thaw, mid-culture, and before harvest."*

Gene expression data not only informs batch release decisions but also feeds into continuous process verification efforts. Interviewee 7 mentioned, *"Certain cell lines express best at specific passages. If we go beyond, expression drops unpredictably."* Consistency in gene expression is crucial to avoid deviations that could compromise safety, efficacy, or manufacturability.

4.2.1.4 Contamination Detection and Mitigation

Contamination remains one of the most pressing risks in biopharmaceutical manufacturing. It can originate from raw materials, equipment, or human error and has the potential to invalidate entire batches. Interviewee 2 shared, *"…you would have to fumigate the entire room, do a study to see what contaminated the product…"*, highlighting the significant operational and financial costs associated with contamination events. Interviewee 4 emphasized the root causes: *"Most contamination is from human error—glove tears, improper gowning, or open reagents."*

Interviewee 5 discussed microbial testing protocols: *"We routinely run Mycoplasma, sterility, and endotoxin assays on all harvested material."*

Contamination control strategies include the use of cleanroom environments, high efficiency particulate air (HEPA) filtration, validated cleaning procedures, and environmental monitoring. The implementation of contamination detection assays—such as Mycoplasma testing, bioburden assays, and host cell Deoxyribonucleic acid (DNA) quantification—is mandated by global regulatory bodies (EMA, 2023; Capes-Davis, 2018).

An effective QC program integrates risk assessments and routine audits to proactively identify contamination sources. Moreover, when contamination is detected, root cause analysis and CAPA implementation are crucial for preventing recurrence. These systems not only preserve product integrity but also safeguard operator health and prevent costly delays. Interviewee 6 mentioned, *"Since we implemented pre-use filter integrity tests, our contamination events have dropped significantly."* Literature affirms that robust contamination control systems are essential to protect biologic integrity (Zia et al., 2024).

4.2.1.5 Environmental Monitoring and Contamination Control

Environmental monitoring (EM) complements direct contamination detection by providing ongoing assurance of facility cleanliness. It involves regular sampling of air, surfaces, and personnel garments, and culture-based analysis to detect microbial load. Interviewee 2 stated, *"...we're regularly taking swabs of the BSC, of the flow, of the air..."*, reflecting a structured EM program typical in GMP-compliant settings. Interviewee 7 added, *"We had to revise gowning SOPs after consistent EM failures around glove cuffs."*

According to Zia et al. (2024), environmental monitoring is a proactive quality assurance measure. It allows early identification of adverse trends that could compromise product quality. Facilities typically employ alert and action levels based on regulatory standards, and excursions from these levels trigger predefined responses including disinfection, retesting, or investigations.

In Ireland, HPRA audits emphasize EM records as key indicators of facility control. This requirement is echoed in EMA guidelines, which categorize EM as a critical component of sterility assurance programs (EMA, 2023). When executed effectively, EM enhances data reliability, supports regulatory compliance, and prevents contamination-related failures.

4.2.2 Challenges in QC Implementation

The effective implementation of Quality Control (QC) protocols in biopharmaceutical manufacturing is fraught with multifaceted challenges, particularly due to the biologically complex nature of products derived from genetically engineered cell lines. While QC is crucial for ensuring safety, efficacy, and regulatory compliance, its processes are often impeded by technical failures, operator variability, regulatory complexity, and resource limitations (Eder, 2024; Thompson, 2023).

Interviewee 1 noted the significance of this complexity, stating, *"Sometimes the parameters are out of spec… could be analyst error or instrument error."* Interviewee 2 emphasized the burden of stringent oversight: *"We have EU approval but not FDA approval because they require further testing."* These insights reflect the dual pressures of ensuring internal process reliability and meeting external regulatory expectations.

Interviewees across multiple organizations echoed similar frustrations with infrastructure, documentation, and process robustness. Interviewee 6 said, *"We're still relying on some legacy systems... and you can't scale quality with outdated tools."* Regulatory compliance was a common pressure point. As Interviewee 4 described, *"Even small changes in software must be documented and approved—it slows everything down."*

Smaller companies face added strain. Interviewee 7 highlighted, *"We don't have the funds for the kind of QC systems that big companies have—we do what we can with what we have."* These constraints create operational fragility, often leaving firms reliant on third-party services, which in turn increases the risk of data fragmentation and quality oversight gaps (Playter, 2023).

The literature reinforces these themes, citing technical validation gaps, non-harmonized global regulations, and limitations in workforce training as persistent issues facing the biopharmaceutical sector (Li et al., 2022; Hyde, 2024). Therefore, addressing these challenges is vital for ensuring that QC systems not only comply but thrive under scrutiny.

4.2.2.1 Technical and Operational Challenges

Equipment calibration issues, software inconsistencies, and analyst variability are central to the technical difficulties experienced in QC operations. Interviewee 1 explained, *"We had issues with the spectrophotometer not giving consistent readings—we had to recalibrate every other week."* Interviewee 4 added, *"Sometimes the software crashes mid-run, and the data has to be reviewed and justified manually—it delays everything."*

Even routine operational errors can have severe consequences. Interviewee 2 shared a relatable incident: *"We were supposed to return in 30 minutes… we weren't. Now the assay's invalid."* Such occurrences highlight how tightly linked time-sensitive procedures are to technical outcomes.

Interviewee 5 pointed out that newer analytical platforms often require revalidation every time software is updated: *"We got a new patch for the chromatography software and had to do a partial revalidation to ensure data integrity."*

These challenges are corroborated by literature, which calls for lifecycle management of instruments, periodic method revalidation, and increased automation to reduce variability (Thompson, 2023; O'Flaherty et al., 2020). Without such controls, operational inconsistencies directly translate into product risk.

4.2.2.2 Regulatory Compliance and Data Integrity

Regulatory frameworks require meticulous alignment between testing protocols, documentation, and system validation. Interviewee 2 stated, *"The FDA and EMA want different formats for data submission—it's like doing the same test twice in two different ways."* Interviewee 4 noted, *"Even editing a template requires change control—it slows down decision-making."*

Data integrity has become one of the most intensely scrutinized areas. Interviewee 1 said, *"Nowadays we use electronic notebooks and logbooks—earlier it was all manual, and errors were frequent."* Interviewee 5 echoed this shift, emphasizing that *"Data is only credible if it's traceable. Everything must have an audit trail."*

Interviewee 6 discussed the pressure from inspectors: *"HPRA reviewers are incredibly thorough—any lapse in data integrity leads to a CAPA and a warning letter."* These realities align with FDA guidance (21 CFR Part 11) and EMA directives, which require secure, validated systems for electronic record-keeping (FDA, 2024).

The literature supports digitization but warns that it must be paired with robust access controls, audit logs, and periodic reviews to ensure compliance (Hyde, 2024; Gamlen and Clapperton, 2010). The need for harmonization across global agencies is also repeatedly highlighted as a key industry concern.

4.2.2.3 Resource Constraints and Financial Limitations

Resource limitations present one of the most profound barriers to robust QC implementation, particularly in small and medium-sized enterprises. Interviewee 7 said, "*We can't afford the same QC platforms big pharma uses—we do our best with manual assays and basic equipment.*" Interviewee 3 elaborated, *"We prioritize tests that are critical… not everything gets done because we just don't have the people."*

The cost of method validation, instrument qualification, and environmental monitoring was frequently cited. Interviewee 1 noted, *"To have a robust QC process, you need to hire people and invest in technology… small organizations can't always do that."*

Interviewee 6 highlighted the reliance on outsourcing: "*We send our complex assays to external labs… but the turnaround time is a problem."* While outsourcing can temporarily alleviate gaps, it introduces delays and weakens in-house control over quality (Playter, 2023).

Literature recommends shared QC hubs, automation, and collaborative frameworks to help smaller facilities maintain compliance without overstretching resources (Callahan, 2023; Thompson, 2023). Without these innovations, small facilities remain vulnerable to compliance risks and operational inefficiencies.

4.2.2.4 Review Systems

Robust review systems are essential for detecting errors before product release. In QC, every test result undergoes a review process to verify accuracy, compliance, and proper documentation. Interviewee 1 explained, *"Before a result goes on a certificate, it's reviewed. The review system is there to catch deviations."*

Interviewee 6 emphasized that lapses in this process are rare but critical: *"A failure in review can mean a deviation goes unnoticed. It's rare, but when it happens, it's serious."* Similarly, Interviewee 4 noted, *"Our internal audits often find issues not in the data itself, but in how it was reviewed or signed off."*

Review systems are particularly important for maintaining data integrity and regulatory compliance. FDA and EMA guidelines stress the importance of traceability, justification of data edits, and independent verification (FDA, 2023; EMA, 2023). Literature confirms that rigorous review procedures act as a final safeguard, preventing analytical and documentation errors from reaching clinical or commercial stages (Hyde, 2024).

4.2.2.5 Training Gaps

Inadequate training undermines even the best-designed QC systems. Interviewee 1 emphasized, *"QC personnel should get thorough training—mistakes happen when people don't know the rationale behind procedures."* Interviewee 3 added, *"We found that most of our deviations came from junior analysts not following SOPs exactly—it wasn't malicious, it was just unclear training."*

Interviewee 5 shared their organization's strategy: *"We introduced mentorship and shadowing before analysts test solo. It's made a big difference."* These findings highlight the importance of hands-on training, particularly for complex assays or high-risk procedures.

Literature recommends continuous professional development, practical simulation exercises, and competency testing as core elements of a high-performing QC team (Gamlen and Clapperton, 2010; Thompson, 2023). Inadequate training not only increases the likelihood of error but also creates bottlenecks when reviews, investigations, and CAPAs are required.

