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TITLE OF DISSERTATION

BIOSIMILARS OF ADALIMUMAB IN EU: ADDRESSING REGULATORY BARRIERS AND MARKET DYNAMICS TO ENHANCE ACCESSIBILITY AND AFFORDABILITY

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

Griffith College Dublin

Dissertation Supervisor: **Alessandra Vecchi**

Student Name: Manjusha Shajimon

Date of submission: 24/08/2025

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Candidate Declaration

Candidate Name: Manjusha Shajimon

I certify that the dissertation entitled "**BIOSIMILARS OF ADALIMUMAB IN EU: ADDRESSING REGULATORY BARRIERS AND MARKET DYNAMICS TO ENHANCE ACCESSIBILITY AND AFFORDABILITY"** submitted for the degree of: **MSc in Pharmaceutical Business and Technology** is the result of the my own work and that where reference is made to the work of others, due acknowledgment is given.

Candidate signature: 

Date: 24/08/2025

Supervisor Name: Alessandra Vecchi

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Date: 24/08/2025

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Abstract

The research examined regulatory obstacles together with market dynamics which affect EU adalimumab biosimilars adoption to enhance their market availability and economic value. The research examined regulatory variations together with market elements and pricing systems and stakeholder perspectives to create evidence-based solutions. A quantitative survey method served as the research methodology to gather data from healthcare professionals and policymakers and patient representatives across multiple EU member states. SPSS analysis of data included descriptive statistics as well as correlation and regression techniques.

The European Medicines Agency (EMA) centralised approval did not eliminate significant regulatory fragmentation. National policies regarding substitution practices together with reimbursement systems and procurement procedures determine how much biosimilar market adoption will take place. Germany and France showed high biosimilar adoption because their substitution and reimbursement policies were supportive yet Italy and Spain and Bulgaria showed slow adoption because their policies were restrictive and procurement systems were limited. The market dynamics played a significant role in biosimilar adoption because both transparent competitive tendering and originator companies' aggressive discounting and single-supplier contracts affected market competition.

Stakeholder opinions regarding biosimilars were influenced by knowledge deficits alongside safety concerns and patient unwillingness to transition from original products. The substitution policy and sustainable pricing strategies emerged as the leading determinants of EU policy harmonisation support according to the correlation analysis. The regression analysis showed that regulatory and market and stakeholder-related factors explain 28.1% of the variance in support for harmonisation indicating multiple barriers to adoption exist.

The study demonstrates that EU-wide standardised substitution and reimbursement systems combined with clear procurement methods and targeted educational initiatives for stakeholders will drive biosimilar acceptance by promoting trust and comprehension. The study advises that policy alignment should be supported while long-term multi-supplier contracts should be established and savings from cost reduction should fund

patient care and structured switching protocols with effective communication should be created.

The economic and accessibility benefits of EU adalimumab biosimilars depend on solving fragmented regulations and market inefficiencies. The EU will create a sustainable biosimilar market with universal access through unified policy reforms combined with stakeholder education and member state cooperation. The proposed method would reduce healthcare costs while extending access to treatment for patients suffering from chronic inflammatory conditions.

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1 Introduction

1.1 Overview

The first chapter presents a survey of the empirical literature on investigating the post-patent expiration uptake of the adalimumab biosimilars in the European Union. It defines the wider scope of the arrival of biosimilars into the market and describes the effects of regulatory guidelines and market situation on both the availability and the cost of biosimilars. The purpose, objectives and research questions are mentioned, and it is realised that there should be a study on the inconsistency of regulations, market barriers, and opinions of stakeholders. The importance of the study to the public health systems and policy actors is also highlighted, and the outline of the structure of the dissertation is briefly presented, thus establishing a base for the following chapters.

1.2 Research Purpose

One such monoclonal antibody is Adalimumab (also known as Humira in the rest of the world) that has completely changed the paradigm of tackling chronic inflammatory conditions like rheumatoid arthritis, Crohn's disease, and psoriasis.

Its clinical and commercial achievement is factored in by the net worldwide sales coming in at about $14.4 billion in 2023, making Humira the top-selling biologic product over a succession of years (Global Data Healthcare, 2024). The loss of Humira (of its main patent) in the European Union, October 2018, set the stage for to put of biosimilar competitors into place occurrence. It has far-ranging repercussions on the access of patients, healthcare expenditure and the pharmaceutical marketplace (SECURITIES and EXCHANGE COMMISSION, 2023).

However, the adoption of adalimumab biosimilars has proved to differ significantly in Europe. Some countries have market shares as high as more than 90% whereas some have it less than 30% (Moorkens *et al.*, 2021). A comparative study conducted in 2023 concluded that the initial entrant of a biosimilar product typically captured a minimum of two times the market shares relative to successive biosimilars. In addition, in countries where biosimilar policies are aggressive, price-cutting by the originator can limit penetration by discouraging further competition (Wilsdon *et al.*, 2021). In Germany and the United Kingdom, penetration has been strong, but in Italy and Spain, stronger regulatory effects and market obstacles have produced a more moderate level of uptake.

European regulatory system of actions with biosimilar has been harmonised and fragmented at once. EMA operates a centralised scientific appraisal and approval procedure and hence ensures efficacy, safety and stringent standards of quality of biosimilars (European Medicines Agency, 2024). However, policy relating to substitution and reimbursement is left to national governments, and this has led to a rather patchwork policy. In some countries, substitution is permitted or even encouraged (e.g., France and Germany), whereas that is not the case in others (Spain and Italy) or in the process of substitution (Medicines for Europe, 2024). This may require prescriber authorisation (and this can often be a requirement upon reimbursement of the new drug). Such regulatory differences have a direct impact on market access and penetration. Those nations with transparent and supportive substitution and switching measures are more likely to demonstrate greater biosimilar usage, but confusing or conservative national regulations may stifle market take-up and inhibit cost savings.

Procurement mechanisms also influence market access. In most of the EU countries, hospital and regional tenders are set that determine which goods to offer at what price (Leopold et al., 2020). Although competitive tendering can drive prices downwards, it also prompts the opportunity of causing market distortions, especially when the contract is given to a single supplier, or when short-term cost saving is placed ahead of the long-term existence of a market. Research reveals that the practice of aggressive discounting by the originator (Humira) in certain markets has resulted in the exclusion of biosimilar in tenders, thus limiting competition and innovation. The 2024 analysis of the biosimilar trends in Europe documented an average of 9.10, 9.30 per cent reduction in the volume-weighted average price per defined daily dose (DDD) on the entry of the biosimilars of TNF-alpha inhibitors, which also includes adalimumab (Car *et al.*, 2023a). However, this does not necessarily translate into higher rates of biosimilar use, especially in places where other more restrictive practices are in place about procurement or involvement of the various stakeholders.

According to Marín-Jiménez et al. (2021), just 55% said they were very confident in prescribing biosimilars, and confidence was closely related to national educational efforts and clarity of regulations. Uptake of course is further stunted by patient disinclination to switch, especially among those established on Humira making sensible education and clear conversation all the more necessary. The iatrogenic usage of adalimumab biosimilars has huge economic repercussions. Although research indicates that the

potential biosimilar competition can save countries a vast amount of money as more than 1.5 billion euros on an annual basis throughout the EU countries with regulatory or market impediments do not enjoy the advantage of such savings (IQVIA, 2022). In addition, low penetration of biosimilars has the potential to continue existing access disparities so that not all patients have the opportunity to use cheaper substitutes.

Since, the clinical and economic effects of adalimumab can hardly be doubted, an extensive exploration of barriers to the adoption of biosimilars is of paramount importance. The current study fills some of the most crucial knowledge gaps as well by determining how regulatory frameworks and market dynamics interact in European contexts, as well as how they are perceived by stakeholders. The research provides recommendations that policymakers, regulators, and healthcare providers can take to improve the affordability and accessibility of adalimumab biosimilars, incorporating the most recent statistical evidence and policy analysis. Finally, the work is aimed at voicing a more patient-centred, sustainable and equitable biosimilar market in Europe.

1.3 Significance of the Study

This research is of great importance since it aims to fill critical gaps when it comes to adopting adalimumab biosimilars and their use within the European Union. The examination process contemplates a strategic examination of the regulatory impediments, market forces, and stakeholder opinions to lay down guidelines that can perpetuate evidence-based policies to increase the accessibility and affordability of these life-saving treatments. It is crucial to examine contemporary biosimilars uptake inequalities to reduce long-term sustainability challenges in healthcare systems, as rising healthcare costs and less access to healthcare services are the primary concerns in the state of healthcare.

In addition, the study results can help managed-care organisations and policymakers to be more efficient in allocating their resources and, thus, treat more patients and ensure more equal health outcomes. The potential significance of this study lies in the fact that it can help to uncover the major barriers which are in the way of adalimumab biosimilars uptake in the European Union. Therefore, provide empirical evidence against which the future policies should be built in the framework of patient access improvement, cost-effectiveness, and health care sustainability protection.

1.4 Research Objective

Aim

To analyse the regulatory barriers and market dynamics of biosimilars of Adalimumab in the EU to enhance their accessibility and affordability.

Objectives

- To discuss regulatory discrepancies in the approval and implementation of adalimumab biosimilar in the EU member states.
- To evaluate the pricing and market factors impacting the adoption of adalimumab biosimilar in the chosen EU states.
- To assess the attitude of healthcare providers and patients on the safety and efficacy of adalimumab biosimilar.
- To formulate evidence-based solutions that can enhance the biosimilar adalimumab accessibility and affordability in the EU.

Questions

- What are the regulatory discrepancies in the approval and implementation of adalimumab biosimilar in the EU member states?
- How do the pricing and market factors impact the adoption of adalimumab biosimilar in the chosen EU states?
- What is the attitude of healthcare providers and patients on the safety and efficacy of adalimumab biosimilar?
- What can be the evidence-based solutions that can enhance the biosimilar adalimumab accessibility and affordability in the EU?

1.5 Structure of the Study

In this dissertation, there are five key chapters that are organised to ensure clarity and logical flow. In Chapter 1, the study is placed into context and the aims of the research are identified, and the importance of the study described. The literature about the regulatory and market dynamics of biosimilars of adalimumab in Europe is a source of

critical review in chapter 2. In Chapter 3, the research methodology is mentioned, which identifies the data collection and data analysis plans. In Chapter 4 findings are presented and discussed in terms of the research questions. Chapter 5 ends in noting key insights, recommendations, and scopes of research. This chapter wraps up the research work by drawing a conclusion based on major points, recommendations and policy and practice implications.

2 Literature Review

2.1 Overview

The current chapter involves a critical literature review of the present studies conducted on the adoption of adalimumab biosimilars in the European Union. It is a consideration of the dynamism between regulatory, market, stakeholder and economic factors. It explores in detail the effect of regulatory gaps and incomplete access to the market, barriers to procurement and the mentality of stakeholders on the uptake as well as the sustainability of biosimilars. The review will offer a theoretical approach to addressing the barriers and enablers of biosimilar intake using the Diffusion of Innovations and Institutional Theory. The synthesis reveals research gaps to be filled by reporting the results of several studies and providing a highlight of the knowledge gap that still exists in the field. Finally, important challenges and opportunities associated with improving the accessibility and affordability of adalimumab biosimilars are presented to establish the framework for the onset of further analysis. Hence, this chapter provides evidence of the creation of evidence-based methods to enhance patient outcomes to improve the efficiency of the health system in such an environment as the EU.

2.2 Definitions of Key-terms

Biosimilar: A biological medicine, which has no clinically meaningful differences regarding safety, purity, and potency with an already approved reference biologic (originator), is called a biosimilar (Poquet-Jornet et al., 2024).

Biopharmaceuticals: Avoidance of the risk of therapeutic equivalence is what makes biosimilars undergo tough comparability investigations to show reliability in quality, efficiency, and safety to their reference medicines (Barbier et al., 2021).

Adalimumab: Adalimumab is a monoclonal antibody also known as a tumour necrosis factor-alpha (TNF-alpha) inhibitor, which is marketed under the name Humira. It is used in many chronic inflammatory disorders such as rheumatoid arthritis, psoriatic arthritis, Crohn's disease, ulcerative colitis and plaque psoriasis (Clarke et al., 2024).

European Medicines Agency (EMA): EMA is the European Medicines Agency, whose role is to facilitate scientific evaluation, oversight, and safety surveillance of medicines

in the UK (Mascarenhas-Melo et al., (2024). It reviews the centralised procedure of approval of biosimilars, which is of their quality, safety, and efficacy at the EU level.

Regulatory Barriers: Regulatory barriers are those barriers caused by regulatory differences between the countries and between the EU and the country of origin, i.e., approval procedures, substitutability and reimbursement rules (Bas and Duarte, 2024). Such obstacles are able to impede the uniform utilisation and availability of biosimilars in the EU member states.

Market Dynamics: Market dynamics refer to the economic and competitive activities that govern the entry, pricing, adoption and sustainability of biosimilars within the healthcare market (Wilsdon et al., 2022). This comprises the arrangements of procurement, tendering and rivalry among the suppliers.

Accessibility: Accessibility refers to how easily patients and health professionals can access biosimilars as a result of regulatory processes, market access, costs/prices, and channels of distribution (Clarke et al., 2024).

Affordability: Affordability can be described as the cost-effective value of biosimilars on patients and healthcare systems as monitored by the pricing strategies, reimbursement policy, and the level of cost reduction of originator biologics (Clarke et al., 2024).

Reimbursement Policy: Reimbursement policy determines the extent and the manner in which the healthcare payers (public or private) will cover the cost of biosimilars. Such policies affect both market accessibility and accessibility of biosimilars (Edgar et al., 2021).

2.3 Discussing Regulatory Discrepancies in Biosimilar Approval and Implementation of adalimumab biosimilar in the EU member states

Existing literature on the subject of regulatory discrepancies and fragmentation in the approval and implementation of biosimilar products substantiates the continuing presence of structural and procedural obstacles at both global and European levels. Cordeiro et al. (2024) propose a critical comparative assessment of the regulations on biosimilars and develop the idea that, despite the numerous standards released by the European Medicines Agency (EMA). It makes differences persist and affect the ways of judging and approving biosimilars of different regions and even within the European Union. Compared to

generics, biosimilars require complex investigations due to their biotechnological nature, lack of harmonised scientific and regulatory standards has led to delayed and uneven approval mechanisms and schedules. This fragmentation is further compounded by the co-existence of EMA-centralised authorisation and national determination with regard to substitution and reimbursement, leading to a patchwork-like access and rate of adoption in the market.

Mascarenhas-Melo et al. (2024) confirm that the EMA developed an effective scientific system of biosimilar approval, but their implementation at the level of the nation remains uneven, especially in terms of interchangeability, pharmacovigilance, and post-marketing requirements. The authors can argue that discrepancies will undermine the confidence of prescribers and patients in its application in the country, and this will result in poor uptake. They also indicate that very different nomenclature and labelling systems in different countries pose further regulatory challenges, which make distribution across countries and pharmacovigilance more difficult. Niazi (2022), in turn, tends toward a more negative position, arguing that the absence of harmonisation in the guidelines on the approval of biosimilars on the global level leads to further inefficiency and redundancy. The author describes the International Council for Harmonisation (ICH) as a step in the right direction, but it is nonetheless not enough to achieve a harmonised approach. Since ICH guidance deals with technical questions, not a process of approvals and a body of post-approval requirements.