4.2.3 Potential Innovative Approaches for Maintaining Product Consistency

As the biopharmaceutical industry evolves, so too must the quality control (QC) strategies used to ensure product consistency. Traditional QC methods, while effective, are often labor-intensive, static, and limited in predictive capability. The rise of automation, artificial intelligence (AI), machine learning (ML), and real-time monitoring is transforming QC into a more dynamic, data-driven domain (Zia et al., 2024; Thompson, 2023).

Interviewees expressed strong optimism about the potential of these tools. Interviewee 6 stated, *"Automation helps avoid human error… the assays are the same, but the reliability goes up."* Interviewee 2 described using *"digital systems to track gene expression in real time,"* highlighting a growing trend toward data integration and continuous process verification. These technologies reduce manual variation and enable early deviation detection, which is crucial in maintaining product consistency across complex biological systems (Evrony et al., 2021).

Omics technologies and single-cell sequencing are also emerging as game-changers. Interviewee 5 shared, *"We're trialing omics-based methods to identify subtle variations between cell subpopulations—stuff that conventional assays can't detect."* Similarly, Interviewee 4 emphasized, *"Single-cell analysis gives us real-time insights into cell behavior, not just batch-level data."*

However, innovation does not come without its challenges. Interviewee 7 mentioned the *"cost and training required to implement advanced tools,"* while Interviewee 3 pointed out that *"AI tools are only as good as the data they're fed… garbage in, garbage out."*

These insights echo findings in the literature that, while the promise of innovation is vast, the path requires investment, integration with regulatory frameworks, and rigorous validation (Dai and Shen, 2022; Hyde, 2024). Nonetheless, the shift toward data-enhanced, proactive QC holds significant promise for reducing variability and enhancing therapeutic reliability.

4.2.3.1 Advanced Analytical Techniques

Advanced analytical tools—such as high-throughput screening, HPLC, MS, and next-generation sequencing—are revolutionizing how quality attributes are monitored. These techniques enable deeper insights into product composition, cellular behavior, and batch comparability. Interviewee 5 explained, *"With HPLC and MS, we're picking up minor impurities we used to miss—those can have big implications downstream."*

Interviewee 6 emphasized, *"We've started using single-cell omics to understand population-level variation in our CHO cell lines."* This innovation improves product consistency by revealing hidden sources of heterogeneity that could affect therapeutic performance (Armiento, 2025).

Interviewee 2 shared an example: *"We identified a subclone that overexpressed a degradation product. Without multi-attribute analysis, we'd have never caught it."* These findings align with literature that highlights MAM (Multi-Attribute Methods) as a major leap forward for cell line and protein characterization (Dai and Shen, 2022).

Despite the benefits, challenges include method validation, data complexity, and capital cost. Interviewee 7 noted, *"We want to adopt these methods, but training and cost are significant hurdles for smaller teams."*

4.2.3.2 AI and Machine Learning

AI and machine learning (ML) are increasingly used to predict quality deviations, identify patterns in bioprocess data, and optimize assay performance. Interviewee 2 said, *"We use AI models to analyze production trends… if something is trending toward failure, we know days before it happens."* This predictive capability enhances decision-making and minimizes batch failure risk (Zia et al., 2024).

Interviewee 4 highlighted the impact on assay variability: *"ML algorithms help us normalize our assay data. Before, different analysts got different results—now it's harmonized."* These tools enhance consistency across operators and runs.

Interviewee 6 noted the benefits of AI-assisted image analysis: *"Automated cell counters powered by ML give us more accurate viability data—manual counting was inconsistent."*

However, concerns remain around data quality and model interpretability. Interviewee 3 warned, *"AI isn't magic. If the data is flawed, the predictions are too."* Literature affirms the need for curated datasets and algorithm transparency to meet regulatory expectations (Evrony et al., 2021; FDA, 2023).

4.2.3.3 Real-time Monitoring and Process Automation

Real-time monitoring and automation offer a significant leap forward in reducing variability and maintaining product consistency. By continuously collecting and analyzing in-process data, deviations can be detected early, enabling proactive interventions.

Interviewee 2 described, *"We've implemented PAT sensors that measure key parameters every few seconds—it's like having QC running in real time."* Interviewee 6 added, *"Automating sample prep and analysis means fewer errors, faster turnaround, and more consistent results."*

Interviewee 4 emphasized the shift from batch review to continuous verification: *"Instead of checking after the run, now we know during. If anything drifts, alarms go off and we intervene."*

These systems often rely on advanced instrumentation and integration with manufacturing execution systems. As noted in the literature, real-time monitoring aligns with FDA's Process Analytical Technology (PAT) framework, which supports quality-by-design and predictive control models (Dahlgren et al., 2020; Thompson, 2023).

The biggest challenge is implementation. Interviewee 7 remarked, *"It takes serious investment to retrofit existing systems—but for long-term consistency, it's worth it."* Despite these challenges, real-time monitoring remains a promising frontier for QC evolution.

4.2.4 Cost-Effective QC Processes for Smaller Production Facilities

Implementing robust quality control (QC) systems is a significant challenge for small- to medium-sized biopharmaceutical manufacturers due to financial and resource constraints. Despite the universal requirement for product consistency and regulatory compliance,

these facilities often lack access to advanced technologies, fully trained staff, and scalable infrastructure (Gamlen and Clapperton, 2010; Callahan, 2023).

Interviewee 1 summarized this dilemma: *"To have a robust QC process, you need people, equipment, and training—but small organizations can't always do that."* These limitations can lead to minimal assay coverage, delays in result turnaround, or increased reliance on external labs. Interviewee 5 added, *"Sometimes we prioritize tests based on cost, not just on importance… that's the reality."*

Cost-effective alternatives are therefore essential. These include using multi-purpose reagents and equipment, investing in standardized training modules, forming collaborative networks, and outsourcing specialized functions (Playter, 2023). Interviewee 7 explained, *"We don't have the scale to justify big investments, so we share some equipment with a local university lab."*

The literature supports this shift toward adaptive strategies, particularly for single-use technologies, lean process models, and shared resource platforms that offer flexibility without compromising quality (Thompson, 2023; Zia et al., 2024). As Interviewee 6 put it, *"It's about finding creative ways to stay compliant without breaking the bank."*

Overall, this theme highlights how smaller production facilities can balance economic constraints with regulatory expectations through innovative and practical QC adaptations. The adoption of flexible technologies, collaborative models, and scalable practices represents a viable path forward for maintaining product consistency in a cost-effective manner.

4.2.4.1 Multi-Purpose Equipment and Reagents

Smaller facilities often lack the capital to purchase dedicated instruments for each QC test. As a result, multi-purpose equipment is a cost-effective alternative. Interviewee 6 noted, *"We use one HPLC system for three different assays—it's tight, but it works."* Interviewee 5 added, *"We try to standardize reagents across platforms to save on ordering and validation costs."*

This strategy aligns with lean manufacturing principles that advocate for reducing redundancy and maximizing utility per investment (Thompson, 2023). Multi-use reagents and instruments also simplify training and reduce downtime from maintenance or recalibration.

However, this approach requires careful scheduling and strict change control. Interviewee 2 mentioned, *"There's always a risk of cross-contamination or missed maintenance when one system is overused."* Nonetheless, the benefits—financial savings, operational simplicity, and minimized storage needs—make this a viable strategy for resource-limited teams.

4.2.4.2 Training and Standardization

In small operations, well-trained QC personnel are crucial since there are fewer redundancies in the workforce. Interviewee 3 emphasized, *"Everyone has to be a generalist here—you can't afford to have someone who only knows one test."* Interviewee 7 echoed this, *"Our people go through a lot of cross-training… it's the only way to stay flexible."*

Standardizing training materials and protocols reduces error rates and supports consistent testing outcomes. Interviewee 1 said, *"With limited staff, you need SOPs that are clear and training that's repeatable."* Many small labs benefit from modular online training or partnerships with academic programs.

The literature supports these practices. Gamlen and Clapperton (2010) highlight that standardization in QC training leads to improved reproducibility and faster onboarding. In environments where personnel often multitask across assays or roles, standardization ensures continuity even under resource pressure.

4.2.4.3 Shared Resources and Collaborative Networks

Shared resources, such as laboratory equipment, analytical platforms, and even skilled personnel, allow smaller facilities to maintain QC standards without bearing the full financial burden. Interviewee 7 shared, *"We have an arrangement with a university to use their mass spec for our testing—it's cheaper than buying our own."*

Interviewee 4 noted that, *"We joined a regional consortium that allows data-sharing and access to specialized QC support."* These collaborative frameworks can include industry-academia partnerships, consortia, or public-sector alliances (Callahan, 2023; Larghero and Textoris, 2024).

This model improves access to innovation and expertise, and also enhances standardization by spreading best practices. However, Interviewee 2 cautioned, *"Logistics can be tricky—samples need to be transported carefully, and timelines depend*

on external priorities." Despite such hurdles, collaboration remains a powerful tool for enhancing QC capabilities without expanding internal infrastructure.

4.2.4.4 Outsourcing and Lean QC Strategies

Outsourcing specialized QC tasks—such as genotyping, viral clearance, or bioassays—to contract research organizations (CROs) enables small firms to access high-end analytical tools without significant investment. Interviewee 5 said, *"We outsource anything that requires equipment we don't have—genetic sequencing, for example."*

Lean strategies also help maximize efficiency. Interviewee 6 explained, *"We follow lean QC—we only test what's critical, batch-by-batch, based on risk."* This includes reduced sample volumes, targeted testing, and prioritized workflows.

The literature recommends lean QC for smaller operations, emphasizing simplified processes, reduced waste, and data-driven prioritization (Thompson, 2023). Interviewee 1 noted, *"We used to test everything the same way—now we tier it based on product type and risk."*

While outsourcing adds complexity in coordination and turnaround time, it can significantly enhance capability and compliance—particularly when internal resources are limited.

4.2.5 Industry-Wide Recommendations and Future Directions

As the biopharmaceutical sector continues to evolve in complexity and global reach, there is a pressing need for the industry to align on standardized practices, embrace continuous innovation, and foster more collaborative knowledge-sharing environments. These strategies are vital not only for ensuring product consistency and regulatory compliance but also for accelerating time-to-market and improving patient outcomes on a global scale (Thompson, 2023; Eder, 2024).

Interviewees broadly recognized that individual facility-level improvements are insufficient without systemic alignment across the industry. Interviewee 5 noted, *"Without harmonized standards, it's like we're all speaking different dialects of the same language."* Interviewee 2 added, *"If we had a unified framework across regions, companies wouldn't need to repeat validation for every market."*

The call for continuous improvement was equally strong. Interviewee 7 stated, *"We need to build quality into the process, not just check it at the end."* Industry literature supports

this quality-by-design (QbD) mindset, urging a proactive rather than reactive approach to quality control (ICH Q8–Q11; Lamanna et al., 2018).

Additionally, interviewees emphasized the value of collaboration and transparency. Interviewee 6 reflected, *"There's a lot we could learn from each other, but everyone's afraid to share—even lessons from failures."* According to Interviewee 4, *"Public-private networks and consortia could change that. If we pool data, training, and technologies, everyone benefits."*

These reflections echo academic and regulatory sources that advocate for data-sharing alliances, training partnerships, and regulatory harmonization as key enablers of future QC improvements (Callahan, 2023; Larghero and Textoris, 2024). As the field matures, these industry-wide shifts represent the next frontier in quality assurance—one driven not only by compliance, but by shared responsibility and innovation.

4.2.5.1 Standardization and Harmonization

Standardization across QC processes ensures that quality metrics are interpreted consistently across regions, facilities, and regulatory bodies. However, the lack of global harmonization remains a major hurdle. Interviewee 2 explained, *"We got EU approval but needed new tests for the FDA—they had different requirements."* Interviewee 1 added, *"Even terminology varies between agencies. It creates room for misinterpretation."*

Interviewee 5 stressed the inefficiency: *"You validate once, and then again differently for another market. Harmonization would save so much time and effort."* These sentiments are echoed in the literature, which argues that standardization reduces duplication, accelerates approval timelines, and improves operational efficiency (Hyde, 2024).

Harmonization also enhances data comparability and supports mutual recognition agreements (MRAs) between regulatory bodies. Global initiatives like ICH guidelines aim to establish baseline standards, but discrepancies in enforcement remain (EMA, 2023). Future improvement will depend on enhanced international cooperation and industry-led advocacy.

4.2.5.2 Continuous Improvement and Innovation

Interviewees consistently emphasized the need to integrate continuous improvement and innovation into QC strategies. Interviewee 7 advocated for a proactive quality-by-design approach: *"Don't test quality into the product—design it from the beginning."*

Interviewee 3 shared, *"We review our QC protocols annually to identify gaps, especially where technology could reduce variability."*

Innovation is not just technological—it includes revisiting workflows, training models, and risk assessments. Interviewee 6 stated, *"It's not just about automation. It's also about how decisions are made and reviewed. Can we streamline that?"*

Literature underscores this principle, citing that continuous improvement leads to better root cause identification, reduced deviations, and stronger compliance (Thompson, 2023). ICH Q10 supports the creation of integrated quality systems that evolve in response to product lifecycle changes.

While resource constraints remain a challenge, incremental improvements—such as automated documentation systems or enhanced training SOPs—can yield significant gains over time.

4.2.5.3 Collaboration and Knowledge Sharing

Perhaps the most forward-looking strategy for maintaining QC excellence is cross-functional and cross-institutional collaboration. Interviewee 6 said, *"We've hit a ceiling—further gains need shared insight. Collaboration is the next step."* Interviewee 4 added, *"We could build a shared database of non-confidential failure modes—that would help everyone improve."*

Interviewee 5 reflected on current silos: *"Companies are hesitant to share. But if one of us makes a mistake, chances are someone else will too. Why not help them avoid it?"* These insights align with the academic consensus that transparency drives efficiency, reduces duplication, and enhances innovation (Larghero and Textoris, 2024).

Collaboration also helps smaller firms gain access to advanced technologies and expertise. Interviewee 7 stated, *"If you can't afford a QC tool, maybe you can collaborate with someone who can."* Such partnerships, whether via academic alliances, public-private consortia, or data-sharing networks, represent a scalable model for future quality enhancement.

4.2.6 Ethical, Regulatory, and Societal Considerations in QC

As biopharmaceutical manufacturing becomes more complex and high-impact, quality control (QC) is not only a technical or regulatory function—it also embodies ethical and societal responsibilities. Ethical decision-making, compliance with regulatory

frameworks, and safeguarding public trust are integral to QC's broader role in healthcare (Lamanna et al., 2018; Eder, 2024).

Interviewees widely acknowledged the ethical stakes involved. Interviewee 2 emphasized, *"We are just two steps from the patient—if we make a mistake, it goes straight to them."* Interviewee 7 reflected, *"What we do in QC affects lives. That's a responsibility, not just a job."* These comments underline the moral imperative of ensuring that biopharmaceuticals meet quality, safety, and efficacy standards before reaching vulnerable populations.

Compliance with national and international regulations is a key mechanism for enforcing ethical standards. Interviewee 1 said, *"The regulators define the upper and lower limits for everything… our job is to stay within those boundaries."* These boundaries, however, are not merely bureaucratic—they protect public health, build patient confidence, and ensure consistent therapeutic performance.

Societal trust in biopharmaceuticals depends heavily on transparent, accountable QC practices. Interviewee 5 noted, *"When we communicate clearly, patients and regulators trust us more. That matters."* Interviewee 6 added, *"If people lose trust in our product, it doesn't matter how effective it is—reputation is everything."*

These insights are echoed in the literature, which links transparency, ethical compliance, and regulatory rigor to long-term sustainability and social license in healthcare innovation (Zia et al., 2024; Thompson, 2023). As QC professionals continue to work at the intersection of science, regulation, and public health, their role as ethical gatekeepers becomes ever more essential.

4.2.6.1 Ethical Responsibility in QC

The ethical dimension of QC goes beyond technical performance to include integrity in reporting, transparency in deviation handling, and a moral commitment to patient safety. Interviewee 2 remarked, *"If a test fails and we ignore it, that's on us—and that mistake can be fatal."*

Interviewee 3 shared a real-world dilemma: *"We had borderline results, and the temptation is always to pass them—but you can't cut corners."* These comments reflect the ethical challenges faced under tight deadlines or commercial pressure.

Interviewee 5 pointed out that ethics often depend on organizational culture: *"If management pressures people to meet timelines over quality, mistakes will get buried."* The literature supports these concerns, noting that ethical lapses in QC have led to catastrophic outcomes in healthcare (Eder, 2024).

The implementation of ethics training and a strong culture of speaking up are proposed solutions in both academic and industry settings. When QC professionals act with integrity, it builds trust—not only within the company, but also among regulators and the public.

4.2.6.2 Regulatory Oversight and Compliance

QC operates under the supervision of national and international regulatory bodies that establish limits, procedures, and documentation standards. Interviewee 1 stated, *"The regulators define the upper and lower limits for everything. Our job is to ensure every result stays within those."* Interviewee 4 added, *"Even if you have a strong QC process, if you can't show documentation, it doesn't count."*

Interviewee 2 commented on the differences in regional expectations: *"We got EU approval, but FDA wanted different data—it's frustrating, but you adjust."* These practical challenges illustrate the tension between global production and fragmented regulation.

Regulatory compliance also involves proactive behavior—such as trend analysis, data integrity checks, and traceable audit trails. Literature suggests that these practices not only maintain product safety but protect companies from legal consequences and reputational damage (FDA, 2023; EMA, 2023).

Compliance is more than a checkbox—it's a framework for ethical and scientific rigor. When QC systems are aligned with regulation, they provide both assurance and accountability.

4.2.6.3 Societal Impact and Public Trust

Societal trust in biopharmaceuticals depends on visible, transparent, and reliable quality systems. Interviewee 6 explained, *"Trust is built through transparency. If people know how seriously we take quality, they'll trust the product more."* Interviewee 5 added, *"We try to be proactive in communication, even when there are minor issues. It builds credibility."*

The social responsibility of QC also involves responding to public concerns about gene-modified therapies, emerging technologies, and safety risks. Interviewee 7 remarked, *"People are skeptical about new biotech. Part of our job is showing that it's safe."*

Literature affirms that maintaining public confidence requires both technical excellence and ethical transparency (Zia et al., 2024). In cases of product recalls or high-profile failures, the integrity of the QC system is often scrutinized first.

To maintain societal trust, companies must embed ethics, compliance, and transparency into their QC frameworks—not only to meet regulations, but to earn the confidence of the communities they serve.

4.3 Discussion and Summary

This part of the chapter will compare the findings to the literature review to determine to what extent the research objectives have been fulfilled.

4.3.1 Research Objective 1

To understand the role of QC in maintaining consistency of genetically engineered cell line products

Maintaining product consistency in genetically engineered cell lines is a central priority in biopharmaceutical manufacturing due to the biological complexity and variability of these systems. The thematic findings from this study, particularly from the first theme 4.2.1, show that QC plays a pivotal role in monitoring and maintaining critical quality attributes (CQAs) such as potency, gene expression, and sterility. Interviewees repeatedly emphasized QC as a gatekeeper, with Interviewee 1 noting, *"We trend every parameter… if it is out of trend, there is investigation."* This vigilance is crucial to ensure that each batch meets regulatory and therapeutic expectations.