Country	Centralised EMA Approval	National Substitution Policy	Reimbursement Policy	Market Access Level
Germany	Yes	Permitted	Supportive	High
France	Yes	Permitted	Supportive	High
Italy	Yes	Restricted	Variable	Moderate
Spain	Yes	Restricted	Variable	Moderate

Country	Centralised EMA Approval	National Substitution Policy	Reimbursement Policy	Market Access Level
Bulgaria	Yes	Restricted	Limited	Low

Table 2.1: Comparative Regulatory Frameworks in Selected EU Countries

Gherghescu and Delgado-Charro (2021) provide a case of regulatory fragmentation using empirical evidence through the comparison of EMA and Food and Drug Administration (FDA) approval routes. Their analysis shows that, in spite of the fact that the biosimilar market in the EU has been growing at a faster pace than its equivalent in the USA. Both markets are defined by the exclusivity period and patent fields on the one hand and the dissimilar regulatory demands on the other. Bas and Duarte (2024) extend the discussion by comparing high-income countries and low- and middle-income ones and underline the point that discrepancies in regulation are even more significant on the international scale. The lack of international agreement on biosimilar standards and diverse regulatory capabilities leads to an imbalance in quality, safety, and effectiveness standards across international boundaries. Hence, based on the literature, it is analysed that the recent advancement in biotechnology and the implementation of artificial intelligence in regulatory science threaten to further increase such gaps unless there is harmonisation of the structures.

2.4 Market Factors and Pricing Strategies Affecting Biosimilar Adoption

In light of a critical and comparative literature review of the strategic approach to pricing and market forces concerning the adoption of biosimilars, one can observe the trend of both improvement and resistance towards structural barriers in both European and world areas. Tachkov et al. (2021) provide the Bulgarian experience that proves that biosimilar entry is associated with impressive price decreases in biologic DMARDs prices. In Bulgaria, the prices decreased by up to 48%. Nevertheless, the changes affecting utilisation are quite subtle: the number of defined daily dose (DDD) utilisation increased, alongside only half of the authorised biosimilars in Europe being reimbursed at the national level, which leads to low market penetration. It indicates that the best adoption of biosimilars is not guaranteed with price cutting but through the regulation of reimbursement policies, as well as market access bottlenecks on a national level. The

Bulgarian case represents a Central and Eastern Europe, as the related technological complex is included in Central Europe by regulations and limitations put on their procurement.

Moorkens et al. (2021) show a considerable regional difference in the market shares of biosimilars against infliximab and etanercept. On other hand, Alsaif and Blumer (2025) present the UK viewpoint in the prism of insulin glargine biosimilars, demonstrating that with new biosimilars, the price of the original product diminished significantly. Biosimilar market shares of over 80% in one market, in other regions, the share never passed the figure of 25%. This figure exists even though both regions had similar frameworks of pricing and reimbursement of biologics on a national level. The authors explain such differences using the regional procurement strategies, local stakeholder involvement, and the point in time at which biosimilar adoption is reached. However, the price reduction was geographically and the number of biosimilars was usually small. Their results coincide with those of Tachkov et al. (2021) because the price decreased, but it was not enough; the utilisation and market share are still low without active policy intervention and expanding reimbursement. The UK experience also teaches the key of open pricing and competitive tendering, which, when not present, dulls the blow of biosimilar competition.

Bas (2025) focuses attention on the innovational formulation of the strategies and intellectual property (IP) issues, stating that a growing number of market dynamics happen due to non-price factors. Delivery systems and devices can both offer competitive differentiation through the use of buffer-free formulations (which may create new IP barriers, as well as prolong exclusivity periods). This is because this relationship makes it slow to enter with biosimilars and diminishes the size of price warfare, which weakens cost savings. The analysis provided by Bas (2025) identifies an essential dilemma: innovation could not only enhance safety and patient experience but also act as a strategic device of the originator firms to preserve their position in the market and control the price.

Wilsdon et al. (2021) state that additional price reductions are not enough to achieve sustainable biosimilar markets. This study reveals potential threats to the viability of the market, including price fluctuations, misaligned provider incentives that may incentivise originator products at the expense of biosimilars. The report proposes long-term contracts, a minimum volume of purchase and transparent prices as solutions to stabilise

the market and keep competition going. Therefore, these list of studies shows that the proposed effective pricing strategies should exist within a larger policy to consider procurement, reimbursement, innovation, and stakeholder alignment to make biosimilar adoption sustainable and generate the maximum savings for the health system.

2.5 Attitudes Healthcare Providers and Patients on Adoption Barriers on Adalimumab Biosimilar

The systematic and comparative analysis of the stakeholder attitudes and adoption barriers to adalimumab biosimilars has shown a sophisticated interdependence of the knowledge gaps, lack of trust, policy gaps, and the influence of professional networks and patient networks. Rieger et al. (2024) substantively divide barriers and facilitators into three categories, namely healthcare professional (HCP), patient, and systemic, using which they evidence that the lack of policy, financial incentives, and information are the main impediments to implementation. The knowledge gap presents the most important challenge to practitioners; safety and efficacy can be cited as the main concerns of patients. Patients have limited influence as compared to clinical providers as well as systemic actors, who are most likely to be guided by information given by clinicians.

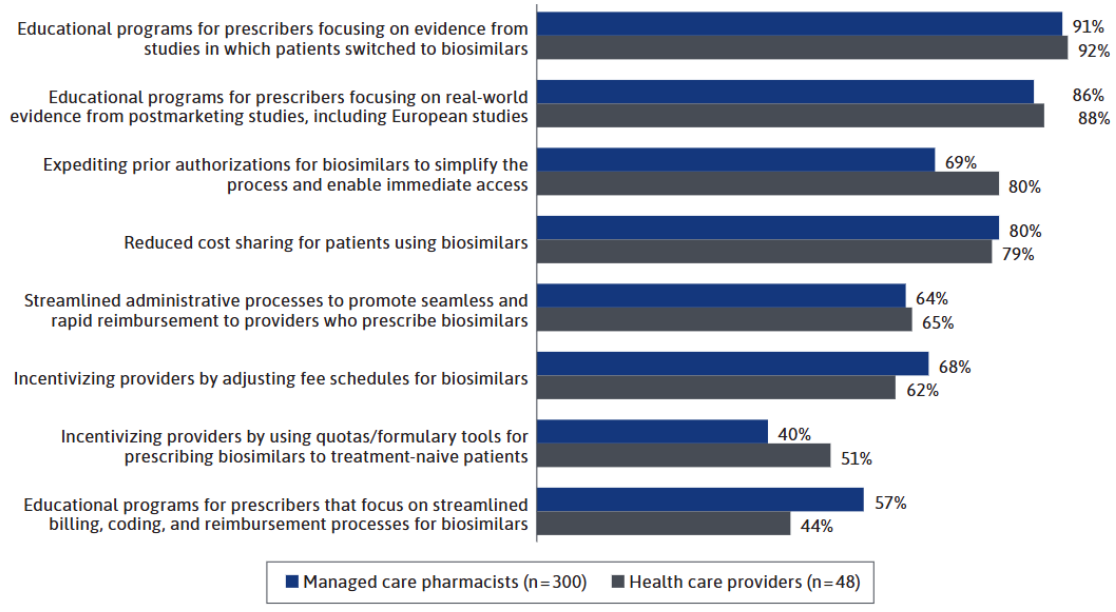

Figure 2.1: Payer and Provider Perceptions of the Likelihood That Designated Strategies Can Overcome Barriers to Biosimilar Adoption

(Source: Edgar et al., 2021)

In line with these findings, two publications by Barbier et al. (2021) outline the low to moderate awareness and trust rates of European HCPs and patients towards biosimilars. It continues to demonstrate misconceptions about the similarity of biosimilars to their originators. Confidence is further undermined through misinformation, promote in many cases by the manufacturers who are the initiators. Their data suggest that multi-level and wide-reaching educational systems are more effective than campaigns used in isolation. Oskouei and Kusmierczyk (2021) and Edgar et al. (2021) emphasise education as the most significant determinant of biosimilar uptake in HCPs. However, the existing education is disunified, and, in most cases, it does not cope with the practice of prescribing, pharmacovigilance, and switching. Edgar et al. (2021) also show that payer-provider collaboration through concerted efforts can bend the curve of prescribing, provided they are, in turn, complemented by intensive and comprehensive educational approaches ***[refer to figure 2.1]***.

According to patient opinion, as explained by Vandenplas et al. (2021), the knowledge gap is heavily pronounced, with most patients ignorant of biosimilars or having a false idea that they are clinically less effective than originators. Even in those who are familiar with the science of biosimilars, the knowledge is superficial and is often channelled through physicians or patient associations. The fact that patient attitudes are strongly reliant on the quality and consistency of the information provided demonstrates that poor education and health literacy may hamper the adoption of the biosimilar. It is also observed in the Belgian scenario, where biosimilar availability has not led to the actual uptake.

Factor	Barrier	Enabler
Regulatory	Fragmented national policies	Harmonised EMA guidelines
Market	Aggressive originator discounting	Transparent tendering

Factor	Barrier	Enabler
Stakeholder Attitudes	Knowledge gaps, mistrust	Targeted education
Procurement	Single-supplier contracts	Multi-supplier, long-term contracts
Patient Perception	Fear of switching	Clear communication

Table 2.2: Key Barriers and Enablers for Adalimumab Biosimilar Uptake

Krstic et al. (2022) also note that in Western Switzerland, the competence and readiness to prescribe biosimilars among experts differ significantly; most of them feel reluctant. This is based on the lack of clinical experience and the fear of having their products accepted by patients. Such results highlight variations in provider attitudes as well as the context, experience and institutional support. Overall, current literature points to the fact that the stakeholder attitude to adalimumab biosimilars is informed by a complex interaction of knowledge, trust, policy, and network processes. The most powerful intervention is education, which is targeted, practical, and multi-stakeholder in nature, but it should be accompanied by effective policies, strong real-world evidence, and direct anti-misinformation measures. Unless there are collective endeavours to take up the concerns of clinicians and patients, these adoption obstacles will limit the health system and patient benefits related to biosimilar competition.

2.6 Evidence-Based Solutions to Enhance Accessibility and Affordability on Adalimumab Biosimilar

These are the recommendations for action shown in the critical and comparative evidence-based strategy evaluation to improve the access and affordability of adalimumab biosimilars. These are mentioned through extensive collaborative effort at both broad and specific levels of policy and practice. In a large range of healthcare regimes, the literature continues to show that given an adequate level of market penetration, complementary policy provision, and stakeholder involvement, the market

entry of biosimilars in the adalimumab market. It leads to tremendous financial savings as well as improved market access for the patients.

The derivation of Woo et al. (2024) findings is solid cross-country evidence of the idea that the introduction of adalimumab biosimilars in high- and upper-middle-income economies. It results in a significant cost reduction of adalimumab, as a whole, without reducing patient consumption. The difference-in-difference conducted by them indicates that the countries that embraced biosimilars recorded a 14% reduction in spending, primarily due to price competition and drug-mix impacts (Woo et al., 2024). The comparison countries that opted not to adopt biosimilars recorded an increase in spending due to higher utilisation. Those findings are supported by Clarke et al. (2024), who developed a model to estimate the potential for cost reduction and attracting additional patients in key European markets. Their findings prove that a complete switch to biosimilars of adalimumab might bring savings in Germany up to 187 million euros, and thousands of new patients could be treated.

As stated in Kvien, Patel and Strand (2022) and Zhai, Sarpatwari and Kesselheim (2021), cost savings are not an absolute indicator of improved access and long-term affordability. Kvien, Patel and Strand (2022), suggest that even realised savings cannot be used to cover additional patients and eliminate access obstacles due to financial means. Zhai, Sarpatwari and Kesselheim (2021) mention that the experience of the US market shows that, despite the approval of biosimilars, access gaps persist. It takes time to spread out and avoid the traps of rebates, and formularies inhibit access to the market. The literature demands clear policy requirements not only to channel savings into patient reach but also to enforce changes in regulatory structures to abolish perverse incentives that give an advantage to the originator products. The change-in and how-in the policies are another serious area of interest.

Tesser, Charabaty and Hebert (2025) review of the real-life switching data provides a conclusion that the originator-to-biosimilar adalimumab switching is possible to be administered whether as mandatory or incentivised, but only in case of effective monitoring of loss of efficacy and adverse events. Notably, they point out that subjective factors, including patient perceptions, device usability, and communication, can contribute to and affect the success of switching programs. The safety and efficacy of adalimumab biosimilars when used in treating inflammatory bowel disease are further

supported by Poquet-Jornet et al. (2024), which strengthens the prospect of population-wide use. The suggested targeted education appears to be a key factor that has the potential to facilitate the adoption of biosimilars.

Leonard et al. (2021) and Donnelly and Paek (2020) highlight the presence of knowledge and trust gaps among healthcare professionals that continue to necessitate management. Leonard et al. (2021) prove that education developed and directed by clinicians, on the topics of immunogenicity, interchangeability, and real-world evidence, is strictly linked to biosimilar prescriptive growth. According to Donnelly and Paek (2020), it is the necessity of convenient tools, peer support, and transparent communication that helps to eradicate inertia and scepticism within clinical practice. Williamson et al. (2020) apply the same argument to oncology, where multidisciplinary education and the inclusion of biosimilar guidance in clinical pathways and electronic health records are proposed. However, both studies note that it is necessary to implement a system of structured switching protocols, patient education, and pharmacovigilance to reduce the risk of switchbacks and guarantee the long-term effects of treatment.

2.7 Theoretical Underpinning

2.7.1 *Diffusion of Innovations Theory*

Diffusion of Innovations Theory, developed by Everett Rogers, provides a complete picture of exploring the process of the adoption of new technologies and practices in the social system. The theory particularly makes sense in the exploration of adalimumab biosimilar uptake in the EU, since it explains how the spread of innovations, including biosimilars. It is disseminated, assimilated, and adopted by healthcare administrators, patients and policymakers. Rogers identifies five major characteristics affecting the adoption, which are relative advantage, compatibility, complexity, trialability and observability (Rogers, 2003) ***[refer to figure 2.2]***.

The relative advantage in terms of biosimilars refers to perceived advantages like possible cost savings and enhanced access, whereas compatibility deals with alignment with the current clinical practices and regulatory systems. Complexity is about the understanding of biosimilar science, regulatory pathways, and switching protocols by the stakeholders, which can be considered a barrier to accomplishing this when not acting appropriately. Trialability and observability involve the possibility of healthcare systems testing the use

of biosimilars and monitoring real-life effects, which are important factors in gaining the confidence of late adopters.

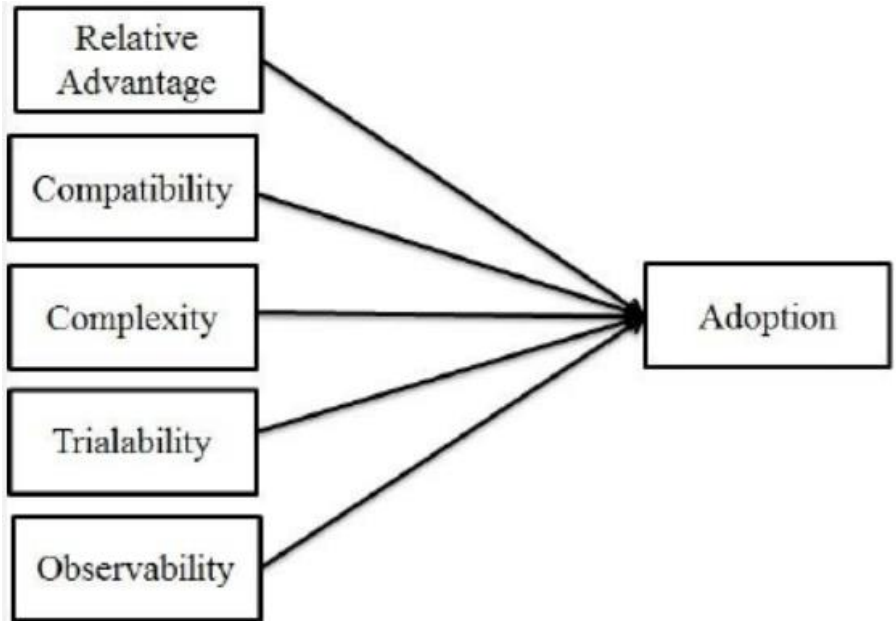

Figure 2.2: Diffusion of Innovations Theory

(Source: Rogers, 2003)

When considered with regard to the objectives of the research, the adoption pattern of adalimumab biosimilars in the EU would be viewed in terms of the innovation diffusion concept. Countries that implement early adopters offer a combination of high regulatory support, procurement that is transparent, and proactive education, which helps improve the perceived relative advantage as well as compatibility of biosimilars. On the other hand, laggard states are typically faced with distorted regulations, a lack of stakeholder inclusion, and real-world evidence influence, which augment the apparent complexity and slacken adoption rates. The theory also supports the focus on the stakeholder attitudes and the educational counterparts, as the opinion leaders and local champions are critical in the adoption decision (Khan et al., 2022). This framework allows examining the identified barriers and strategies to overcome them in an organised manner by following the model of adoption stages presented in this paper, which includes knowledge, persuasion, decision, implementation, and confirmation.