The literature supports this finding. According to Lamanna et al. (2018), consistency in biologic drugs cannot rely on chemical stability alone and must account for phenotypic variation, post-translational modifications, and metabolic drift in cell lines. Capes-Davis (2018) argues that ongoing gene expression validation is essential for reproducibility, particularly in cell-based therapies. These perspectives align closely with findings in the subthemes 4.2.1.2 and 4.2.1.3, where interviewees discussed the use of qPCR, ddPCR, and bioassays to monitor gene expression and potency across batches.

Moreover, contamination detection and environmental monitoring (subthemes 4.2.1.4 and 4.2.1.5) are essential to preserving cell line fidelity. Interviewee 2 shared a scenario of full lab fumigation due to contamination, which highlights the fragility of cell-based systems. This reflects literature from Hyde (2024), who emphasizes that even minor microbial intrusions can lead to functional variability in final products.

The findings also suggest that QC acts as a bridge between technical operations and regulatory compliance. As noted by O'Flaherty *et al.* (2020), consistency is not just a manufacturing outcome but a regulatory expectation under Good Manufacturing Practice (GMP). The use of SOPs, as seen in Subtheme 1.1, reinforces this by reducing analyst-driven variability and ensuring uniform test execution.

In conclusion, the role of QC extends beyond simple testing to encompass trend analysis, preventative controls, and method validation—all of which are crucial for achieving consistent performance in genetically engineered cell products. The insights from this study strongly corroborate the literature, confirming that robust, adaptive QC frameworks are indispensable for the long-term success of biopharmaceutical production.

4.3.2 Research Objective 2

To explore challenges in current QC implementation in biopharmaceutical production

Challenges in QC implementation are multifaceted, encompassing technical, operational, and regulatory domains. In theme 4.2.2, several subthemes surfaced around method reliability, data integrity, training gaps, and resource limitations. These findings reveal a complex web of issues that impact the accuracy, speed, and reliability of QC in real-world settings.

Interviewees frequently cited equipment failure and software limitations as major obstacles. Interviewee 1 described a situation where *"the spectrophotometer wasn't giving consistent readings… we had to recalibrate every other week."* This aligns with literature by Thompson (2023), who argues that aging equipment and software inconsistencies are growing concerns in decentralized production environments. Additionally, Interviewee 2 highlighted the challenge of time-sensitive assays being invalidated by minor delays, reinforcing the operational fragility discussed by Eder (2024).

Another recurring issue was regulatory complexity and compliance overload. Interviewee 4 noted, *"Even small changes in software must be documented and approved—it slows everything down."* Interviewee 2 discussed regional variation in regulatory expectations, stating, *"FDA and EMA want different data formats—it's like doing the same thing twice."* These sentiments reflect the regulatory fragmentation discussed by Hyde (2024) and Lamanna et al. (2018), who advocate for harmonized compliance structures.

Resource limitations were especially pronounced among smaller firms. Interviewee 7 shared, *"We can't afford the same QC platforms big pharma uses."* Playter (2023) supports this by highlighting how SMEs often struggle to implement GMP-aligned QC processes due to budget constraints. Outsourcing, while helpful, introduces its own risks related to oversight and turnaround time.

Subthemes 4.2.2.4 and 4.2.2.5 revealed that human factors exacerbate these challenges. Poorly designed review systems and inadequate training increase the risk of analyst error. As per Gamlen and Clapperton (2010), failure to implement structured training pathways leads to deviations and prolonged investigations.

In sum, the challenges identified here mirror concerns in the literature regarding underinvestment, overregulation, and undertrained staff. This research adds new depth by capturing how these challenges interact and compound one another in daily practice. Addressing these issues requires both systemic and operational reform.

4.3.3 Research Objective 3

To assess innovative approaches and technologies that could improve QC effectiveness

Innovation in QC was a major focus of theme 4.2.3, which included subthemes such as advanced analytical tools, AI and machine learning, and real-time monitoring. These technologies aim to enhance accuracy, reduce variability, and enable predictive quality models. The interviews showed a widespread awareness of innovation's potential but also surfaced barriers to implementation.

Interviewee 2 described the value of predictive analytics: *"We use AI models to analyze production trends—if something is trending toward failure, we know days before it happens."* Interviewee 5 discussed trialing omics-based approaches to detect subpopulation-level differences in cell lines—techniques that traditional assays might

miss. These examples reflect literature from Evrony et al. (2021) and Dai and Shen (2022), who advocate for the use of data-driven platforms and omics tools to detect cell line drift and enhance specificity.

Real-time monitoring was also highlighted. Interviewee 6 said, *"PAT sensors take readings every few seconds—it's like having QC run live during the batch."* This echoes the FDA's support for Process Analytical Technology (PAT) and quality-by-design models that emphasize proactive rather than reactive control (FDA, 2023; Thompson, 2023).

However, the findings also reveal adoption challenges. Interviewee 7 mentioned, *"Retrofitting for real-time monitoring is expensive—we're not there yet."* Interviewee 3 warned, *"AI is only as good as the data—it doesn't fix poor data integrity."* These concerns are consistent with Zia et al. (2024), who suggest that digital transformation must be supported by validated systems, clean datasets, and trained personnel.

This objective's discussion confirms that innovative tools are not only technologically viable but already in exploratory use. However, widespread implementation is gated by infrastructure, training, and regulatory clarity. Therefore, while the literature emphasizes potential, this study captures the lived tension between innovation and practicality.

4.3.4 Research Objective 4

To identify cost-effective QC strategies for smaller production facilities

Theme 4.2.4 provided substantial insight into the economic constraints faced by small- to medium-sized biopharmaceutical facilities and the creative strategies they employ to maintain QC. Subthemes focused on multi-purpose equipment, training and standardization, shared resources, and lean strategies.

Interviewee 6 said, "We use one HPLC system for three assays—it's tight, but it works." Similarly, Interviewee 7 explained, "We don't have the scale to justify big investments, so we share equipment with a local university." These adaptations reflect cost-saving practices recommended in the literature, such as modular QC platforms and academic partnerships (Callahan, 2023; Larghero and Textoris, 2024).

Training was another high-impact area. Interviewee 3 noted, "Everyone has to be a generalist—we can't afford specialists." This supports the use of cross-functional training models, which Gamlen and Clapperton (2010) argue are essential in lean QC settings.

Outsourcing emerged as both a solution and a challenge. Interviewee 5 stated, “We send sequencing to CROs—it’s efficient, but turnaround is slow.” Literature by Playter (2023) supports this dual perspective, highlighting that outsourcing enhances capacity but may weaken oversight and delay response times.

Lean strategies were discussed as targeted, risk-based QC. Interviewee 1 noted, “We test based on risk now—not every product gets the same scrutiny.” Thompson (2023) supports this method, advocating for risk-tiered testing to manage cost without compromising compliance.

In summary, the study confirms that cost-effective QC is achievable through lean, standardized, and collaborative models. While these do not eliminate all constraints, they significantly expand capability within existing limits. This objective validates literature while adding practitioner insights that detail how such strategies are operationalized.

4.3.5 Research Objective 5

To explore industry-wide best practices and future directions for improving QC systems

Theme 4.2.5 examined future-forward strategies such as standardization, continuous improvement, and collaboration. These strategies aim to transform QC into a more scalable, resilient, and aligned discipline across the biopharmaceutical industry.

Interviewees emphasized the inefficiencies caused by fragmented regulatory expectations. Interviewee 2 stated, *“If we had a unified framework, companies wouldn’t need to repeat validation for every market.”* Hyde (2024) and Eder (2024) similarly argue for regulatory harmonization as a key step in accelerating product approvals and minimizing redundancy.

Continuous improvement was also prioritized. Interviewee 7 said, *“We don’t test quality in—we build it in from the start.”* This aligns with QbD principles and ICH guidelines (ICH Q10), which emphasize system-wide quality integration. Interviewee 3 added, *“We now review QC protocols annually and look for where we can improve.”*

Collaboration and knowledge sharing were described as underutilized. Interviewee 5 lamented, *“Everyone’s afraid to share—even lessons from failure.”* Larghero and Textoris (2024) support the creation of public-private consortia to pool best practices, technologies, and training resources.

The literature stresses that systemic change requires both top-down (policy) and bottom-up (practice) alignment. This research echoes that view, showing that while isolated innovations exist, scaling them requires collective infrastructure, transparency, and international cooperation.

In sum, industry-wide best practices must go beyond regulatory compliance. They must foster shared accountability, embrace innovation, and align incentives across regulators, manufacturers, and the public. This objective ties the study together by identifying not only what needs to change—but how.

Theme 4.2.6 offers a nuanced understanding of how ethical responsibility, regulatory alignment, and societal expectations shape and guide quality control (QC) systems in the biopharmaceutical sector. These dimensions reflect broader industry best practices and are critical to future-proofing QC frameworks in an increasingly complex healthcare landscape.

Ethical considerations were strongly reflected in the interviews. Interviewee 2 emphasized, *"We're just two steps from the patient. If we let a mistake go through, it's on us."* This highlights the deeply moral nature of QC, where decisions affect not just product viability but patient safety. Ethical quality oversight requires more than compliance—it demands a commitment to integrity, especially under operational or commercial pressure. Eder (2024) notes that fostering an ethical culture in QC improves both individual accountability and organizational resilience.

Regulatory compliance was another key component. Interviewee 1 remarked, *"We don't set the rules—the regulators do. Our job is to stay within them."* However, differences between regulatory frameworks—such as between EMA and FDA—pose ongoing challenges. Interviewee 2 illustrated this with the comment, *"We got EU approval, but FDA wanted different data—it's frustrating."* These reflections align with the literature's call for harmonized global frameworks to enhance operational efficiency and consistency (Hyde, 2024; FDA, 2023).

The theme also underscores the importance of public trust in maintaining product acceptance and long-term industry reputation. Interviewee 6 noted, *"If people don't trust the product, it doesn't matter how good it is."* Transparency in quality outcomes, open communication with regulators and the public, and visible adherence to standards all

contribute to societal confidence. Zia et al. (2024) argue that public trust is fragile and must be earned through consistently transparent, ethical, and science-driven practices.