2.7.2 *Institutional Theory*

Institutional Theory looks into how structures, norms and rules of an organisation determine the behaviour of actors within a specified system. Institutional Theory holds

that organisations are gearing up to regulatory, normative and cognitive pressures to achieve legitimacy, resources and stability (Scott, 2005) ***[refer to figure 2.3]***. Regulatory pressure in the EU biosimilar landscape is evidenced by centralised EMA approval, national reimbursement policy and procurement system. Normative pressure emerges in terms of professional guidelines, clinical societies, and peer networks, and cognitive pressure emerges in terms of shared beliefs regarding whether or not biosimilars are safe, effective, and of value.

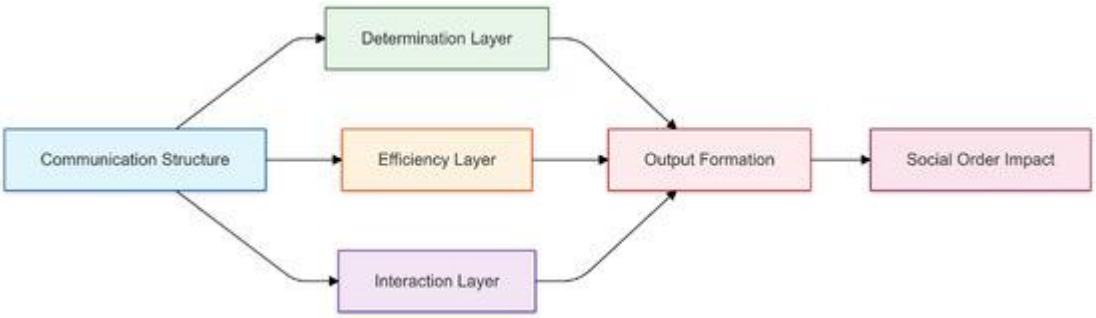

Figure 2.3: Institutional Theory

(Source: Scott, 2005)

This theoretical paradigm has a direct fit within the research objectives, especially the study of regulatory mismatches and market dispersion. Institutional Theory explains the existence of fragmented market access and uneven adoption, even with harmonised EMA approval, due to the variation in substitutability, reimbursement and procurement at the national level. It also explains why the attitudes of stakeholders, as formulated by institutional norms and frames of reference, may promote or hamper the process of biosimilar uptake irrespective of clinical evidence (El-Garaihy et al., 2022). Therefore, the theory warrants the study of both official obstacles to policy and informal factors of adoption that would allow the comprehensive analysis of accessibility and affordability issues. Institutional Theory helps to consider the interaction of regulatory frameworks, professional standards, and the perception of the stakeholders to see an entire picture of legacy barriers to the uptake of biosimilars and develop interventions. This may overcome both institutional and behavioural components of the issue.

2.8 Thematic Summary

Theme	Research Question	Theoretical Concept(s)
Regulatory Fragmentation & Harmonisation	How do national regulatory differences impact biosimilar uptake in EU member states?	Regulatory Theory; Policy Implementation
Market Dynamics & Pricing Strategies	What market factors drive or hinder adalimumab biosimilar adoption across countries?	Market Competition; Health Economics
Stakeholder Knowledge Gaps & Attitudes	How do stakeholder knowledge and confidence influence biosimilar implementation?	Diffusion of Innovation; Knowledge Translation
Procurement and Tendering Practices	How do procurement strategies affect biosimilar market access?	Health Systems Management; Institutional Theory
Patient Perceptions & Adoption Barriers	What patient-level factors promote or deter switching to biosimilars?	Patient-Centred Care; Behavioural Economics
Economic and Access Outcomes	What are the observed economic and access benefits of wider biosimilar adoption?	Value-based Healthcare; Accessibility Theory

Table 2.3: Summary Table

2.9 Literature Gap

A growing number of studies on adalimumab biosimilars have appeared throughout the European Union, although there are a number of fundamental gaps that still need to be covered. The existing studies provide detailed accounts of regulatory inconsistency,

market fragmentation, and the obstacles to stakeholders, although, to date, there has been no synthesis that consolidates the influences of such variables on biosimilar uptake and long-term sustainability. Barbier et al. (2021) and Bas and Duarte (2024) highlight regulatory and procurement anomalies, but they do not explain how the specific process in question influences adalimumab biosimilar coverage and pricing options in single-member states.

In addition, despite the consistent recognition of stakeholder attitudes as relevant barriers, the majority of studies take them as individual determinants and do not focus on how they interrelate with more encompassing institutional arrangements, purchase schemes, and competition. Policy changes or educational programs designed to increase biosimilar availability and affordability have also been made quite rarely, and there is a lack of empirical assessments of their impacts on economic stability and patient outcomes. This fragmented research has stood in the way of a comprehensive view of the reciprocal, multi-faceted relationship between regulation and market forces and stakeholder behaviour in the EU context.

2.10 Conceptual Framework

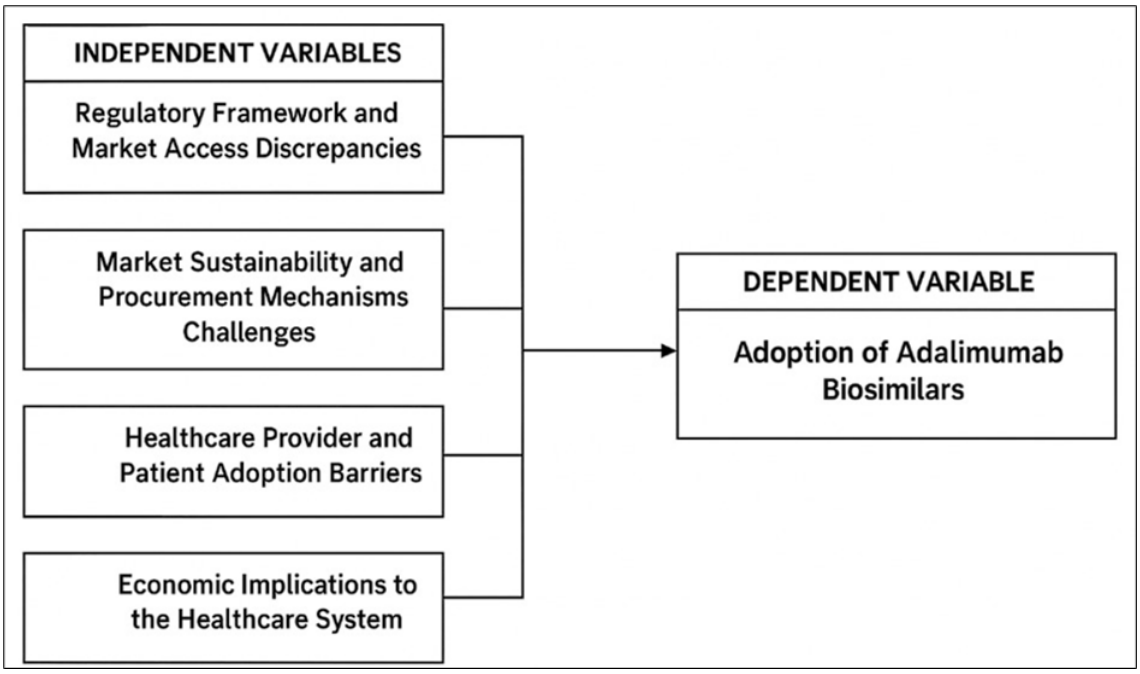

Figure 2.4: Conceptual Framework

2.11 Research Questions

RQ1: What are the regulatory discrepancies in the approval and implementation of adalimumab biosimilar in the EU member states?

The review finds that the centralised approval of EMA contrasts with the national policies on substitution, reimbursement, and pharmacovigilance to produce uneven access and acceleration of adalimumab biosimilars based in country.

RQ2: How do the pricing and market factors impact the adoption of adalimumab biosimilar in the chosen EU states?

The review of the literatures reveals that there were considerable regional differences in pricing mechanisms, procurement styles and competition. It indicates that price decrease per se will not certainly lead to biosimilar uptake since it is also determined by the reimbursement policies, tendering and activity of originator businesses, thus justifying this research question.

RQ3: What is the attitude of healthcare providers and patients on the safety and efficacy of adalimumab biosimilar?

The origin of this question is the results that reported by the researchers which say that gaps in knowledge, trust, and misinformation among medical workers and patients represent a significant obstacle to the use of biosimilars.

RQ4: What can be the evidence-based solutions that can enhance the biosimilar adalimumab accessibility and affordability in the EU?

The literature review summarises the suggestions on how to enhance the adoption of biosimilars, including you are familiar with standardised policies, specialised education and transparent procurement.

2.12 Conclusion

The overall literature review indicates that there are numerous obstacles that deter EU citizens against using adalimumab biosimilars. The access and the price are different because of regulations and pricing rules. The healthcare professionals and patients are usually deprived of information and mistrustful, which decelerates uptake. Solutions to these can be in the form of harmonised policies, improved education and also clear rules

of the market. There is evidence that we need further researches in order to observe the interaction of these issues. Addressing these aspects, healthcare providers will be able to provide safe and affordable biosimilars to a larger number of patients. Future studies would be informed by the results found here.

3 Methodology and Research Design

3.1 Overview

The chapter presents the methodological outline followed to research regulatory barriers and market factors affecting the order of availability and affordability of adalimumab biosimilars in the European Union. The project uses interpretivist philosophy, where the clarity of opinions of the most crucial stakeholders, regulators, healthcare professionals, and patient representatives shall be achieved. The study is done using an inductive approach that takes the empirical observations to help shape the formation of conceptual understanding. The major methods of the research is quantitative, which implies the use of survey to obtain voluminous data. The purposive sampling will allow recruiting a diverse group of participants and having interactions with people with the background knowledge relevant to various EU settings. Ethical considerations like informed consent, confidentiality and adherence to the regulations on data protection are strictly observed. Thematic analysis is employed in order to systematically determine and code trends in the gathered sources of information so that a deeper and broader comprehension of the influence leading to biosimilar adoption and market sustainability is achieved.

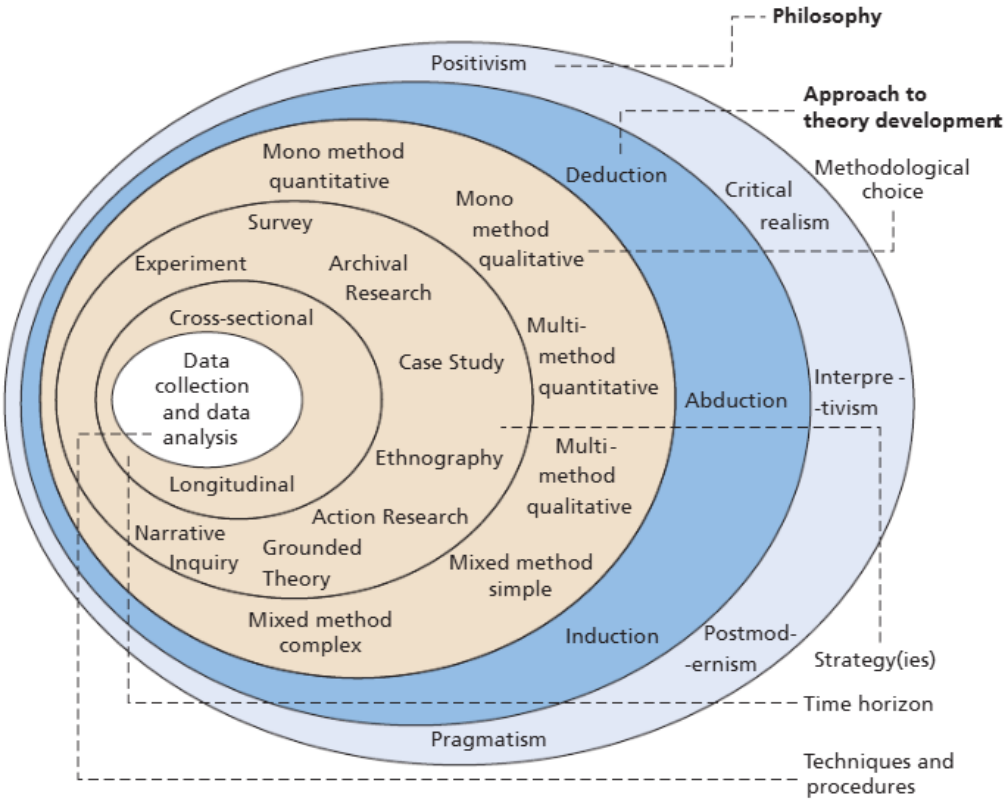

Figure 3.1: Research Onion

(Source: Saunders, Lewis and Thornhill, 2019)

In order to provide a clear description of the philosophical and the methodological framework, the Research Onion developed by Saunders is used ***(see Figure 3.1)***. The model graphically organises philosophical positions, approaches, strategies and time horizons and provides an inter-layered take on research design.

3.2 Research Philosophy and Approach

3.2.1 *Research Philosophy*

Philosophy of research is the belief or opinion on the creation and comprehension of knowledge in research. It informs a researcher on how to think, collect and interpret data on the world (Gannon, Taheri and Azer, 2022). A number of primary research philosophies exist: positivism, interpretivism, pragmatism and realism. Positivism also has the view that reality is unarguable and could be quantifiable through facts and figures. Interpretivism views reality as personal, which is determined through experiences and the meaning of people. Pragmatism is pragmatic and adopts any technique that will assist in obtaining the answer to the research question (Kelly and Cordeiro, 2020).

Interpretivism enables the researcher to gather information that is rich and detailed during the survey. ***Positivism research philosophy*** is selected in this study. (Gannon, Taheri and Azer, 2022). The positivism approach is applicable in the present study since it involves objective analysis using objective and measurable information like regulatory schedules, market share and pricing schedules. It can be used to perform a hypothesis test and enable a researcher to generalise the findings. The impact of regulatory and market conditions on the availability and affordability of biosimilars within the EU to create scientific rigour and policy applicability are also analyse through this process. In this study interpretivism and critical realism are less appropriate that concentrate either on subjective experiences, social constructions, or other cascade layers of causation. This research requires an empirical, policy-oriented knowledge and not an interpretative one. Pragmatism does not provide theoretical predictability to test cause-effect relationship in regulatory conditions and thus, positivism will be more consistent with the objectives of the study.