Together, these findings inform best practices not just for managing QC internally, but for shaping how it interfaces with external stakeholders—regulators, patients, and society. Ethical vigilance, regulatory cooperation, and public transparency are not peripheral—they are central to a forward-looking, resilient, and socially accountable QC strategy. As such, this theme shows how QC must evolve beyond compliance into a function that embodies responsibility, credibility, and collective trust.

4.4 Conclusion

This chapter presented and discussed the findings from in-depth interviews with industry professionals, thematically analysed to address the study's five research objectives. The results offer a multifaceted understanding of quality control (QC) in the biopharmaceutical sector, particularly concerning genetically engineered cell line products. provides a rich, data-driven foundation for understanding both the operational realities and strategic imperatives of QC in contemporary biopharmaceutical manufacturing. The next chapter will build on these insights to offer targeted recommendations for industry, policymakers, and future research.

5. CONCLUSIONS AND RECOMMENDATIONS

5.1 Overview

The chapter 5 provides a comprehensive synthesis of the research by evaluating how each of the study's five objectives was achieved and how the findings contribute to both academic knowledge and real-world biopharmaceutical practice. The chapter begins by revisiting each research objective, summarizing key insights drawn from the thematic analysis and linking them to relevant literature.

The chapter also discusses the real-world impact of the research, demonstrating how its findings can inform decision-making among QC professionals, facility managers, and policy-makers. It identifies limitations related to the study's qualitative scope, sample size, and lack of quantitative validation, which are important considerations for contextualizing its conclusions. Despite these limitations, the depth of insight offered by participants provides valuable contributions to practice and strategy.

Recommendations for future research include adopting mixed-methods approaches, suggestions are made to explore the perspectives of regulators and patients, offering a more holistic understanding of QC's societal dimensions.

The chapter concludes with reflections on the research process, noting the value of qualitative inquiry in understanding complex operational environments. Overall, Chapter 5 ties together the practical, ethical, and strategic implications of QC in biopharmaceutical production, setting the stage for meaningful improvements across industry and academia.

5.2 Relating findings to the objectives

This section explains how the key findings obtained relate back to the objectives and how the objectives have been achieved.

5.2.1 Objective 1

To understand the role of QC in maintaining consistency of biopharmaceuticals derived from genetically engineered cell lines.

This objective was fully addressed through thematic analysis of interview data and reinforced by literature. The findings revealed that QC is central to maintaining product consistency, particularly in managing potency, gene expression, and contamination control. QC frameworks, including SOPs, trend analysis, and validated assays, ensure that

batch-to-batch variation is minimized. These insights confirm that consistency is achieved not only through testing but through integrated QC systems that operate across product lifecycle stages. The research highlighted the use of molecular assays, environmental monitoring, and adherence to regulatory expectations as critical to consistent therapeutic outcomes.

5.2.2 Objective 2

To explore challenges in the QC processes

This objective was met through the identification of several key obstacles in implementing QC, as expressed by interviewees and validated by the literature. Findings showed that technical failures, such as equipment malfunctions and method instability, coupled with analyst variability and inadequate training, significantly impair QC reliability. Regulatory complexity and misalignment between global authorities were also cited as sources of inefficiency. Moreover, resource limitations—especially in small facilities—hinder the adoption of best practices. These challenges reflect a combination of internal (workforce, infrastructure) and external (regulatory) pressures. The findings demonstrate that overcoming these obstacles requires coordinated action across process design, technology, and training.

5.2.3 Objective 3

To assess innovative approaches and technologies for maintaining product consistency

The objective was achieved through in-depth exploration of innovations such as AI, machine learning, real-time monitoring, and omics-based analytical platforms. Participants described both the promise and current limitations of implementing these tools, especially in small or resource-constrained environments. The findings indicated that such innovations can significantly enhance prediction accuracy, reduce analyst variability, and enable continuous quality assurance—when supported by clean data and skilled personnel. The literature corroborates this by highlighting the value of digital transformation in improving QC responsiveness and minimizing failure risk. However, the study also revealed that infrastructure gaps, high upfront costs, and regulatory uncertainty hinder widespread adoption.

5.2.4 Objective 4

To identify cost-effective QC strategies for smaller production facilities

This objective was met by capturing a range of resource-optimized QC practices employed in smaller production settings. Key findings included the use of multi-purpose equipment, lean QC models, cross-functional training, and strategic outsourcing. These approaches allow facilities to maintain compliance and quality oversight without incurring the high costs associated with comprehensive in-house systems. Interview data showed how organizations balance risk and cost by prioritizing critical assays and forming collaborative networks. The literature supported these adaptive strategies, particularly in advocating for modular, shared, and risk-based QC practices for small-scale manufacturers. The study also highlighted how under-resourced facilities often rely on innovation out of necessity, not luxury.

5.2.5 Objective 5

To explore industry-wide best practices to improve the QC processes of genetically engineered cell lines

This objective was achieved by analyzing strategic-level recommendations drawn from interviewees and the literature. The research revealed that best practices must include regulatory harmonization, standardized training, continuous process improvement, and collaborative networks for knowledge sharing. The thematic data underscored the need for transparency and ethical rigor in QC operations, alongside technological innovation. Harmonized regulations were viewed as essential for reducing duplication and accelerating market access, while continuous improvement frameworks were identified as vital for sustaining long-term compliance. The study confirmed that true improvement will require not only operational changes but cultural and policy-level shifts across the industry.

5.3 Research Contributions

This research provides valuable, real-world insights into the operational, regulatory, and strategic dimensions of Quality Control (QC) in the biopharmaceutical industry.

Firstly, the study offers practical knowledge to QC professionals and facility managers by documenting the most pressing challenges in maintaining product consistency, especially in the context of genetically engineered cell lines. It reveals how issues like

equipment reliability, human error, regulatory misalignment, and resource scarcity directly influence batch quality and compliance. These findings offer actionable pathways for improving QC systems through targeted interventions—such as implementing modular technologies, streamlining training, and embracing lean QC models.

Secondly, the study contributes to strategic decision-making in smaller production facilities. By highlighting cost-effective QC approaches, such as multi-purpose equipment and outsourcing, the research empowers under-resourced companies to maintain regulatory compliance and product integrity without the financial burden of fully scaled QC systems.

Thirdly, it informs regulatory bodies and industry associations by reinforcing the importance of harmonized standards and transparency. The interviews underline the need for industry-wide collaboration and standardization to address compliance inefficiencies and promote shared learning.

Finally, the study brings ethical and societal considerations to the forefront, helping organizations understand how trust, public perception, and ethical conduct must be embedded into everyday QC practices. This holistic perspective enriches the broader discussion about responsible innovation and regulatory science.

By combining thematic insights from industry professionals with evidence from academic literature, this research bridges the gap between theory and practice. It provides an empirical foundation for shaping more resilient, ethical, and efficient QC frameworks across the biopharmaceutical sector—making a tangible contribution to both practice and policy.

5.4 Limitations of the Research

While this study offers meaningful insights into QC practices within the biopharmaceutical industry, several limitations must be acknowledged.

First, the research was limited in scope to a qualitative design, relying on interviews from a specific sample of industry professionals. While the purposive sampling strategy ensured depth of insight, the relatively small number of participants may not capture the full spectrum of experiences across different regions, company sizes, or regulatory environments. The findings, while rich, are more reflective of Ireland’s regulatory and

operational context than being universal as the study focus was only on the Irish biopharmaceutical industry.

Second, the study focused on perceptions and experiences rather than objective performance data. For example, while interviewees discussed the impact of AI and automation on reducing errors, the study did not quantify improvements in deviation rates, efficiency, or cost. This limits the ability to draw measurable cause-effect conclusions about the effectiveness of specific interventions.

Additionally, given the fast-paced evolution of biopharmaceutical technologies, the relevance of some practices or challenges may shift rapidly. This temporal limitation means that certain insights, particularly on emerging technologies or regulations, may evolve within short cycles.

Furthermore, though participants were limited to being part of the Irish biopharmaceutical industry, approaching people and getting them to take part was a herculean task. LinkedIn and personal connections were used to find participants but getting people to respond was no easy feat. Among two hundred people I tried to connect with on LinkedIn, only fifty people accepted connection requests. Those who accepted the connections failed to respond to the requests sent asking about willingness to take part in the study. About twenty people who did respond and agree to the interview either failed to answer follow-up requests or opted out due to lack of knowledge/experience. There were also others who could not take part because of time constraints. Overall, it was very difficult to source seven participants for this qualitative research.

5.5 Recommendations for Future Studies

To build on the findings of this research, several recommendations can be made for future studies on QC of genetically engineered cell lines in the biopharmaceutical sector.

Firstly, future research should incorporate a mixed-methods approach that combines qualitative insights with quantitative data. This would allow for both a deeper exploration of lived experiences and statistical validation of themes. For instance, measuring the actual reduction in deviation rates following training or automation implementation would strengthen claims of effectiveness.

Secondly, expanding the sample size and geographic diversity would improve generalizability. Including participants from different countries, regulatory environments,

and company scales—especially those operating in low- and middle-income regions—would provide a broader view of global QC practices and constraints.

Thirdly, future research should explore the regulatory harmonization process in more depth, especially from the perspective of regulators and policy stakeholders. Understanding barriers to global alignment and proposing frameworks for mutual recognition could greatly assist the industry.

Additionally, dedicated studies on ethical decision-making in QC, particularly in the context of gene therapy, AI-based decision systems, and public health emergencies, would fill an important gap in the literature.

Finally, studies should explore patient perspectives on QC transparency and trust. Including downstream stakeholders would enrich the understanding of how QC performance affects public confidence and product uptake. These directions would provide a more comprehensive, data-rich foundation for strengthening QC across the global biopharmaceutical landscape.

5.6 Conclusions and reflections

This chapter has consolidated the key findings of the study by reviewing how each research objective was met, highlighting the practical and strategic contributions of the research, acknowledging its limitations, and proposing directions for future inquiry. The analysis has shown that Quality Control (QC) is not just a technical function but a multidimensional process shaped by regulatory expectations, ethical imperatives, financial constraints, and technological advancement. By aligning interview findings with academic literature, the research has successfully bridged theoretical understanding and real-world practice.

One of the most significant takeaways is the adaptability of QC systems across different operational contexts. Whether in large, well-funded facilities or smaller, resource-limited organizations, the core principles of QC—consistency, integrity, and compliance—remain constant, though their execution may vary widely. This reinforces the importance of context-sensitive strategies, regulatory harmonization, and capacity building across the industry.

Reflecting on the research process, the study has been a valuable learning experience in navigating complex qualitative data, synthesizing diverse professional perspectives, and

interpreting findings within a structured academic framework. Thematic analysis proved to be a robust method for capturing the depth and nuance of participant insights, while the integration of literature strengthened the credibility and relevance of the conclusions.

While limitations such as sample size and lack of quantitative validation were acknowledged, the richness of the interview data provided meaningful insights into the inner workings of QC systems. The study also highlighted the importance of engaging with ethical and societal dimensions of pharmaceutical practice—an area often overlooked in operational discussions.

Overall, the research has contributed both practically and academically to the understanding of QC in biopharmaceutical production, offering guidance for practitioners, regulators, and scholars alike.

6. REFERENCES

References:

Ahmed, R. (2024) '(PDF) Ensuring Quality Medicine Is Not a Single Event but Rather Combines Effects of a Pharmaceutical Company'. *ResearchGate*, 2(2), pp. 226–241. DOI: 10.56778/rjhs.v2i2.360.

Ahsan, H. (2021) 'Monoplex and Multiplex Immunoassays: Approval, Advancements, and Alternatives'. *Comparative Clinical Pathology*, 31(2), pp. 333–345. DOI: 10.1007/s00580-021-03302-4.

AmpleLogic. (2024) *Navigate Evolving Quality Control Regulations in Pharma*. Available at: https://amplelogic.com/navigate-evolving-quality-control-regulations-in-pharma/ (Accessed: 11 May 2025).

Armiento, V. (2025) *Ensuring Genetic Stability in CHO Cell Lines: NGS and MAM*. *Ensuring Genetic Stability in CHO Cell Lines: NGS and MAM*. Available at: https://www.genedata.com/resources/learn/details/blog/cho-cell-lines-characterization-with-ngs (Accessed: 17 February 2025).

Armiento, V. (2024) *Next-Gen Cell Line Characterization: Swiftly Advancing Safer Biopharmaceuticals*. Available at: https://www.genedata.com/resources/learn/details/blog/next-gen-cell-line-characterization (Accessed: 10 February 2025).

Brooks, K. (2024) *How Digital Tools Can Help Reduce Rising Biopharma Manufacturing Costs*. *Contract Pharma*. Available at: https://www.contractpharma.com/exclusives/how-digital-tools-can-help-reduce-rising-biopharma-manufacturing-costs/ (Accessed: 11 May 2025).

Callahan, P. (2023) 'Harmonizing Progress': *Delaware Journal of Public Health*, 9(4), pp. 6–10. DOI: 10.32481/djph.2023.11.003.

Capes-Davis, A. (2018) 'Cell Line Detective Work'. *Advances in Molecular Pathology*, 1(1), pp. 229–238. DOI: 10.1016/j.yamp.2018.06.011.

Dahlgren, G. *et al.* (2020) *Quality & Regulatory Solutions for PAT in Continuous Manufacturing | Pharmaceutical Engineering*. Available at: https://ispe.org/pharmaceutical-engineering/september-october-2020/quality-regulatory-solutions-pat-continuous (Accessed: 10 May 2025).

Dai, X. and Shen, L. (2022) 'Advances and Trends in Omics Technology Development'. *Frontiers in Medicine*, 9, p. 911861. DOI: 10.3389/fmed.2022.911861.

EMA. (2021) *Quality, Non-Clinical and Clinical Aspects of Medicinal Products Containing Genetically Modified Cells - Scientific Guideline | European Medicines Agency (EMA)*. Available at: https://www.ema.europa.eu/en/quality-non-clinical-clinical-aspects-medicinal-products-containing-genetically-modified-cells-scientific-guideline (Accessed: 10 May 2025).

European Medicines Agency (2022) *ICH guideline M10 on bioanalytical method validation*. Available at: https://www.ema.europa.eu/en/documents/scientific-guideline/ich-guideline-m10-bioanalytical-method-validation-step-5_en.pdf

Evrony, G.D., Hinch, A.G. and Luo, C. (2021) ‘Applications of Single-Cell DNA Sequencing’. *Annual Review of Genomics and Human Genetics*, 22(1), pp. 171–197. DOI: 10.1146/annurev-genom-111320-090436.

FDA. (2024) *Human Gene Therapy Products Incorporating Human Genome Editing*. Available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/human-gene-therapy-products-incorporating-human-genome-editing (Accessed: 10 May 2025).

Gamlen, M. and Clapperton, G. (2010) ‘Quality Management Systems for Small Biopharmaceutical Organizations’. 23, pp. 40–45.

Gemble, S. *et al.* (2022) (7904) ‘Genetic Instability from a Single S Phase after Whole-Genome Duplication’. *Nature*, 604(7904), pp. 146–151. DOI: 10.1038/s41586-022-04578-4.

Ghelani, J.H. (2021) ‘(PDF) Advances in Lean Manufacturing: Improving Quality and Efficiency in Modern Production Systems’. *ResearchGate*, 9(6), pp. 611–625. DOI: 10.18535/ijsrm/v9i06.ec02.

Haigney, S. (2024) ‘Enhancing Quality Through Training’. 48(12), pp. 10–15.

HPRA. (2025) *Regulatory Guidance Documents | Medicines for Human Use*. *Guidance documents – medicines for human use*. Available at: https://www.hpra.ie/regulation/human-medicine/marketing-authorisation-holders/guidance-documents (Accessed: 10 May 2025).

Hyde. (2024) *Cell Line Development in Drug Discovery*. Available at: https://www.biocompare.com/Editorial-Articles/614252-Cell-Line-Development-in-Drug-Discovery/ (Accessed: 10 May 2025).

ICH. (2024) *ICH Official Web Site : ICH*. *Quality Guidelines*. Available at: https://www.ich.org/page/quality-guidelines (Accessed: 26 November 2024).

Lamanna, W.C. *et al.* (2018) ‘Maintaining Consistent Quality and Clinical Performance of Biopharmaceuticals’. *Expert Opinion on Biological Therapy*, 18(4), pp. 369–379. DOI: 10.1080/14712598.2018.1421169.

Larghero, J. and Textoris, J. (2024) *Collaborative Research and Quality Control Supports Cell & Gene Therapy Development & Manufacturing*. *bioMérieux Website*. Available at: https://www.biomerieux.com/corp/en/blog/pharmaceutical-qc/Collaborative_Research_Quality_Control_Cell_Gene_Therapy_Development_Manufacturing.html (Accessed: 11 May 2025).

Li, Z.-M. *et al.* (2022) ‘Factors Affecting the Expression of Recombinant Protein and Improvement Strategies in Chinese Hamster Ovary Cells’. *Frontiers in Bioengineering and Biotechnology*, 10, p. 880155. DOI: 10.3389/fbioe.2022.880155.

Machina, H.K. and Wild, D.J. (2013) ‘Electronic Laboratory Notebooks Progress and Challenges in Implementation’. *SLAS Technology*, 18(4), pp. 264–268. DOI: 10.1177/2211068213484471.

Manzano, T. and Whitford, W. (2024) *Artificial Intelligence in the Biopharmaceutical Industry*. Available at: https://www.bioprocessintl.com/information-technology/artificial-intelligence-in-the-biopharmaceutical-industry-treacherous-or-transformative- (Accessed: 11 May 2025).

Mirasol, F. (2025) ‘Accelerating Adoption of Smart Tools to Advance Manufacturing’. 49(2), pp. 10–13.

Mirasol, F. (2018) ‘Maintaining Cell Line Integrity’. *BioPharm International*, 31, pp. 10–15.

Naeem, M. *et al.* (2023) ‘A Step-by-Step Process of Thematic Analysis to Develop a Conceptual Model in Qualitative Research’. *International Journal of Qualitative Methods*, 22, p. 16094069231205789. DOI: 10.1177/16094069231205789.

Narayanan, T.N. *et al.* (2024) *(PDF) Digital Pharma: How Software Solutions Are Shaping the Pharmaceutical Industry*. *ResearchGate*. Available at: https://www.researchgate.net/publication/385554007_Digital_Pharma_How_Software_Solutions_are_Shaping_the_Pharmaceutical_Industry (Accessed: 11 May 2025).

O’Flaherty, R. *et al.* (2020) ‘Mammalian Cell Culture for Production of Recombinant Proteins: A Review of the Critical Steps in Their Biomanufacturing’. *Biotechnology Advances*, 43, p. 107552. DOI: 10.1016/j.biotechadv.2020.107552.

Playter, G. (2023) ‘The Logistics of Outsourcing Biologics’. 47(3), pp. 48–49.

Pluta, P. (2024) ‘Application of Validation Principles to the Training Quality System: Part 9, Quality Risk Management Hazard Identification’. 48(11), pp. 20–26.

Robertsone, G. and Markova, Z. (2023) ‘(PDF) Lean Implementation Benefits for the Pharmaceutical Company - From Project to Implementation’. *ResearchGate*, pp. 88–99. DOI: 10.7250/scee.2022.009.