3.2.2 *Research Approach*

A research approach is a plan or method that the researcher will utilise in collecting and analysing data. These three approaches mainly apply in research, namely deductive, inductive, or abductive (Khatri, 2020). The deductive method begins with a theory or a hypothesis and puts it to the test with information. It shifts to the particular outcomes. The abductive approach attempts to get the most reasonable explanation of what data is observed by alternating data and theory. It is commonly employed in cases where insufficient data to be for use in the deduction or induction process alone (Kaushik and Walsh, 2019).

In the current research, the ***deductive research approach*** is selected. The deductive methodology is of relevance in this study because it uses the well-established regulatory and economic theories and examines them to the actual situation of adalimumab biosimilars in the EU. It allows systematic assessments of the impacts of existing regulatory regimes and market actors on affordability, access, and yields well-grounded, prima facie-theoretically explicit conclusions that can be used as policy and industry strategies. The inductive and abductive methods are unsuitable since they are concerned with formulating of new theories based on observations. The abductive approach is not selected because the research does not have to alternate between the data and the theory, but has to construct an understanding based on the data. The study involves the need to test out the available theories concerning regulation and market conduct as applies to the situation of biosimilars. The structure of the exploratory methods might not be sufficient in answering complicated, policy-oriented questions on which this research paper is based.

3.3 Research Strategy

The research strategy is the global plan that serves as a guide for how an article can be comprehensively carried out. It assists the researcher to determine the type of data to collect, the collection methodology and the method of analysis (Taherdoost, 2021). Research strategies can be of three major categories, that is, qualitative, quantitative as well and mixed strategy (Khan *et al.*, 2023). Qualitative research strategy is aimed at gathering non-statistical information that may consist of words, opinions, and experiences. It is applied to get a deceptive interpretation of the thoughts, feelings and behaviours of people (Laryeafio and Ogbewe, 2023). Interviews, focus groups, and

observations are the popular methods of qualitative research. This is the ideal strategy when the study aims at getting acquainted with complicated matters, discovering the meanings, or understanding the thinking of people.

A quantitative research approach gathers numerical information which is measurable and can be statistically analysed. It applies surveys, tests or existing data to test hypotheses or to evaluate a relationship between variables. One can use this method when what one wants to do is to measure a pattern or test a theory, or make a generalisation about a large population. This methods strategy entails a combination of quantitative strategies. It gathers the two forms of data to offer a clearer précis on the research problem (Oranga and Matere, 2023). Forming a strategy is applicable where depth and breadth are required.

The ***quantitative research strategy*** is selected in the present study. This is simply because the research aims to determine the regulatory obstruction and market forces surrounding adalimumab biosimilars in the EU. The aims are aimed at getting insight into the experiences of actors, including regulators, healthcare professionals, and patients, attitudes, and opinions. Formal survey methods enable more detailed and richer information ensuring quantitative raw primary data collection. Such a strategy will assist in unleashing some underlying problems, values and incentives that drive biosimilar uptake.

The integration of quantitative data will take place primarily at the stage of the interpretation of the results and will be based exclusively on the results of survey analysis. Findings achieved in the quantitative context will be contrasted and alongside with the qualitative ones synthesised to triangulate evidence and strengthen the cogency of decisions. In particular, there will be a presentation of statistical overviews next to related qualitative themes with a view of supporting or contrasting perspectives. This congruent strategy will confirm, complete, or discredit thematic interpretations that come out of interviews so that a more holistic overview of barriers and enablers is presented. Its synthesis will take place in the discussion chapter, which is aimed at using statistical data to support or refute arising qualitative narratives.

3.4 Collection Primary Data

3.4.1 *Sources*

This research applies ***primary data collection method*** to collect raw primary data from research responses directly. The primary data implies gathering new data or the data that is directly collected with people being involved in the subject (Dhudasia, Grundmeier and Mukhopadhyay, 2021). This is significant since the research focuses on comprehending the experience, views, and issues of the stakeholders regarding adalimumab biosimilars within the EU. The primary data is selected since it will provide original, first-hand information which cannot be built on other stored reports or articles (Diatta and Berchtold, 2022). It enables the researcher to raise certain questions and chase new ideas which might emerge in the course of study. The secondary data is not the primary way. Secondary data is the evidence gathered through other people, such as books, articles and reports (Wickham, 2019). Although the secondary data may offer the background and context, it cannot offer any background or up-to-date information regarding the current attitude and the barriers experienced by the stakeholders. It can also omit valuable local or personal experiences which are central to this research.

The primary data sources can be persons with direct experience of adalimumab biosimilars. These include biosimilar approval and policy working regulators and policymakers, medical practitioners like physicians, pharmacists and hospital administrators and patient groups representatives. The sample will be selected through purposive sampling. This will provide a broad picture by taking a sample that encompasses a variety of countries and functions. The process of recruiting people implies addressing the potential participants within the professional networks, institutional contacts, and public lists. They will be sent an email invitation, which will contain information on the study and the consent form. It should not be under any obligation to participate, and it should be confidential.

This research study involves survey data on stakeholders, which include healthcare professionals, policymakers, and patients representatives on the quantitative analysis. Descriptive statistics, including frequencies, percentage values, and indicators of the central tendency of demographic distributions, will be drawn up, and the main tendencies of answers will be distinguished with regard to regulatory and market barriers to adalimumab biosimilars. Inferential statistics In cases where it is suitable and the sample

size permits, associations or correlations between the respondent groups or significant differences will be tested by use of inferential statistics such as chi-square tests or t-tests. The overall capabilities of the programs like SPSS will be used to conduct all analyses and provide precision, effective data handling, and definite presentation of important quantitative results.

3.4.2 *Access and Ethical Issues*

This study is governed by strict regulations to safeguard the participants and their data. The participants are reached via professional contacts, publication lists and invitation via email. Each of the participants is well informed about the research and has to sign his or her consent to participate. The studies comply with the ***"Data Protection Act 2018"*** of the UK, which implies that all individual information is secured and can be used only to conduct the research and is destroyed at the culmination of the study (Act, 2018). The data is saved on password-encrypted equipment, and only the supervisor and the researcher can access it. All records have their names and personal information stripped away so that information remains confidential.

The ethical approval is based on the ***guidelines of Griffith University*** (Griffith College, 2025). This implies that the study upholds the rights of all participants, including the right to quit at any time. Validity and reliability will be achieved in the research, which will encompass the adoption of clear approaches and authentic reporting. Confidentiality is absolutely kept, and no data is passed on that can show the identity of a participant. It is the goal of the study to be just, find it secure, and respectful, and ensure that all the information is managed with caution and that the findings are reliable and precise. The practice will safeguard all the parties involved and ensure that the research is highly ethical.

3.5 Approach to Data Analysis

The style of data analysis applied in the study is aimed to be comprehensible, orderly, and convenient. The primary aim is to interpret data gathered on adalimumab biosimilars in the EU with the stakeholders. The primary method to extract analysis of the data is statistical and thematic analysis (Jowsey, Deng and Weller, 2021). The study applies statistical and thematic data analysis technique as developed by Braun and Clarke. Based on this technique, preparation of data marks the first step in data analysis. Each and every response is recorded (with consent) and this is in transcribed form. These recordings are

referred to as transcripts. This assists in comprehending major thoughts and emotions expressed among the participants.

Then, the researcher begins to code data. Coding refers to the identification or marking of the significant words, phrases, or sentences concerning the research questions. Every code denotes a tiny idea or a topic which is significant to the study. As an example, when a participant mentions a product of interest as a regulatory barrier, then the section of the text will be coded as regulation (Mennella *et al.*, 2024). Following the coding, the researcher searches for patterns in the code. Groupings of similar codes make up themes. A theme is the larger concept that ties several codes together. As an example, the codes relating to the themes of regulation, approval delays and policy differences could go under an overall theme of regulatory challenges. The researcher verifies whether the themes can align with the research aims and whether themes can drive responses to the principal questions of the research (Jowsey, Deng and Weller, 2021).

In the given study, quantitative data collected through surveys will be incorporated in the data collection and analysis phase. The survey will be shared among the stakeholders working within the industry and those in the regulation circles to develop quantitative information on regulatory issues, market dynamics, and attitudes towards biosimilar availability. The process of the integration is done after the literature review, and it plays the role of confirmation of the theoretical assumptions with practical evidence. This is meant to determine trends, test hypothesis and provide evidence-based findings that will provide policy recommendations to enhance access and affordability of adalimumab biosimilars in the EU.

This shall be followed by revising the survey response analysis and narrowing down the themes. The researcher uses a retreating strategy whereby he checks the data given to ensure that every theme is supported by sufficient data from the surveys. On rare occasions, new themes can be generated, others are merged, or eliminated. The aim is that there should be clear and powerful themes explaining the findings of the research. After finalising the themes, the researcher describes each theme in detail. This involves the direct attribution of the participants by providing their words and how they relate to the topic. The researcher gives the meaning of each theme and the reason why it is significant in the comprehension of the accessibility and the affordability of adalimumab biosimilars in the EU.

In the quantitative part of the survey, descriptive statistics will be applied to the response of participants, pointing out the trends in questions concerning the regulatory obstacles to the utilisation of adalimumab biosimilars and its influence on the pricing and accessibility of adalimumab biosimilars. The use of SPSS software will assist in cleaning up, tabulation and visualisation of data. This method delivers clear and concise view of the perception of the stakeholders in line with the objectives of the study.

3.6 Conclusion

This chapter has described the methodological approach taken to explore the regulatory barriers and market dynamics that are shaping the adoption of adalimumab biosimilars within the European Union. This research employs an interpretivist philosophy and an inductive methodology that facilitates a subtle insight into stakeholders' views using quantitative approaches. Survey are the principal method of data collection, providing in-depth information from purposively sampled participants, including regulators, healthcare professionals, and patient representatives. Ethical practice is stringently maintained, respecting confidentiality and informed consent according to data protection legislation and institutional policies.

Both thematic and statistical analysis approach allows for the detection of frequent themes and patterns in participant responses and enables detailed exploration of the structural and behavioural determinants influencing biosimilar uptake. The methodology chosen is consonant with the research aims, with the latter seeking to address intricate regulatory and market settings from the perspective of pivotal stakeholders. By its concentration on experiential information and contextual knowledge, the adopted research approach stands to produce valuable insights into biosimilar accessibility and affordability within the EU. This methodological framework paves the way for the ensuing chapter, which offers the findings and discussion in light of the data gathered by this strong and ethically upright research procedure.

4 Presentation and Discussion of the Findings

4.1 Overview

The chapter on data presentation and the discussion of the findings synthesises survey, statistics, and literature data as well to clarify how stakeholders view the implementation of adalimumab biosimilar adoption into the EU. It begins by describing the trend, regulatory experience, procurement practice, as well as safety concerns, then it proceeds to correlation and regression analyses in revealing important drivers behind the provision of support to the harmonised EU-wide policies. Every analytical segment is critically construed on the backdrop of the ascertained market forces and factual learning inadequacies. This well-organised story explains how the chapter develops the influence of multiple-faced barriers and enablers that combine to create access and affordability of biosimilar adalimumab amongst various member states.

4.2 Analysis of SPSS

4.2.1 Descriptive statistics

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
What is your professional role?	100	1	5	3.18	1.321
How many years of experience do you have in your current field?	100	1	4	1.81	.918
Do you think that national regulations to biosimilar vary so much compared with that of EU?	100	1	5	1.89	1.024
Have you any experience of delay in the use of biosimilar adalimumab because of the regulatory processes of use in your country?	100	1	2	1.91	.288
Does non-harmonised policy on substitution and interchangeability influence your readiness to prescribe/ dispense bio-similar products?	100	1	2	1.81	.394
Does your institution have transparent and inclusive procedures of procurement or tendering to biosimilar suppliers?	100	1	4	1.84	1.070
Are you keen that the existing pricing policy promotes a sustainable competition between the producers of biosimilars and original manufacturers?	100	1	2	1.86	.349
Has your facility developed shortages or instability on biosimilar adalimumab?	100	1	2	1.78	.416
Are you satisfied with the level of safety and efficacy of adalimumab biosimilar information?	100	1	2	1.80	.402
Does a fear of immunogenicity or adverse effects present a significant obstacle to prescribing biosimilar adalimumab practice?	100	1	5	1.72	1.036
Do you think that patients under your care are adequately informed concerning biosimilars to make informed choices?	100	1	5	1.75	1.086
Have you noticed how patients have not wanted to change to biosimilar adalimumab when they had originator?	100	1	2	1.83	.378
Has your institution/healthcare system realised any cost savings by the introduction of adalimumab biosimilars?	99	1	5	1.73	1.067
In your environment, is the savings of biosimilar adoption used to better access or services to the patients?	100	1	5	1.78	1.151
Would aligned EU-wide approaches on the authorisation of biosimilars, their substitution and the procurement of adalimumab biosimilars enhance uptake and access of biosimilar adalimumab?	100	1	2	1.92	.273
Valid N (listwise)	99				

Figure 4.1: Descriptive statistics

Descriptive statistics given on the fifteen survey questions provide the trend of variability in the responses, which are related to the research topic of interest of biosimilar adoption and access (Sooksriwong *et al.*, 2025). When the standard deviations exceed one, it means that the responses are spread around the mean, and when it is less than one, it means that

the responses are grouped around the mean. Dispersion questions are the professional roles of the respondents (SD = 1.321), the views on national regulatory variability relative to EU standards (SD = 1.024), the institutional procurement/tendering procedures (SD = 1.070), the fear of immunogenicity or adverse events (SD = 1.036), the thoughts about the adequacy of patient information (SD = 1.086), the cost savings realised in an institution (SD = 1.067) and the utilisation of biosimilars. This dispersion carries an implication of non-homogeneous opinions or experiences among the respondents based on their role, regulatory awareness, institutional practice, safety concern, patient communication, financial performance and savings re-investment. Such heterogeneity is in line with the literature stressing the fragmented national policies and different stakeholder confidence in biosimilars.

By contrast, questions with clustered responses encompass years of professional experience (SD = 0.918), exposure to regulatory delays (SD = 0.288), policy influence on prescribing readiness (SD = 0.394), perceptions of pricing policy sustainability (SD = 0.349), experiences of biosimilar shortages or instability (SD = 0.416), satisfaction with safety and efficacy information (SD = 0.402), observations of patient reluctance to switch from originator products (SD = 0.378), and views on whether aligned EU-wide authorisation, substitution and procurement would enhance uptake and access (SD = 0.273). Low dispersion scores in these domains imply that respondents could largely agree with each other regarding their tenure, the proliferation of regulatory delays, effects of dissimilar substitution policies, expensive tendering protocols, the sustainability of supply, satisfaction with information, switching behavioural patterns of patients, and the perceived advantage of harmonised EU regulations. That consensus supports the consistency of findings Barbier et al. (2021) that there is a uniform effect of regulatory complexities on the uptake of biosimilars in different jurisdictions and on a favourable attitude of stakeholders in relation to harmonisation.

The central tendencies are reflected by the means. For example, the mean rating for perceived regulatory variation (Mean = 1.89) lies below the neutral mid-point on a five-point scale. It signalling a general tendency to agree that national regulations vary significantly from EU directives as per analysis of Alsaif and Blumer (2025). In combination with the high SD, this highlights the difference in experiences of regulatory fragmentation around countries as reported in the dissertation. Similarly, the mean satisfaction with safety and efficacy information (Mean = 1.80 on a 1–2 scale) and patient

reluctance to switch (Mean = 1.83) reflect widespread concerns about communication and trust, though clustered responses imply uniformity of concern. Both the procurement procedures and cost-savings realisation institutional procedures yielded a score close to 1.84 and 1.73, respectively, indicating a moderate level of agreement on the presence of transparent procurement and realisation of savings, respectively, but dispersion in these items indicates disparity in institutional preparedness and financial implication.

In short, it can conclude that the merger of dispersal and clustering across survey items indicates that although there is general agreement between healthcare stakeholders in their perceptions of the burden of non-harmonised policies, stability of supply, and unwillingness of patients to disengage, there is marked heterogeneity in their experiences of professional role, institutional processes, perceptions of safety, and financial reinvestment. These results complement the research proposal through its focus on multidimensional obstacles such as regulatory fragmentation, distortions of procurement, knowledge gaps, and economic incentives to adalimumab biosimilar use, and its findings confirm the dissertation suggestion to implement multi-stakeholder educational actions and harmonised policies to support the circumstances shared and divergent barriers identified by respondents.

4.2.2 Correlation analysis

Correlations

		Do you think that national regulations to biosimilar vary so much compared with that of EU?	Have you any experience of delay in the use of biosimilar adalimumab because of the regulatory processes of use in your country?	Does non-harmonised policy on substitution and interchangeability influence your readiness to prescribe/ dispense bio-similar products?	Does your institution have transparent and inclusive procedures of procurement or tendering to biosimilar suppliers?	Are you keen that the existing pricing policy promotes a sustainable competition between the producers of biosimilars and original manufacturers?	Has your facility developed shortages or instability on biosimilar adalimumab?	Are you satisfied with the level of safety and efficacy of adalimumab biosimilar information?	Does a fear of immunogenicity or adverse effects present a significant obstacle to prescribing biosimilar adalimumab practice?	Do you think that patients under your care are adequately informed concerning biosimilars to make informed choices?	Have you noticed how patients have not wanted to change to biosimilar adalimumab when they had originator?	Has your institution/healthcare system realised any cost savings by the introduction of adalimumab biosimilars?	In your environment, is the savings of biosimilar adoption used to better access or services to the patients?	Would aligned EU-wide approaches on the authorisation of biosimilars, their substitution and the procurement of adalimumab biosimilars enhance uptake and access of biosimilar adalimumab?
Do you think that national regulations to biosimilar vary so much compared with that of EU?	Pearson Correlation	1	.035	.023	.288**	-.185	-.010	-.152	.266**	.375**	-.153	.114	.271**	-.104
	Sig. (2-tailed)		.732	.822	.004	.065	.922	.131	.007	<.001	.128	.259	.006	.302
	N	100	100	100	100	100	100	100	100	100	100	99	100	100
Have you any experience of delay in the use of biosimilar adalimumab because of the regulatory processes of use in your country?	Pearson Correlation	.035	1	.293**	-.080	.276**	.255*	.192	-.187	-.073	.230*	-.048	-.182	.294**
	Sig. (2-tailed)	.732		.003	.429	.005	.011	.055	.062	.472	.021	.636	.069	.003
	N	100	100	100	100	100	100	100	100	100	100	99	100	100
Does non-harmonised policy on substitution and interchangeability influence your readiness to prescribe/ dispense bio-similar products?	Pearson Correlation	.023	.293**	1	-.073	.539**	.297**	.331**	-.008	-.206*	.324**	-.125	-.049	.233*
	Sig. (2-tailed)	.822	.003		.472	<.001	.003	<.001	.938	.039	.001	.217	.632	.020
	N	100	100	100	100	100	100	100	100	100	100	99	100	100
Does your institution have transparent and inclusive procedures of procurement or tendering to biosimilar suppliers?	Pearson Correlation	.288**	-.080	-.073	1	.048	-.057	.042	.242*	.122	-.143	.151	.176	.060
	Sig. (2-tailed)	.004	.429	.472		.638	.572	.676	.015	.228	.156	.136	.080	.556
	N	100	100	100	100	100	100	100	100	100	100	99	100	100
Are you keen that the existing pricing policy promotes a sustainable competition between the producers of biosimilars and original manufacturers?	Pearson Correlation	-.185	.276**	.539**	.048	1	.481**	.735**	-.026	-.333**	.508**	-.241*	-.228*	.518**
	Sig. (2-tailed)	.065	.005	<.001	.638		<.001	<.001	.799	<.001	<.001	.016	.022	<.001
	N	100	100	100	100	100	100	100	100	100	100	99	100	100
Has your facility developed shortages or instability on biosimilar adalimumab?	Pearson Correlation	-.010	.255*	.297**	-.057	.481**	1	.579**	-.097	-.101	.595**	-.110	-.228*	.377**
	Sig. (2-tailed)	.922	.011	.003	.572	<.001		<.001	.335	.320	<.001	.278	.022	<.001
	N	100	100	100	100	100	100	100	100	100	100	99	100	100
Are you satisfied with the level of safety and efficacy of adalimumab biosimilar information?	Pearson Correlation	-.152	.192	.331**	.042	.735**	.579**	1	-.087	-.347**	.506**	-.200*	-.227*	.498**
	Sig. (2-tailed)	.131	.055	<.001	.676	<.001	<.001		.387	<.001	<.001	.047	.023	<.001
	N	100	100	100	100	100	100	100	100	100	100	99	100	100
Does a fear of immunogenicity or adverse effects present a significant obstacle to prescribing biosimilar adalimumab practice?	Pearson Correlation	.266**	-.187	-.008	.242*	-.026	-.097	-.087	1	.260**	-.149	.126	.321**	.027
	Sig. (2-tailed)	.007	.062	.938	.015	.799	.335	.387		.009	.139	.216	.001	.788
	N	100	100	100	100	100	100	100	100	100	100	99	100	100
Do you think that patients under your care are adequately informed concerning biosimilars to make informed choices?	Pearson Correlation	.375**	-.073	-.206*	.122	-.333**	-.101	-.347**	.260**	1	-.228*	.373**	.311**	-.205*
	Sig. (2-tailed)	<.001	.472	.039	.228	<.001	.320	<.001	.009		.023	<.001	.002	.041
	N	100	100	100	100	100	100	100	100	100	100	99	100	100
Have you noticed how patients have not wanted to change to biosimilar adalimumab when they had originator?	Pearson Correlation	-.153	.230*	.324**	-.143	.508**	.595**	.506**	-.149	-.228*	1	-.041	-.203*	.357**
	Sig. (2-tailed)	.128	.021	.001	.156	<.001	<.001	<.001	.139	.023		.685	.043	<.001
	N	100	100	100	100	100	100	100	100	100	100	99	100	100
Has your institution/healthcare system realised any cost savings by the introduction of adalimumab biosimilars?	Pearson Correlation	.114	-.048	-.125	.151	-.241*	-.110	-.200*	.126	.373**	-.041	1	.358**	-.216*
	Sig. (2-tailed)	.259	.636	.217	.136	.016	.278	.047	.216	<.001	.685		<.001	.032
	N	99	99	99	99	99	99	99	99	99	99	99	99	99
In your environment, is the savings of biosimilar adoption used to better access or services to the patients?	Pearson Correlation	.271**	-.182	-.049	.176	-.228*	-.228*	-.227*	.321**	.311**	-.203*	.358**	1	-.250*
	Sig. (2-tailed)	.006	.069	.632	.080	.022	.022	.023	.001	.002	.043	<.001		.012
	N	100	100	100	100	100	100	100	100	100	100	99	100	100
Would aligned EU-wide approaches on the authorisation of biosimilars, their substitution and the procurement of adalimumab biosimilars enhance uptake and access of biosimilar adalimumab?	Pearson Correlation	-.104	.294**	.233*	.060	.518**	.377**	.498**	.027	-.205*	.357**	-.216*	-.250*	1
	Sig. (2-tailed)	.302	.003	.020	.556	<.001	<.001	<.001	.788	.041	<.001	.032	.012	
	N	100	100	100	100	100	100	100	100	100	100	99	100	100

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

Figure 4.2: Correlation analysis

The connection between responses to the fifteen questions surveyed about adopting adalimumab biosimilar in EU healthcare facilities is termed the correlation matrix. Correlation coefficients may have values between -1 and +1, where the values between 0.5 and 1.0 are considered strong positive correlation and below 0.5 a weak positive relationship, and, surprisingly, negative correlation with varying strength.

The strongest positive correlate of Question 15 is Question 5 (“Does non-harmonised policy on substitution and interchangeability influence your readiness to prescribe/dispense biosimilar products?”) at r = 0.518, denoting a strong positive relationship. This is an indication that the respondents who feel that existing replacement policies are obstacles are also most likely to want homogenisation across the EU to enhance adoption. A similarly strong correlation appears with Question 7 (“Are you keen that the existing pricing policy promotes sustainable competition…?”) at r = 0.498,

indicating that belief in competitive pricing strategies aligns closely with endorsement of harmonised frameworks.

Question 6 ("Does your institution have transparent and inclusive procedures of procurement or tendering to biosimilar suppliers?") correlates moderately strongly with Question 15 at r = 0.377, signifying that institutional procurement transparency relates to support for EU-wide alignment. A weaker yet statistically significant positive relationship emerges with Question 10 ("Does a fear of immunogenicity or adverse effects present an obstacle…?") at r = 0.357, implying that safety concerns also motivate calls for harmonisation. Question 11 ("Do you think that patients under your care are adequately informed…?") shows a modest correlation of r = 0.216, suggesting that perceptions of patient education modestly align with support for unified policies.

In comparison, there are a couple of variables that either show little or negative relationships with the dependent variable. Question 8 ("Has your facility developed shortages or instability…?") correlates at r = 0.027, essentially null, indicating that supply-side instability is unrelated to attitudes on EU-wide harmonisation. Question 13 ("Has your institution realised any cost savings by introduction of adalimumab biosimilars?") correlates at r = 0.032, likewise negligible, suggesting that actual financial outcomes do not influence harmonisation support.

Negative correlations appear with Question 1 (professional role; r = –0.104), Question 2 (years of experience; r = –0.294), Question 9 (satisfaction with safety and efficacy information; r = –0.205), and Question 12 (patient reluctance to switch; r = –0.250). The moderate negative correlation with experience means that the very experienced stakeholders are somewhat less persuaded that EU-wide methods will lead to an improvement in the uptake, and perhaps they have entrenched interests with national mechanisms. Any negative connotations with satisfaction in the current information and the reluctance of observed patients imply that any individuals satisfied with the current communications or that fewer switching obstacles may more readily be satisfied without harmonisation demands.

These findings demonstrate that perception of policy fragmentation and pricing competition are the most powerful sources of arguments in supporting EU-wide harmonised strategies regarding the uptake of adalimumab biosimilar (Car *et al.*, 2023b). There is also a significant difference in determining the role of institutional procurement

transparency and safety concerns, and only a minimal or even negative effect on such practical issues as the lack of supply, actual cost savings, and inclination to participate by the patients (Donnelly and Paek, 2020). This trend supports the thesis of this dissertation on the importance of regulatory harmonisation and procurement change, which will assist with the introduction of biosimilars across EU member states in terms of accessibility and affordability.

4.2.3 Regression analysis

Model Summary

Model Summary

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.608[a]	.369	.281	.232

a. Predictors: (Constant), In your environment, is the savings of biosimilar adoption used to better access or services to the patients?, Does non-harmonised policy on substitution and interchangeability influence your readiness to prescribe/ dispense bio-similar products?, Does your institution have transparent and inclusive procedures of procurement or tendering to biosimilar suppliers?, Have you any experience of delay in the use of biosimilar adalimumab because of the regulatory processes of use in your country?, Do you think that patients under your care are adequately informed concerning biosimilars to make informed choices?, Have you noticed how patients have not wanted to change to biosimilar adalimumab when they had originator?, Does a fear of immunogenicity or adverse effects present a significant obstacle to prescribing biosimilar adalimumab practice?, Has your institution/healthcare system realised any cost savings by the introduction of adalimumab biosimilars?, Do you think that national regulations to biosimilar vary so much compared with that of EU?, Are you satisfied with the level of safety and efficacy of adalimumab biosimilar information?, Has your facility developed shortages or instability on biosimilar adalimumab?, Are you keen that the existing pricing policy promotes a sustainable competition between the producers of biosimilars and original manufacturers?

Figure 4.3: Model Summary

The model summary table reports several key metrics that assess the strength and explanatory power of the regression model predicting stakeholder support for aligned EU-wide approaches to authorisation, substitution, and procurement of adalimumab biosimilars (the dependent variable) (Plevris *et al.*, 2022). First, the multiple correlation

coefficient, R = 0.608, indicates a moderate overall association between the set of predictor variables (survey questions on regulatory fragmentation, procurement transparency, safety concerns, cost savings, and related factors) and the outcome. This effect of R is indicative of the fact that the predictor meets a kind of overall significant, but not trivial, heterogeneous linear correlation with the perceived probability of respondents that the normalisation of policy would stimulate the uptake of bio-similarity.

The R^2 figure (0.369) shows that almost 36.9% of the variance in the dependent variable was explained by the independent variables in the model. What this is to imply, in practice, is that more than a third of the support of the respondents in embracing the EU-wide alignment can be described by their encounters and feelings with regulations of the nation, procurement practices, policing of white prices, safety updates, and other aspects engaged in the poll. Although an R^2 of less than 0.5 may seem modest in purely statistical matters, when applied in a study in the social sciences, a figure of 0.37 has an acceptable level of explanatory power, especially in a multi-factorial attitude being modelled.

Even more importantly, an adjusted R^2 of 0.281 has to be pointed out. The adjusted R^2 is more realistic because, unlike R^2, the number of predictors of a variable does not increase with each additional predictor, but rather it penalises too many or irrelevant ones and gives a more realistic impression of how well the model will work in the population. An adjusted R^2 of 0.281 hints that, considering the predictors, nearly 28.1% of the variation in respondents to go with EU-wide on consistency is explained by the model. This value highlights the fact that though the predictors are of substantive interest, a large percentage, i.e., more than 70% of the variance, goes unaccounted. Most probably that such residual variance indicates another impact of other factors which are not reflected by the survey, such as country-specific policies, individual attitudes, institutional culture, and unmeasured behavioural determinants. The 0.232 standard error of estimate is a measure of how far, on average, the observed values are from their regression line. A smaller standard error indicates that predicted values closely track actual responses; here, a value of approximately 0.23 on a binary (yes/no) or Likert-type scale suggests reasonably tight clustering of residuals, reinforcing the model's relative precision in forecasting stakeholder support.

Collectively, these statistics translate into the idea that the regression model offers a rather strong but incomplete explanation of what determines biosimilar uptake support. The

moderate values of R and R^2 are an assurance that dimensions like the perceived policy fragmentation, transparency, the competitiveness of prices, and the safety considerations would act as crucial determinants towards harmonisation endorsement (Mascarenhas-Melo et al., 2024). However, the gap between R^2 (0.369) and adjusted R^2 (0.281) signals that not all included survey items contributed equally; some predictors may have limited unique explanatory value and could be reconsidered or refined in subsequent studies. In addition, the large unexplained variance indicates the necessity to consider additional factors that could promote the accuracy of prediction, including leadership in the institutions, patient advocacy power, real-life data on prescribing, and national budgeting shortfalls (Donnelly and Paek, 2020).

These results are consistent with the established multidimensional obstacles to adoption, namely, regulatory fragmentation, distortion in procurement, knowledge gaps among stakeholders, and economic incentives, and reveal the necessity of specific educational programmes and policy harmonisation. Practically, the model indicates that the interventions focusing on the substitution policy and the issue of competition in price will most probably lead to the maximum growth of the stakeholders support to EU-wide approaches, although also, of course, recalling the researchers that it will be necessary to investigate more contextual and psychological drivers of the given approach to better explain the attitudes toward the biosimilar uptake under the conditions of different EU health systems.