Steiner, R. (2018) *Taking a Collaborative Approach to Continuous Pharmaceutical Manufacturing*. *European Pharmaceutical Review*. Available at: https://www.europeanpharmaceuticalreview.com/article/80580/collaborative-continuous-manufacturing/ (Accessed: 11 May 2025).

Thompson, P. (2023) ‘Bioprocessing Challenges and Solutions in Modern Drug Manufacturing’. *Pharmaceutical Bioprocessing*, 11(4), pp. 1–3. DOI: 10.37532/2048-9145.2023.11(4).74-76.

Tricht, E. van. (2025) *Quality Control in the (Bio)Pharmaceutical Industry: Safeguarding Medicines for Global Health*. *BioQC | Quality Experts*. Available at: https://bio-qc.com/quality-control-in-the-biopharmaceutical-industry-safeguarding-medicines-for-global-health/ (Accessed: 11 May 2025).

Weiser, W. (2020) ‘How an Integrated LIMS Platform Can Transform Drug Development and Manufacturing Workflows’. *European Pharmaceutical Review*, 25(5), pp. 43–46.

Zhang, H. *et al.* (2021) (1) ‘Application of the CRISPR/Cas9-Based Gene Editing Technique in Basic Research, Diagnosis, and Therapy of Cancer’. *Molecular Cancer*, 20(1), pp. 1–22. DOI: 10.1186/s12943-021-01431-6.

Zia, S. *et al.* (2024) ‘Emerging Technologies for Quality Control of Cell-Based, Advanced Therapy Medicinal Products’. *Journal of Pharmaceutical and Biomedical Analysis*, 246, p. 116182. DOI: 10.1016/j.jpba.2024.116182.

APPENDIX A

Ethics Application & Declaration Form

DISSERTATION TITLE:
Assessment of Quality Control Processes in Genetically Engineered Cell Lines in Ireland: An Impact on Biopharmaceutical Product Consistency.

RESEARCHER'S NAME: Jeamy Sera Johnson

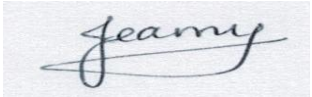
PROGRAMME OF STUDY: MSc. Pharmaceutical Business and Technology

SUPERVISOR'S NAME: Ganiru Priscilla Ugwu

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:



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

For Supervisor:

Yes ☐ No ☑

SUPERVISOR SIGNATURE:

For Ethics Committee (if required): Ethics Committee

Yes ☐ No ☐

ETHICS COMMITTEE MEMBER SIGNATURE:

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 objectives of research

Genetically engineered cell lines are the critical foundation for modern biopharmaceutical manufacturing, enabling the production of complex therapeutic proteins, monoclonal antibodies, and advanced biological treatments. Cell lines are established cell cultures that have uniform genetic make-up. These cultures proliferate indefinitely when adequate culture medium and space is available. Genetically engineering the genetic material of cell lines using biotechnological processes results in genetically engineered cell lines. They are indispensable tools in biomedical research, biotechnology, and therapeutic development. Ensuring the quality and authenticity of these cell lines is paramount, as inconsistencies can lead to irreproducible results and compromised data integrity. This necessitates robust quality control (QC) processes to maintain the reliability of experimental outcomes.

The rapid evolution of genetic engineering technologies necessitates continuous adaptation of quality control methodologies to maintain pace with scientific advancements. The biopharmaceutical industry faces increasing pressure from regulatory bodies to implement more sophisticated quality control mechanisms. Agencies like the Food and Drug Administration (FDA) and the European Medicines Agency (EMA) require increasingly detailed documentation and validation of genetic engineering processes, emphasizing the need for robust, reproducible quality control strategies.

The aim of this research is to examine how quality control processes in influence the consistency of biopharmaceutical products that are derived from genetically engineered cell lines, in Ireland, by identifying common challenges faced and possible improvement areas in the processes. This would help to develop insights into the processes, come up with innovative approaches and findings that could lead to industry-wide best practice recommendations for improving the QC processes of genetically engineered cell lines.

The objectives of this research are to:

- Evaluate the different QC processes and understand its influence in the product consistency of biopharmaceuticals derived from genetically engineered cell lines.
- Examine common challenges and areas of improvement in the QC processes.
- Identify potential innovative approaches for maintaining product consistency.
- Identify cost-effective QC processes that can be implemented, particularly in facilities of smaller production.
- Develop possible recommendations for industry-wide best practices to improve the QC processes of genetically engineered cell lines.

1.2 Research methodology:

A qualitative approach (interviews) will be employed for this research due to the need for a detailed understanding of how quality control processes are implemented and managed. In-depth interviews will allow participants to discuss their experiences in their own words, leading to a greater understanding of the factors influencing quality control in genetically engineered cell lines. This aligns with the study's objective to explore industry practices, challenges, and areas for enhancement rather than merely measuring predefined variables.

This study on quality control processes in genetically engineered cell lines will adopt an interpretivist

philosophy. The interpretivist paradigm acknowledges that research is affected by human perspectives and experiences, making it ideal for understanding the complex dynamics of quality control implementation and challenges. Since quality control processes involve human judgment, decision-making, and varied organizational contexts, this philosophical stance will enable a deeper understanding of how different facilities approach and maintain product consistency. This philosophy allows for a more flexible and open-ended investigation, enabling the researcher to uncover unexpected insights and adapt the research process as new information emerges. Interpretivism supports an inductive research approach, in which data is collected from industry experts to generate theories and develop insights about the quality control processes. This approach allows for the emergence of patterns and themes from the experts' experiences rather than testing predetermined hypotheses. This is particularly important in a field where regulatory standards, technological advancements, and quality control practices evolve dynamically.

Data will be collected through in-depth interviews of quality control related professionals in Ireland. The interview will consist of open-ended questions that will help to draw in-depth insights about the processes that influence product consistency and potential innovative approaches. They study participants will be contacted and selected through LinkedIn and personal connections the data obtained will be analysed thematically.

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

RESEARCH PROCEDURES

Does the research proposal involve:

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

PARTICIPANTS

Does the research proposal involve:

People who are not competent and/or fluent in English	Yes **No**
Does your research group include any of the following vulnerable groups *(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)*	Yes **No**

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 current study revolves around the influence of quality control (QC) processes in the consistency of biopharmaceutical products that are derived from genetically engineered cell lines. Therefore, the interviewees for the study will be professionals who hold positions in Irish biopharmaceutical companies, such as QC managers, analysts, quality assurance analysts, process development scientists, facility managers overseeing quality systems or regulatory affairs specialists. The interviewees will be selected from multiple organizations so there is uniform representation across the industry.

4.2 How do you plan to gain access to/contact/approach your participant(s).

The participants for this study will be approached or contacted through my professional network in LinkedIn and through personal connections. After initial contact, participants will be formally requested to take part in the study with the help of participant information leaflet and informed consent forms, and approved questions will be asked during the interview.

SECTION 5: INFORMATION, CONSENT AND CONFIDENTIALITY

5.1 Participant Information Letter

(PIL) for participants Please confirm

below that your information letter covers:

Description of the research topic and method	**Yes** No
Details of what participation will involve	**Yes** No
Rights to anonymity	**Yes** No

Confidentiality	**Yes** No
Rights to withdraw from the research	**Yes** No
The contact details of the researcher and supervisor (if necessary)	**Yes** No

5.2 Informed Consent Form (ICF) for participants

Please indicate below if your research requires a signed consent form by selecting the relevant option only:

Yes: my research requires signed consent and I have attached an ICF in the appendices of my application.
No: my research study involves an online survey only and/or does not require signed consent

---

SECTION 6: STORAGE OF DATA

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

All the data collected as part of this research will be stored in conformation with Data protection law and will abide by General Data Protection Regulation (GDPR). Signed consent forms and original audio recordings will be retained in password protected personal computer of the researcher and a copy of these will be stored in password protected cloud storage as backup until the exam boards confirms the results of their dissertation. A transcript of the interviews will be created for data analysis and stored like the recordings and a copy of these will be retained for a further two years after this. Only the researcher, supervisor and Griffith College staff will have access to the stored recordings and consent forms. The data submitted to college for review or future publication will be devoid of any identification of the participants and there will be no risk of confidentiality breach.

SECTION 7: NON-DISCLOSURE AGREEMENT & STUDENT CONSENT

7.1 Non-Disclosure Agreement (NDA)

Will the final dissertation contain any information pertaining to any source what would warrant the use of a Non-Disclosure Agreement (NDA) e.g. industry-based research?

Yes **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 No

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

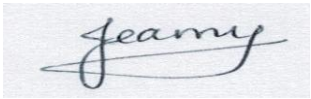
NOTE: Applicants must attach the following documents in electronic format to the appendix.

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

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

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

For Student:



SECTION 10: APPENDIX

APPENDIX B

GRIFFITH COLLEGE

Participant Information Letter

TITLE OF THE STUDY: Assessment of Quality Control Processes in Genetically Engineered Cell Lines in Ireland: An Impact on Biopharmaceutical Product Consistency.

I would like to invite you to take part in a research study. Before you decide you need to understand why the research is being done and what it would involve for you. Please take time to read the following information carefully. Ask questions if anything you read is not clear or if you would like more information. Take time to decide whether or not to take part.

WHO I AM AND WHAT THIS STUDY IS ABOUT

I am Jeamy Sera Johnson, a student pursuing MSc. Pharmaceutical Business and Technology at Griffith College, Dublin. I am doing this research as part of my dissertation module. On successful completion, I will be awarded the Master's degree. This study will examine how quality control processes influence the consistency of biopharmaceutical products that are derived from genetically engineered cell lines within Ireland. The aim is to identify the challenges faced during the processes and to come up with possible areas of improvement.