ANOVA

ANOVA[a]

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	2.716	12	.226	4.196	<.001[b]
	Residual	4.638	86	.054		
	Total	7.354	98			

a. Dependent Variable: Would aligned EU-wide approaches on the authorisation of biosimilars, their substitution and the procurement of adalimumab biosimilars enhance uptake and access of biosimilar adalimumab?

b. Predictors: (Constant), In your environment, is the savings of biosimilar adoption used to better access or services to the patients?, Does non-harmonised policy on substitution and interchangeability influence your readiness to prescribe/ dispense bio-similar products?, Does your institution have transparent and inclusive procedures of procurement or tendering to biosimilar suppliers?, Have you any experience of delay in the use of biosimilar adalimumab because of the regulatory processes of use in your country?, Do you think that patients under your care are adequately informed concerning biosimilars to make informed choices?, Have you noticed how patients have not wanted to change to biosimilar adalimumab when they had originator?, Does a fear of immunogenicity or adverse effects present a significant obstacle to prescribing biosimilar adalimumab practice?, Has your institution/healthcare system realised any cost savings by the introduction of adalimumab biosimilars?, Do you think that national regulations to biosimilar vary so much compared with that of EU?, Are you satisfied with the level of safety and efficacy of adalimumab biosimilar information?, Has your facility developed shortages or instability on biosimilar adalimumab?, Are you keen that the existing pricing policy promotes a sustainable competition between the producers of biosimilars and original manufacturers?

Figure 4.4: ANOVA

The ANOVA table evaluates whether the regression model as a whole provides a statistically significant explanation of variance in respondents' support for aligned EU-wide approaches to authorisation, substitution, and procurement of adalimumab biosimilars (the dependent variable). The F-statistic value of 4.196 of the models and a corresponding significance level of $p < .001$ show that the entire combination of twelve predictor variables includes a contributing share of variance in the stakeholder support that goes beyond what would be expected purely by chance. Academically, the null hypothesis that one of the independent variables would be found to be in tune with perceived harmonisation benefits could be discredited at the same level at the 0.1% level, which indicated the general strength of the model.

The regression sum of squares (SSR) of 2.716 reflects the amount of variability in the dependent variable accounted for by the twelve predictors, whereas the residual sum of squares (SSE) of 4.638 represents unexplained variance. The total sum of squares (SST) of 7.354 partitions into these two components (SSR + SSE). Thus, approximately 36.9%

of total variance is explained by the model (R^2 = 2.716 / 7.354), consistent with earlier model-summary findings. Examining the degrees of freedom, the model uses 12 df for the regression component (equal to the number of predictors) and 86 df for the residual component (total sample of 99 minus the number of parameters, including the intercept). These values of the df make sure that the F-test rightly keeps in mind the complexity of models regarding sample size.

A highly significant F-value indicates that the combination of variables, which include regulatory fragmentation, procurement transparency, price policy perception, safety issues, cost realisation of savings, patient attitude, and the factors therein, provides a meaningful predictive framework regarding the stakeholders' belief in harmonised EU policy, which would further their biosimilar uptake and access (Mascarenhas-Melo et al., 2024). This goes in line with the focus of the dissertation, which is that regulatory harmonisation and procurement changes are key facilitating factors of the adoption of biosimilars in different national healthcare settings.

However, despite the statistical significance of the overall model, the SSR relative to SST indicates that a substantial proportion of variance (approximately 63.1%) remains unexplained, suggesting omitted variables or contextual influences not captured by the survey. Such residual variance can include factors of country-specific reimbursement systems, personal risk-benefit judgement by the clinician and budget limitations among institutions, and patient advocacy pressures and (Bas and Duarte, 2024). These various barriers are complex to deal with, as the proposal observes, but this needs harmonised policy frameworks along with effective educational programs as well as clear tendering procedures and stakeholder engagement strategies so as to maximise the theoretical rewards of biosimilar competition.

Overall, the ANOVA findings confirm that the set of predictors constitutes a statistically significant model of explaining support to EU-wide alignment, which validates the conjoining nature of predictors pertinent to shaping the perception towards the uptake of biosimilars (Mestre-Ferrandiz *et al.*, 2024). However, the level of unexplained variance serves to underline the importance of ongoing research into other determinants, qualitative, organisational, and cultural, which motivate real-life use of adalimumab biosimilars within the European Union.

Coefficients

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients		
		B	Std. Error	Beta	t	Sig.
1	(Constant)	.912	.222		4.102	<.001
	Do you think that national regulations to biosimilar vary so much compared with that of EU?	-.012	.027	-.045	-.441	.660
	Have you any experience of delay in the use of biosimilar adalimumab because of the regulatory processes of use in your country?	.177	.090	.187	1.976	.051
	Does non-harmonised policy on substitution and interchangeability influence your readiness to prescribe/ dispense bio-similar products?	-.046	.075	-.067	-.618	.538
	Does your institution have transparent and inclusive procedures of procurement or tendering to biosimilar suppliers?	.020	.024	.078	.820	.414
	Are you keen that the existing pricing policy promotes a sustainable competition between the producers of biosimilars and original manufacturers?	.182	.119	.233	1.532	.129
	Has your facility developed shortages or instability on biosimilar adalimumab?	.042	.084	.064	.508	.613
	Are you satisfied with the level of safety and efficacy of adalimumab biosimilar information?	.131	.097	.193	1.350	.180
	Does a fear of immunogenicity or adverse effects present a significant obstacle to prescribing biosimilar adalimumab practice?	.037	.025	.141	1.461	.148
	Do you think that patients under your care are adequately informed concerning biosimilars to make informed choices?	.002	.027	.006	.058	.954
	Have you noticed how patients have not wanted to change to biosimilar adalimumab when they had originator?	.059	.085	.082	.695	.489
	Has your institution/healthcare system realised any cost savings by the introduction of adalimumab biosimilars?	-.026	.025	-.100	-1.008	.316
	In your environment, is the savings of biosimilar adoption used to better access or services to the patients?	-.024	.024	-.102	-1.002	.319

a. Dependent Variable: Would aligned EU-wide approaches on the authorisation of biosimilars, their substitution and the procurement of adalimumab biosimilars enhance uptake and access of biosimilar adalimumab?

Figure 4.5: Coefficients

The coefficients table presents the unstandardised regression coefficients (B), their standard errors, standardised coefficients (Beta), t-values, and significance levels for each predictor in the model estimating respondents' support for aligned EU-wide approaches to adalimumab biosimilar authorisation, substitution, and procurement (the dependent variable). The constant term (intercept) of B = 0.912 (SE = 0.222, t = 4.102, p < .001) reflects the baseline level of endorsement when all predictors are set to zero, and is highly significant, indicating that on average respondents exhibit a moderately positive predisposition towards harmonisation even in the absence of other measured factors.

Out of the 15 survey items that were put in as independent variables, no single variable met the traditional significance bar of p <.05. The predictor most closely approaching significance is Question 4 ("Have you any experience of delay in the use of biosimilar adalimumab because of regulatory processes in your country?"), with B = 0.177, SE = 0.090, t = 1.976 and p = .051. Even though it is slightly beyond the 0.05 threshold, this positive coefficient indicates that the respondents with regulatory delays would be more likely to say that they were in favour of EU-wide harmonisation, which is in line with the perception that national bottlenecks fostered demand since unified frameworks were preferred. The standardised Beta value, which is 0.187, states that it has a small effect size compared to the other variables.

Collectively, the results of the study indicate that although the stakeholders have diverse experiences and attitudes as provided by the description and correlation analysis, no survey item among those considered has a dominant and direct effect on harmonisation perceptions, even at the expense of others. It is consistent with the multifaceted barriers that have been listed in the dissertation and proposal, regulatory fragmentation, procurement distortions, stakeholder knowledge gaps, and economic incentives, showing that biosimilar uptake attitude is not decided by a single factor but a complex and interacting factors specific (Rieger *et al.*, 2024b). The significance of procedural bottlenecks at the national level, evident in the marginally significant role of regulatory delay. It supports the relevance of a national jurisdiction as a central driving force behind the quest to achieve EU-wide alignment (Bas and Duarte, 2024). Future studies may thus improve the measurement of policy-specific experiences and introduce more contextual variables to explain the residual variance and generate a greater degree of predictability concerning stakeholder support of biosimilar adoption strategies.

4.3 Findings

The detailed statistical data indicate subtle information about the attitudes of the stakeholders towards a harmonisation of policies regarding adalimumab biosimilar at the EU-wide level. The descriptive statistics illustrate the heterogeneous perceptions found across professional roles, regulation perceptions, and institutional practices, whereas there is a convergence of perceptions on regulatory delays, supply stability, and harmonisation advantages. Such a trend captures the idea of the dissertation of policing national policies that generate different stakeholder experiences.

Correlation analysis identifies substitution policy influence ($r=0.518$) and pricing policy sustainability ($r = 0.498$) as the strongest predictors of support for EU-wide alignment, corroborating the literature's focus on regulatory harmonisation and procurement reform as critical enablers. Negative correlations with professional experience ($r=-0.294$) suggest that seasoned practitioners may resist policy changes, potentially reflecting entrenched familiarity with existing national frameworks.

The regression model demonstrates statistical significance ($F = 4.196$, $p < 0.001$), with an adjusted R^2 of 0.281, indicating that 28.1% of the variance in harmonisation support is explained by measured factors. However, the substantial unexplained variance (71.9%) underscores the complexity of biosimilar adoption attitudes, suggesting unmeasured contextual influences such as institutional culture, budgetary constraints, and patient advocacy dynamics.

Notably, no individual predictor achieved statistical significance ($p<0.05$), with only regulatory delays approaching significance ($p = 0.051$). This observation supports the conclusion of the dissertation that the obstacles to biosimilar uptake are multidimensional and interconnected, which imposes the necessity to use complex policy measures to shift them, instead of merely specific solutions. The findings confirm the necessity of complex strategies entailing regulatory harmonisation, transparency in procurement, training of stakeholders, and long-term multi-layer involvement in adalimumab biosimilars access and affordability throughout European Union member states.

4.4 Discussion

4.4.1 Discussion of regulatory discrepancies in the approval and implementation of adalimumab biosimilar in the EU member states

European Medicines Agency (EMA) centralised marketing authorisation for adalimumab biosimilars in 2018 established a unified scientific evaluation process (Mascarenhas-Melo et al., 2024). However, national implementation varies markedly. Germany and France allow automatic substitution and friendly reimbursement, which results in fast biosimilar adoption, while Italy and Spain have restrictive substitution policies and inconsistent reimbursement levels that enable maintenance of originator control. In Bulgaria, reimbursement is restricted and the system of tendering is limited, weakening access even more, which characterises significant national heterogeneities in implementing recommendations despite all products being endorsed similarly at the EMA (Cordeiro et al., 2024). Such differences are the result of different interpretations of interchangeability: The countries that permit pharmacy-level substitution without prescriber input (Estonia and Poland) versus those that necessitate an explicit prescription of biosimilars by the physician to the explicit exclusion of automatic substitution, with Spain and Italy. These disintegrated policies create distortions in procurement that, in jurisdictions unwilling to open up to multi-supplier, longer-term contracting, there in single-supplier, short-term tendering leading to vigorous originator discounting and biosimilar exclusion of hospital tendering.

In addition, the availability of prescriber readiness is affected by non-harmonised guidelines of substitution and interchangeability. Moorkens et al. (2021) demonstrated that a lack of clear national directives correlates with lower physician confidence and slower biosimilar adoption, even when cost savings are realised. In contrast, countries with explicit “best value biological” frameworks (e.g., Ireland’s ambulatory ‘best value’ policy) show higher biosimilar utilisation post-exclusivity. This type of fragmentation in regulation ensures continuation of unequal access to patients and suboptimal competition, which compromises the goals of EMA in terms of creating biosimilar-driven affordability. Such disparities would be caught by harmonisation of national substitution policies, which is consistent with the strong totality of evidence approach by EMA and standardisation of tendering processes using transparent multi-supplier contracts. Unless harmonised reformation occurs, adalimumab biosimilars will delay fully realising the economic and clinical potentials of biosimilars in the European Union.

4.4.2 Pricing and market factors impacting the adoption of adalimumab biosimilar in the chosen EU states

Market forces, including pricing power and competition, have been the most crucial factors influencing the adoption of adalimumab biosimilars in European Union countries. Upon entry, biosimilar competition typically resulted in an average volume-weighted price reduction of about 9.2 to 9.3% per defined daily dose of TNF-alpha inhibitors such as adalimumab, but these gains have not led to significant market shares (Car *et al.*, 2023b). In France and Germany, favourable reimbursement policies that allow inexpensive substitutes- especially when combined with long-term, multi-supplier tenders- increase competitive pressure. This approach enables long-term price reductions for the originator and allows biosimilar suppliers to sustain profitable, long-term market presence. Conversely, in Italy, Spain, and Bulgaria, procurement systems tend to favour single-supplier arrangements and short-term purchases focused on low prices, which enable originator discounts and effectively exclude biosimilars despite EMA approval. Both this aggressive discounting by originator manufacturers and limited substitution policies reinforce the dominance of originators and limit biosimilar use.

Additionally, differences in national pricing policies affect stakeholder confidence. Countries with well-defined frameworks on value, such as Ireland's biological policy, see higher physician willingness to prescribe biosimilars compared to jurisdictions lacking transparent price signals. Pharmacists and hospital administrators note that non-harmonised rebate schemes and unchanneled discounts hinder procurement transparency, reducing competition among smaller biosimilar manufacturers. The market is further influenced by patient-facing factors: when savings are reinvested into improved services and patient education programs, patients- especially in Germany and France- are more willing to switch from originator Humira to biosimilars. Conversely, in regions where cost savings are transferred into general budgets without clear benefits, patients remain hesitant to accept substitution, which further limits biosimilar market penetration.

Altogether, the competitive landscape of adalimumab biosimilars is dictated by the interplay between the strategy of originator discounting, national design of procurement, and transparent cost savings. The effective alignment of the substitution laws, implementation of a multi-supplier tender, and coherent pricing actions are crucial to transforming the theories of long-term price reductions into successful biosimilar usage and equal patient provision in the EU member states.

4.4.3 Assessment of attitude of healthcare providers and patients on the safety and efficacy of adalimumab biosimilar

It can be seen that the approach to prescribing adalimumab biosimilars is characterised by the cautiousness of the fragmented confidence of healthcare professionals, which is indicative of larger issues in clinical practice. Marín-Jiménez et al. (2021) reported that only 55% of surveyed specialists felt "very confident" when initiating biosimilar therapy, with confidence closely tied to the clarity of national regulations and the availability of educational initiatives. This reluctance is further exaggerated by the long-standing concerns of immunogenicity and adverse events; more than 40% of the doctors in Belgium noted safety-related to the prescribing of biosimilars as a deterrent, and recalled that clinical evidence should be sound, and the interchangeability protocols should be clarified. Pharmacists resemble this caution: just a third dispensed biosimilars, and almost half did not feel educated enough to advise their usage, which proves the necessity of specific professional education.

On their part, patients are found to have low awareness but have conditional trust in biosimilars. Vandenplas et al. (2021), found that Belgian patients had encountered the term "biosimilar," yet among those informed, acknowledged that biosimilars match reference products in safety and efficacy. A strong majority expressed willingness to transition if their physician recommended it, contingent on receiving thorough explanations and accessible educational materials. This conditional acceptance can be put in the larger picture of information deficiency: most of the of patients require clear safety and efficacy data on the part of the healthcare provider, as concerns a move off of originator biologics, fearing unknown risks.

Most importantly, such attitudes demonstrate a gap between the theoretical equivalence and confidence in the real world. Although clinical trials and observational studies, such as Poquet-Jornet et al. (2024), demonstrate non-inferiority in immunogenicity and clinical outcomes after switching to biosimilar adalimumab, stakeholders remain unconvinced, often due to opaque procurement and rebate schemes that erode trust in cost-driven decisions rather than evidence-based practice. As pointed out in the literature review, aggressive originator discounting and single-supplier tenders cause distortions in the market, which adds to the professional scepticism concerning biosimilars. To overcome this attitudinal barrier, combination educational programs, price transparency policy, as well as harmonised exchangeability policy are a must. The absence of such actions will

only further undermine the potential of adalimumab biosimilars to introduce more access and save costs in the healthcare sector, as there will be an ongoing disbelief in the safety and efficacy of these types of drugs.

4.4.4 Formulation of evidence-based solutions that can enhance the biosimilar adalimumab accessibility and affordability in the EU

A policy framework based on centralisation should be further supported by enforceable principles of substitution and interchangeability that the countries of the EU have to adhere to in the face of regulatory fragmentation. Based on the positive relationship that was found between perceived policy inconsistency and uptake support ($r = 0.518$), harmonised directives should replace some rights on the pharmacy level should aiming to eliminate national differences and increase the speed of biosimilar implementation. In addition to the totality-of-evidence guidelines used by the EMA, these binding guidelines must impose the obligation to report openly and publicly any national policies regarding substitution and the real-world results of such switching. This plan addresses head-on the literature and survey findings of the barrier of fragmented national policies and provides homogeneous prescriber confidence and patient trust across the jurisdictions.

The reform of procurement should focus on multi-supplier, long-term contracting, not single supplier contracting, on bodies that are rich in competitive tendering, but not based on the lowest price. The findings by Leopold et al. (2020), ANOVA results ($F = 4.196$, $p < .001$) have indicated that procurement transparency is involved in increasing the number of stakeholders in supporting harmonisation. At the EU level, therefore, there are possible frameworks that may encourage member states to share in pooled procurement of adalimumab biosimilar products, which can use the scale effects with a predictable volume and stable cost. These pooled tenders would override the attacking originator discounting strategies that are now leaving out biosimilars and share among suppliers the market risk, maintain long-term competition, and strengthen the market.

Educational programmes aimed at reducing safety and efficacy concerns should be conducted to address knowledge gaps and provide further education to multiple stakeholders. The findings presented by Marín-Jiménez et al. (2021), where 55% physicians expressed confidence in the treatments, evidence that constant evidence-based training is necessary, with the incorporation of clinical trial data, pharmacovigilance reports, and switching protocols. At the same time, patient-directed programs, created

together with patient organisations, must provide understandable and convenient information on the equivalence and cost-efficiency advantages of biosimilars, responding to the conditional trust as disclosed in survey work with patients (Vandenplas et al., 2021). Integrating these programmes into national health systems will create an institutionally informed decision-making process and evade the possibility of immunogenicity fear, and synchronise the perception of stakeholders with the real world.

Lastly, reallocation of economic incentives towards reinvestment in the realisation of savings in patient care and system sustainability is important. The inconsistencies in reinvestment of savings on biosimilars are shown in the survey results (SD = 1.151) or reported as a variable institutional practice. A mandatory re-investment of savings in EU-wide savings with a requirement that a share of procurement savings that are linked to quality-of-care measures and improvement of access would institutionalise transfer of resources to patient service development, training, and monitoring facilities in the specialty, and increase capacity in the specialty. In conjunction with the sound health-economic assessments, such an action would transform the estimated theoretical savings of more than 1.5 billion euros per year into actual enhanced healthcare and shoulder stakeholders to implement biosimilars and guarantee equitable access in the European Union.

4.5 Summary

The chapter shows that although there is a consensus between healthcare providers and the patients regarding the necessity of regulatory harmonisation, cross-country differences in the experiences of transparency in the procurement process, pricing approaches, and views of safety are extensive. One of the key insights presented by correlation analyses is the impact that substitution policies and competitive pricing have on the harmonisation support, whereas by using regression models one can see how the measured factors have partial yet potent explanatory properties. The discussion can incorporate these findings into the literature-based barriers identified in the literature including policy fragmentation, tendering distortion and knowledge gap and helps reiterate why integrated solutions are needed. Finally, the chapter affirms the need of synchronising policy change, transparency in procurement, and specific education to increase the usage and equity of adalimumab biosimilar across the EU.

5 Concluding Thoughts on the Contribution of this Research, its Limitations and Suggestions for Further Research

5.1 Implications of Findings for the Research Questions

Research question 1:

The approval process for adalimumab biosimilars shows major regulatory differences between EU member states. The European Medicines Agency (EMA) offers a centralised approval system yet each EU member state maintains its own approach to biosimilar substitution and reimbursement which results in varying biosimilar market access. The combination of biosimilar substitution authorisation and favourable reimbursement systems in Germany and France leads to high biosimilar availability for patients. The biosimilar market access remains restricted in Bulgaria because of its strict policies. The existing differences between EU member states create obstacles for biosimilars' adoption consistency and prolong their implementation throughout Europe. The absence of harmonisation leads to confusion among healthcare providers and patients while delaying adoption and working against EU-wide biosimilar adoption. The research shows that regulatory fragmentation stands as the main challenge so harmonised guidelines or enforceable principles across member states would help address these problems to improve biosimilar adoption speed and quality. Health ministry and payer managers should take note of regulatory fragmentation by creating country-level substitution and reimbursement rules that follow EMA principles and implementing automatic pharmacy substitution for adalimumab when appropriate. They should also establish uniform prior-authorisation criteria with neighbouring states to decrease access time and minimise provider confusion.

Research question 2:

The adoption of adalimumab biosimilars throughout EU member states depends heavily on pricing elements together with market-related factors. The introduction of biosimilars results in substantial price cuts which can reach as much as 48% thus lowering treatment costs. The market penetration of biosimilars differs because originator companies use aggressive discounting strategies and different procurement methods and national reimbursement systems exist. Biosimilar adoption remains restricted in certain areas even though prices have decreased because patient and provider incentives do not support

broader adoption. The research shows that transparent multi-supplier tendering and pooled European contracts enable savings distribution and promote equal access to biosimilars. The combination of competitive pricing with clear market policies and broad stakeholder engagement will lead to the maximum utilisation of biosimilars for patient and health system benefits. Procurement leads should implement transparent multi-winner tenders with scheduled price-review clauses and enable regional pooled or joint purchasing. They should also align provider and patient incentives through gain-sharing or budget-retention for departments to achieve real uptake from lower prices.

Research question 3:

Healthcare providers and patients maintain conflicting views about adalimumab biosimilars which creates barriers to their adoption. Healthcare professionals demonstrate average knowledge about biosimilars yet they continue to doubt their safety and effectiveness and quality standards. The lack of understanding among healthcare providers leads to widespread misconceptions about biosimilars and some medical staff remain uncertain about transitioning patients from originator biologics. Patients tend to have limited knowledge about biosimilars yet they will trust them when their healthcare providers provide straightforward explanations and safety and efficacy reassurance. Survey results and literature show that education plays a crucial role because patients and providers become more willing to use biosimilars after receiving clear and accessible information. The evidence suggests that specific educational programmes and communication strategies must be developed to establish trust and correct false beliefs while fostering an environment that supports biosimilar adoption. Hospital managers and clinical directors should implement structured switching pathways that combine pharmacist-led education with clinician toolkits such as standard consent scripts, FAQ sheets, nocebo-mitigation guidance. They should also track uptake and adverse events in dashboards to build confidence through local data.

Research question 4:

Research evidence demonstrates multiple operational approaches to enhance EU accessibility and affordability of adalimumab biosimilars. Standardised regulatory policies combined with centralised guidelines would eliminate confusion and speed up the adoption process across different countries. The implementation of transparent procurement practices through multi-supplier contracts and pooled European tenders

promotes competitive pricing and expanded access to healthcare services. The implementation of structured switching protocols together with education programmes for healthcare professionals and patients helps to address knowledge gaps while building trust in biosimilars. The implementation of coordinated policy actions that involve all stakeholder groups including regulators and healthcare providers and patients and payers leads to collective buy-in and streamlined implementation. The evidence-based strategies will help EU member states overcome existing barriers to provide fair access to affordable treatment while achieving meaningful health system savings through biosimilar uptake support. National programme managers coordinating stakeholders should establish a cross-stakeholder steering group with clear milestones such as guideline publication, tender calendar, training completion rates and publish a public progress scorecard. They should also tie reimbursement bonuses to the achievement of safe switching and access targets.

5.2 Contributions and Limitations of the Research

5.2.1 Contributions

The research delivers multiple vital contributions to pharmaceutical policy and biosimilar adoption studies within the EU framework. The research delivers an extensive examination of regulatory barriers and market obstacles and stakeholder challenges which affect the availability and cost-effectiveness of adalimumab biosimilars. The research combines both updated literature review findings with original survey data to gather insights from regulators and healthcare professionals and patient groups. The research extends beyond clinical evidence by studying practical and systemic adoption issues through multi-actor perspectives that include policy fragmentation and procurement practices and educational barriers.

The thematic quantitative approach helps identify essential barriers and enablers which enables evidence-based recommendations for harmonised regulation and better procurement. The research presents policy recommendations together with educational approaches to address the differences between countries and stakeholders. The research stands out through its theoretical development and its practical recommendations which guide EU governments and healthcare providers and payers in their real-world decisions. The research demonstrates ethical rigor through its survey design and data privacy

measures and participant consent procedures which establish best practices for future studies in sensitive and regulated settings.

5.2.2 Limitations

The research study identifies multiple essential gaps but contains certain boundaries. The research depends on survey-based quantitative data from selected EU member states which might not reveal all local variations in regulatory or market practices. Future research needs to conduct individual country studies while collecting additional data from areas that have unique tender rules and prescribing standards to understand regional practices. The thematic analysis sample size provides adequate representation but it might not fully capture the diverse viewpoints within each stakeholder group. The future study should increase the sample size and include purposive quotas for each stakeholder group such as clinicians, pharmacists, payers, patients, industry to ensure balanced representation. The data collection period missed policy changes in certain countries while the research did not thoroughly investigate how AI affects regulation and the quick development of new biologics.

The research lacks specific economic modelling of cost savings because it relies on literature and survey responses which might overlook detailed financial effects. Future research should develop country-level budget impact models that incorporate actual procurement prices together with switching rates and utilisation data and validate these results against payer finance records. The survey response bias exists because people who strongly express opinions or have personal experiences tend to participate in surveys. The research had time and resource constraints which limited the scope of qualitative research and prevented additional interviews that could have provided more detailed insights about regional and institutional differences. A follow-on mixed-methods study should allocate resources for multi-country interviews and focus groups, using a common interview guide to compare regional and institutional differences. The research provides a strong base for additional studies while delivering practical suggestions to advance EU-wide biosimilar policy development.

5.3 Recommendations for Practice

The research findings deliver various operational suggestions to enhance EU-wide accessibility and affordability of adalimumab biosimilars. The recommendations have

immediate managerial value for healthcare administrators, procurement managers and policy decision-makers because they need to implement system-level reforms in practice.

Regulatory Harmonisation:

Health ministry managers and regulatory agency managers should establish standard EU-wide regulatory guidelines as their main priority. The European Medicines Agency should create binding directives which enforce uniform substitution and interchangeability standards for all member states (Slunge *et al.*, 2023). Regulatory officers at the managerial level need to verify national compliance while creating internal monitoring systems and releasing real-world switching results to maintain transparency and accountability.

Procurement Reform

Hospital administrators together with procurement managers should adopt multi-supplier long-term agreements instead of their current practice of single-supplier short-term contracts. The change stops originator companies from using aggressive discounting to block biosimilars from entering the market (Barbier, Simoens, *et al.*, 2021). The evaluation framework of procurement teams needs to be transparent to assess total value through supply reliability and patient outcomes instead of focusing solely on lowest price. European-level coordinated purchasing enables managers to achieve better prices and establish reliable supply networks.

Education and Training Programmes

All stakeholders require complete education programmes because healthcare providers require formal training about biosimilar safety together with their efficacy and switching protocols. Clinical experts can create this training content which should be integrated into electronic health records and clinical pathways (Reddy, 2024). Patient education materials need to be simple to understand and should exist in various languages. Professional medical societies need to actively promote biosimilar awareness while working to correct false beliefs about their safety and effectiveness.

Structured Switching Protocols

Hospitals require operational managers to create standardised switching protocols which guarantee safe patient transfers between originator and biosimilar products. The protocols

need to monitor clinical results including efficacy loss and adverse events. The managers need to establish formal patient consent procedures which include detailed documentation about the switch purpose and anticipated results. The managerial oversight system maintains both regulatory requirements and patient trust.

Stakeholder Collaboration

Healthcare managers and policymakers need to create advisory committees which include regulators together with healthcare providers, patients and pharmaceutical representatives. Managers should create shared decision-making frameworks while involving patient advocacy groups for education and policy development. The collaborative approach ensures policies meet stakeholder requirements and enhances public acceptance of biosimilars.

Financial Incentives

The reimbursement systems need redesign to make provider incentives match biosimilar adoption (Lobo and Río-Álvarez, 2021). Healthcare providers should receive shared savings benefits from biosimilar cost reductions. Insurance systems need to establish specific coverage rules which direct patients toward biosimilars during appropriate clinical situations.

Therefore, the recommendations show that successful biosimilar integration requires EU-level policy as well as managerial capabilities across regulatory bodies, hospitals and insurance systems to implement reforms. The achievement of equitable biosimilar access throughout Europe requires leadership effectiveness together with transparent procurement, structured training and collaborative governance. The success of these initiatives depends on political commitment, adequate funding, and consistent managerial oversight.

5.4 Recommendations for Future Research

In-Depth Qualitative Studies

Future research should include qualitative interviews and focus groups with diverse stakeholders—regulators, physicians, pharmacists, hospital administrators, and patients. These methods can uncover contextual factors and motivations behind biosimilar adoption that surveys may miss. The personal experiences of individuals along with

institutional cultures and local barriers will enhance quantitative findings to develop specific intervention strategies.

Longitudinal Economic Impact Analysis

The study used cross-sectional survey and literature data but future research needs to use longitudinal economic models to measure real-world cost savings and patient access over time. The tracking of budgets, utilisation rates, and health outcomes in countries adopting pooled procurement or multi-supplier contracts will yield robust evidence on financial and clinical benefits.

Comparative Policy Evaluation

The evaluation of early-adopter and laggard EU states through comparative case studies will show which policy elements lead to faster biosimilar uptake. A thorough policy analysis of legal frameworks and reimbursement rules and procurement practices will help identify best practices that can be adapted across other member states.

Effectiveness of Educational Interventions

The development of targeted education programmes proved essential for both healthcare providers and patients. Future research needs to create and evaluate particular training programmes through online modules and workshops and decision aids while assessing their effects on knowledge and attitudes and prescribing behaviour and switching rates through randomised controlled trials or pre-post designs.

Role of Digital Health and AI

Research should examine how digital tools together with artificial intelligence systems can enhance regulatory review processes and pharmacovigilance activities and individualised decision-making capabilities. Research studies should analyse how AI analytics predict market adoption patterns and detect off-label medication use and track immediate adverse events to enhance safety and trust levels.

Patient-centred Outcome Research

The research should focus on patient-reported outcomes such as quality of life, treatment satisfaction and adherence after switching to biosimilars. Mixed-methods studies can capture both quantitative measures and patient narratives to gauge long-term acceptance.

Global Harmonisation Impact

In addition, studies comparing EU experiences with non-EU regions like North America or Asia can assess the effects of harmonised global standards on market entry, price competition, and access, providing lessons for international policy alignment.