WHAT WOULD TAKING PART INVOLVE?

Participation in this study will involve giving an interview on an audio/video conferencing platform (Zoom) or a telephonic interview (whichever is preferable), to share thoughts and opinions on the quality control processes of genetically engineered cell lines and how it impacts product consistency. The interview will be recorded and transcribed later for data analysis in order to derive conclusions that will help achieve the study objectives.

WHY HAVE YOU BEEN INVITED TO TAKE PART?

You have been invited to take part in this study because of your work and functional role within the Irish biopharmaceutical industry. You were identified to be a potential study participant through LinkedIn.

DO YOU HAVE TO TAKE PART?

Please note:

- that participation in this study is voluntary;
- that a decision not to consent will have no adverse consequences;
- that consent can be withdrawn at any time during the research
- If you need to withdraw, please contact the researcher, Jeamy Sera Johnson, at +353 894673827 or email: jeamysera.johnson@student.griffith.ie

WHAT ARE THE POSSIBLE RISKS AND BENEFITS OF TAKING PART?

Please note that no personal benefit will be obtained by participating in this research. There is no risk/disadvantage to taking part in this study other than the time invested by the participant for the interview. However, it is possible that data obtained from the study will be published, in which case, the data published will be anonymised and confidentiality maintained.

WILL TAKING PART BE CONFIDENTIAL?

Confidentiality and anonymity of all participants that take part in this study will be maintained during and after the research. Any personal data that is irrelevant to the research objectives will not be collected during the interview. Non- anonymised data like interview recordings and signed consent forms will be stored in a password protected personal computer and cloud storage of the researcher. Only the researcher, supervisor and Griffith College staff will have access to the stored recordings and consent forms. Confidentiality may have to be broken if there is a serious risk of harm or danger to either the participant or another individual or if a serious crime has been committed.

HOW WILL INFORMATION YOU PROVIDE BE STORED AND PROTECTED?

Signed consent forms and original audio recordings will be retained in password protected personal computer of the researcher and a copy of these will be stored in cloud storage securely as backup until after my degree has been conferred. The stored data will be accessible only to the researcher, supervisor and Griffith College staff. A transcript copy of the interviews in which all identifying information has been removed will be retained for a further two years after this. Under freedom of information legalisation, you are entitled to access the information you have provided at any time.

WHAT WILL HAPPEN TO THE RESULTS OF THE STUDY?

The study results will be submitted to the college for review as part of completing this master's course. All content submitted as part of the dissertation will be made accessible in the college library and could also be potentially published in online e-journals or repositories.

WHO SHOULD YOU CONTACT FOR FURTHER INFORMATION?

Jeamy Sera Johnson (Dissertation Researcher)

Phone: +353 894673827 Email: jeamysera.johnson@student.griffith.ie

[THANK YOU]

APPENDIX C

Consent to take part in research

TITLE OF THE STUDY: Assessment of Quality Control Processes in Genetically Engineered Cell Lines in Ireland: An Impact on Biopharmaceutical Product Consistency.

The researcher retains one copy signed by both themselves and the participant. The participant should also receive a copy of consent form as a record of what they have signed up to.

- I _____ voluntarily agree to participate in this research study.
- I understand that even if I agree to participate now, I can withdraw at any time or refuse to answer any question without any consequences of any kind.
- I understand that I can withdraw permission to use data from my interview within two weeks after the interview, in which case the material will be deleted.
- I have had the purpose and nature of the study explained to me in writing and I have had the opportunity to ask questions about the study.
- I understand that participation involves attending a 20–30 minute interview on an audio/video platform and sharing my thoughts and opinions on the quality control processes of genetically engineered cell lines and how it impacts product consistency.
- I understand that I will not benefit directly from participating in this research.
- I understand that all information I provide for this study will be treated confidentially.
- I understand that in any report on the results of this research my identity will remain anonymous. This will be done by changing my name and disguising any details of my interview which may reveal my identity or the identity of people I speak about.
- I agree to my interview being audio-recorded.
- I understand that disguised extracts from this interview may be quoted in an MSc. dissertation and potentially published papers.
- If data is coming from within one company or specifically pertaining to the one company. I understand that I will adhere to all of the codes of conduct and employee confidentiality for the said company and there is no expectation to breach these by partaking in this research.
- I understand that if I inform the researcher that myself or someone else is at risk of harm, they may have to report this to the relevant authorities - they will discuss this with me first but may be required to report with or without my permission.
- I understand that signed consent forms and original audio recordings will be retained in password protected personal computer of the researcher and a copy of these will be

stored in password protected cloud storage as backup until the exam boards confirms the results of their dissertation. Only the researcher, supervisor and Griffith College staff will have access to the stored recordings and consent forms.

- I understand that a transcript of my interview in which all identifying information has been removed will be retained for two years from the date of the exam board.
- I understand that under freedom of information legalisation I am entitled to access the information I have provided at any time while it is in storage as specified above.
- I understand that I am free to contact any of the people involved in the research to seek further clarification and information.

Researcher Details

Name	: Jeamy Sera Johnson
Degree Programme	: MSc. Pharmaceutical Business and Technology
College Details	: Griffith College, Dublin 8, Ireland
Contact number	: +353 894673827
Contact mail	: jeamysera.johnson@student.griffith.ie

Signature of participant [Full Name – Printed]

Signature of research participant

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Date

Signature of researcher

I believe the participant is giving informed consent to participate in this study

---------- ----------

Date

Signature of researcher

APPENDIX D

Questionnaire 1 for interviews

TITLE OF THE STUDY: Assessment of Quality Control Processes in Genetically Engineered Cell Lines in Ireland: An Impact on Biopharmaceutical Product Consistency.

Objective 1: Evaluating Different QC Processes and Understanding Their Influence on Product Consistency

1. Can you describe the quality control processes currently in place for genetically engineered cell lines in your facility?
2. How do these QC processes influence the consistency of biopharmaceutical products derived from these cell lines?
3. What specific analytical techniques do you use to monitor the quality of genetically engineered cell lines, and how do they contribute to product consistency?

Objective 2: Examining Common Challenges and Areas for Improvement

4. What challenges do you face in implementing and maintaining quality control processes for genetically engineered cell lines?
5. Are there any areas where you believe improvements could be made in the current QC processes?
6. How has your QC approach evolved over time, and what prompted these changes?
7. How do you manage genetic instability and variability in protein expression in genetically engineered cell lines?

Objective 3: Identifying Potential Innovative Approaches for Maintaining Product Consistency

8. Are you aware of any innovative QC techniques or technologies that could enhance the consistency of biopharmaceutical products?
9. How do you see the role of advanced analytical techniques like single-cell sequencing and omics technologies in improving QC processes?
10. What is your experience with the use of digital tools and AI in QC processes?
11. Can you describe a specific instance where QC processes prevented a significant deviation in product quality?

Objective 4: Identifying Cost-Effective QC Processes for Smaller Production Facilities

12. How do you balance the need for robust QC processes with the financial constraints of smaller production facilities?
13. What cost-effective QC alternatives do you think could be beneficial for smaller production facilities?
14. How can regulatory compliance be ensured while managing limited resources? In such cases how do you think QC processes should be changed for improving product consistency?

Objective 5: Developing Recommendations for Industry-Wide Best Practices

15. Are there any specific challenges or considerations unique to the Irish biopharmaceutical industry (when compared to other markets) that affect QC processes and product consistency?
16. What role do you think industry-wide collaboration and standardization could play in improving QC processes?
17. How do you stay updated with evolving regulatory requirements and technological advancements in QC?
18. What do you believe should be industry-wide best practices for QC processes that have not yet been widely adopted?

Questionnaire 2 for interviews

TITLE OF THE STUDY: Assessment of Quality Control Processes in Genetically Engineered Cell Lines in Ireland: An Impact on Biopharmaceutical Product Consistency.

Objective 1: Evaluating Different QC Processes and Understanding Their Influence on Product Consistency

1. What is your understanding of the quality control processes involved in the production of biopharmaceutical products?
2. How do you perceive the influence of QC processes on the consistency and efficacy of biopharmaceutical products?
3. Which QC parameters are most critical for ensuring biopharmaceutical product consistency?

Objective 2: Examining Common Challenges and Areas for Improvement

4. What challenges do you think might exist in the QC processes for biopharmaceutical products?
5. Are there any areas where you believe improvements could be made in the QC processes, based on your observations?
6. How do you think QC processes have evolved over time, and what prompted these changes?
7. How do you think variability in the quality of different batches of biopharmaceutical products can be managed?

Objective 3: Identifying Potential Innovative Approaches for Maintaining Product Consistency

8. Are you aware of any innovative QC techniques or technologies that could enhance the consistency of biopharmaceutical products?
9. How do you see the potential role of analytical techniques like single-cell sequencing and omics technologies in improving QC processes?
10. What is your experience with the use of digital tools and AI in QC processes, if any?
11. Can you describe a specific instance where QC processes prevented a significant deviation in product quality?

Objective 4: Identifying Cost-Effective QC Processes for Smaller Production Facilities

12. How do you think smaller production facilities can balance the need for robust QC processes with financial constraints?

13. What cost-effective QC alternatives do you think could be beneficial for smaller production facilities?
14. How can regulatory compliance be ensured while managing limited resources? In such cases how do you think QC processes should be changed for improving product consistency?

Objective 5: Developing Recommendations for Industry-Wide Best Practices

15. Are there any specific challenges or considerations unique to the Irish biopharmaceutical industry (when compared to other markets) that affect QC processes and product consistency?
16. What role do you think industry-wide collaboration and standardization could play in improving QC processes?
17. How do you stay updated with evolving regulatory requirements and technological advancements in QC?
18. What do you believe should be industry-wide best practices for QC processes that have not yet been widely adopted?