5.5 Final Conclusion and Reflections

5.5.1 Final Conclusion

The research investigated which elements determine EU member states' adoption of adalimumab biosimilars. The main obstacles to biosimilar adoption in EU member states stem from regulatory fragmentation and different procurement methods and pricing strategies and stakeholder attitudes. Countries that implement unified substitution rules and support reimbursement policies achieve better biosimilar adoption rates than nations with restrictive policies. Market transparency together with multi-supplier contracts prove necessary for biosimilar adoption success beyond competitive pricing strategies. The education of healthcare providers together with patients serves to build confidence while addressing existing misconceptions. Standardised regulations combined with transparent procurement and structured switching protocols and targeted training programmes will enhance both accessibility and affordability of evidence-based solutions. The implementation of these strategies collectively will assist EU states to address existing challenges while providing equal biosimilar access to patients and achieving health system cost reductions.

The research holds significance because it demonstrates how actual policy decisions affect medical facilities and drug distribution centres. The study provides policy makers and hospital leaders with a straightforward approach to promote safe biosimilar use through clear rules and open procurement and planned switching with effective communication. These steps when implemented will accelerate patient access while safeguarding supply and generate meaningful savings for additional healthcare needs. The framework together with measures developed in this study enables researchers to monitor progress over time while evaluating the most effective approaches between countries.

5.5.2 Reflections

The research gained strength through the combination of a broad literature review with newly acquired survey data. I achieved balance by involving regulators, healthcare professionals, and patients, who provided real-world perspectives. I used a quantitative thematic approach to identify distinct patterns which led me to specific recommendations. I discovered that policy and market interactions are complex because individual measures usually fail to achieve success on their own. Future research will involve gathering more qualitative data to gain better understanding of particular local aspects. My study provides immediate practical value to policymakers and health leaders despite the time and resource constraints. The success of future policy changes will depend on maintaining open communication with all stakeholders and continuously evaluating policy modifications. The adoption of biosimilar medicines in Europe for successful and sustainable use requires both collaborative approaches and well-informed flexible strategies.

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7 Appendices

7.1.1 *Appendix A – Literature Review Matrix*

Authors	Research Aims	Research Methods	Findings	Research Limitation	Relevance to This Research
Alsaif and Blumer (2025)	Examine prescribing and cost trends of insulin glargine biosimilars in UK primary care	Quantitative analysis of prescription and cost data	Biosimilar entry reduced prices, but uptake varied regionally	Focused on insulin glargine, not adalimumab; UK-specific	Illustrates biosimilar market dynamics and pricing impact
Barbier et al. (2020)	Explore stakeholder learnings to improve biosimilar understanding and adoption in Europe.	Survey and literature review	Knowledge gaps and misinformation hinder adoption; need for multi-stakeholder education	Limited to selected EU countries and stakeholders	Highlight the importance of education and stakeholder engagement
Barbier et al. (2021)	Assess knowledge and perceptions of biosimilars among Belgian pharmacists and physicians	.Survey research	Moderate awareness, persistent misconceptions, low confidence in biosimilars	Belgium-specific; self-reported data	Underlines provider attitudes as barriers to biosimilar uptake

Bas (2025)	Analyse innovative formulation strategies and regulatory/IP challenges for biosimilars	Literature review	New formulations affect competition; IP barriers delay entry	Focus on formulation, not direct market access	Explains how innovation and IP affect biosimilar market sustainability
Bas and Duarte (2024)	Examine international biosimilar regulations and AI use in oncology	Comparative policy analysis	Regulatory fragmentation persists; AI could harmonise processes	Oncology focus: limited empirical data	Shows regulatory discrepancies relevant to adalimumab biosimilars
Clarke et al. (2024)	Model cost-savings and access opportunities with adalimumab and tocilizumab biosimilars	Economic modeling	High conversion to biosimilars yields major savings and access gains	Model-based projections; real-world uptake may differ	Quantifies the economic impact of biosimilar adoption in Europe
Cordeiro et al. (2024)	Provide a regulatory perspective on biosimilar medicines	Regulatory review	EMA guidelines are comprehensive, but national	More descriptive than analytical	Details of regulatory fragmentation in biosimilar approval

			implementation varies		
Donnelly and Paek (2020)	Advocate for biosimilar adoption in clinical practice	Commentary	Education and practical support are key to adoption	Lacks empirical evidence	Supports the need for HCP education for biosimilar uptake
Edgar et al. (2021)	Identify real-world barriers and solutions to biosimilar adoption from the payer/provider view	Mixed-methods: interviews, case study	Coordinated education and incentives increase adoption	US-centric; limited EU data	Informs strategies for overcoming adoption barriers
Gherghescu and Delgado-Charro (2021)	Overview of EMA and FDA biosimilar regulatory approvals	Regulatory analysis	EMA has more biosimilar approvals; national-level barriers persist	Focus on approvals, less on post-approval dynamics	Compares EU/US regulatory pathways and market entry

C

Krstic et al. (2022)	Assess Swiss physicians' expertise and attitudes toward TNF-α biosimilars	Online survey	Varied expertise; concerns about efficacy and patient acceptance	Limited to Switzerland and TNF-α biosimilars	Reveals physician-level barriers to biosimilar adoption
Kvien et al. (2022)	Evaluate cost savings and access from biosimilar use	Policy analysis	Savings can expand access and ease the financial burden	Focus on potential, not realised, outcomes	Supports economic rationale for biosimilar adoption
Leonard et al. (2021)	Systematic review of HCP knowledge and acceptance of biosimilars	Systematic review	Knowledge gaps and misconceptions are common among HCPs	Heterogeneity in included studies	Highlights education as a lever for biosimilar uptake
Mascarenhas-Melo et al. (2024)	Overview of biosimilar development, quality, regulatory issues, and management	Review article	Biosimilars increase access but face regulatory and perception challenges	Broad scope, not adalimumab-specific	Contextualises regulatory and quality challenges for biosimilars

D

Moorkens et al. (2020)	Examine early/late adoption of infliximab/etanercept biosimilars in the UK	Survey analysis	Early adoption is linked to local champions and institutional culture	Focus on the UK and two molecules	Demonstrates local factors in biosimilar adoption patterns
Moorkens et al. (2021)	Analyse regional market dynamics of biosimilars in Germany	Market data analysis	Wide regional variation in biosimilar uptake; procurement strategies matter	Germany-specific	Shows procurement's role in biosimilar market dynamics
Niazi (2022)	Critique biosimilar approval guidelines and harmonisation	Policy and regulatory review	Lack of global harmonisation delays biosimilar entry	Focus on guidelines, not market outcomes	Explains regulatory barriers to biosimilar access
Oskouei and Kusmierczyk (2021)	Assess the importance of HCP education for biosimilar uptake	Review article	Education is key to overcoming provider resistance	Lacks new empirical data	Reinforces education as an adoption facilitator

E

Poquet-Jornet et al. (2024)	Evaluate the effectiveness and safety of adalimumab biosimilars in IBD	Real-world clinical study	Biosimilars are safe and effective in IBD	Single-country, disease-specific	Supports clinical equivalence for biosimilar adoption
Rieger et al. (2024)	Systematic review of barriers/enablers to biosimilar uptake via Actor Network Theory	Systematic review	Policy, incentives, and knowledge are key barriers/enablers	Theory-driven, may miss practical nuances	Integrates multi-actor barriers relevant to adalimumab uptake
Tachkov et al. (2021)	Assess the price and utilisation impact of biosimilars in Bulgaria	Quantitative analysis	Price drops after biosimilar entry, but limited utilisation	Bulgaria-specific; limited generalizability	Illustrates price-utilisation disconnect in biosimilar markets
Tesser et al. (2025)	Review switching from originator to adalimumab biosimilars	Literature review and expert synthesis	Switching is feasible and safe with structured protocols	Focus on non-US settings	Informs switching policy and clinical practice for adalimumab

Vandenplas et al. (2021)	Explore patient association roles in biosimilar information	Survey analysis	Patient associations key in education, but knowledge gaps persist	Limited to European associations	Highlights patient education as a determinant of uptake
Williamson et al. (2020)	Address oncologists' gaps in biosimilar use	Survey and commentary	Education and clinical guidance are needed for oncologists	Oncology focus; US-centric	Underscores the speciality-specific education needs
Wilsdon et al. (2022)	Develop a global roadmap for policy sustainability in biosimilars	Policy analysis and synthesis	Long-term contracts, transparent pricing are needed for sustainability	Broad, not adalimumab-specific	Informs policy recommendations for market sustainability
Woo et al. (2024)	Analyse budget savings from adalimumab biosimilar availability in 14 countries	Difference-in-difference econometric analysis	Biosimilar entry reduces expenditure, increases access	Focus on budget, not clinical outcomes	Quantifies the economic benefit of adalimumab biosimilars

Zhai et al. (2021)	Critically assess why US biosimilars underperform	Policy critique	Uptake hampered by rebates, slow adoption, policy gaps	US-focused	Offers cautionary lessons for EU biosimilar policy

Table 1: Literature Review Matrix

7.1.2 *Appendix B – Ethics Application and Survey Questionnaire*

Ethics Application & Declaration Form – Survey

DISSERTATION TITLE:
BIOSIMILARS OF ADALIMUMAB IN EU: ADDRESSING REGULATORY BARRIERS AND MARKET DYNAMICS TO ENHANCE ACCESSIBILITY AND AFFORDABILITY

RESEARCHER'S NAME: MANJUSHA SHAJIMON

PROGRAMME OF STUDY: MSc in Pharmaceutical Business and Technology

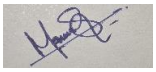
SUPERVISOR'S NAME: Alessandra Vecchi

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:

STUDENT SIGNATURE: 

DATE: 07/07/2025

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

For Supervisor:

X

I

Ethics Committee Approval Required: Yes No

SUPERVISOR SIGNATURE: 

DATE: 08/07/2025

For Ethics Committee (if required):

Ethics Committee Approval Given: Yes ☐ No ☐

ETHICS COMMITTEE MEMBER SIGNATURE:

DATE:

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

SECTION 1: DESCRIPTION OF RESEARCH STUDY

1.1 Purpose and objectives of research

Purpose: This research aims to analyse the regulatory barriers and market dynamics of biosimilars of Adalimumab in the EU to enhance their accessibility and affordability. The clinical and economic effects of adalimumab can hardly be doubted, an extensive exploration of barriers to the adoption of biosimilars is of paramount importance. The current study fills some of the most crucial knowledge gaps as well by determining how regulatory frameworks and market dynamics interact in European contexts, as well as how they are perceived by stakeholders. The research provides recommendations that policymakers, regulators, and healthcare providers can take to improve the affordability and accessibility of adalimumab biosimilars, incorporating the most recent statistical evidence and policy analysis. Finally, the work is aimed at voicing a more patient-centred, sustainable and equitable biosimilar market in Europe.

Objectives:

- To discuss regulatory discrepancies in the approval and implementation of adalimumab biosimilar in the EU member states.
- To evaluate the pricing and market factors impacting the adoption of adalimumab biosimilar in the chosen EU states.
- To assess the attitude of healthcare providers and patients on the safety and efficacy of adalimumab biosimilar.
- To formulate evidence-based solutions that can enhance the biosimilar adalimumab accessibility and affordability in the EU.

1.2 Research methodology:

J

This study is based on quantitative method to provide an accurate overview of the adoption of the adalimumab biosimilar in the European Union. The aim is to explore the complex and situation-specific phenomena through the study of the regulatory bottle necks and market relations that precondition the availability and affordability of the adalimumab biosimilar in the European Union. Survey will be used as a primary data collection methodology that allows exploring the experiences of the participants and their viewpoints in great depth, keeping the possibility to consider emerging topics when discussing them with the participants. The process of sampling begins with purposive techniques and narrows its focus on the people who have a direct exposure or related experience concerning adalimumab biosimilars. Categories within the sample include four major stakeholders:

1. Policy implementation and regulatory organizations (approvers of biosimilar)
2. Policymakers who are responsible in regard to controlling the activities of healthcare and pharmaceuticals
3. Physicians, pharmacists and other healthcare providers who prescribe or handle biosimilars
4. Representatives of patient group capable of communicating the experiences and concerns of patients

SECTION 2: POSSIBLE ETHICAL ISSUES

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

SUBJECT MATTER

Does the research proposal involve:

Research into specific company activities that would be deemed sensitive or confidential	No
Research into politically and/or racially/ethnically and/or commercially sensitive areas	No
Sensitive, personal, professional or corporate issues	No

RESEARCH PROCEDURES

Does the research proposal involve:

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

PARTICIPANTS

Does the research proposal involve:

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

<u>If you have answered NO to ALL questions, please go straight to Section 4.</u>

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

SECTION 3: STEPS TAKEN TO AVOID ETHICAL ISSUES

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 is clearly designed in order to obtain a broad and balanced display of insights associated with adalimumab biosimilar availability and affordability in the European Union (EU). With this purpose, the profile of participants is purposefully composed out of four various and overlapping spheres:

• Regulators: Persons who authorise, actuate and monitoring of biosimilar policies in both domestic and EU jurisdiction.

• Policymakers: They are mainly decision-makers who influence the regulations involved in the care of healthcare and pharmaceuticals with emphasis on biosimilars.

• Healthcare professionals: Healthcare practitioners, dispensers, or arbiters of adalimumab biosimilars in primary care.

• Patient-group representatives: The leaders or representatives of patient organisations who can represent patients in expressing their concerns, experience and expectations on biosimilar therapies.

The subjects will be identified through purposive sampling so that every group of subjects can have distinctive, informed and enlightening information about the regulatory, clinical, and experiential aspects of adopting biosimilar products. It is hoped that these stakeholders, who have a direct interest or stake in the area of biosimilar policy and practices would not only enable the cataloguing of challenges affecting accessibility and affordability in the various EU healthcare settings, but would also help clear up predispositions and create actionable recommendations that would help improve accessibility and affordability.

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

To compile the participants in such a study, the purposive sampling approach shall be used with participants being selected on the basis of having expertise or experience with regards to the adalimumab biosimilars in the European Union. Qualified applicants, or, in other words, regulators, policymakers, healthcare providers, and representatives of patient groups will be selected based on their professional relationships, institutional ties, and publicly maintained lists of related groups.

The first contact will be done through personal email and other professional messaging apps. The consent for participating in the study will be given as a question in the survey. Other communication through email or professional network sites (e.g., LinkedIn) can be implemented to boost the respondents and indeed deal with any concerns.

In all these interactions, the communication shall also be done with respect and according to the ethics so that the participants are comfortable and fully communicated prior to agreeing to participate in the research.

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

5.2 **Informed Consent Form (ICF) for participants**

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

No. my research study involves online surveys. The survey does not require signed consent. Consent will be included in the online survey as follows:

1.Do you consent to participate in this study?

- Yes, I consent to participate.
- No, I do not consent to participate

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?

Data Storage

Any research data, such as audio recording, thematic notes collected out of the survey, will be stored safely in password-protected devices and on encrypted cloud storage as per the regulations established by the institution. It will only be accessed by the main researcher and the supervisor. The data shall remain in storage ten months after the end of the study and summitting this research. Thereafter, every information will be destructed and thus maintaining confidentiality.

Data Protection Management

To address the problem of data protection, it will be ensured that the General Data Protection Regulation (GDPR) is followed strictly. The identity of the participants will remain anonymous throughout all the reports and the personal identifiers will be taken away as early as possible in data processing. An informed consent will be obtained and the purpose and storage as well as use of data will be explained. Analysis and publication of only aggregated, anonymized results will be provided, and the responses of a particular person will be confidential and untraceable.

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?

No

7.2 **Student consent**

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

Yes

SECTION 8: RECORDING AND RETENTION OF DISSERTATION VIVA

8.1 **Viva Recording**

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

SECTION 9: DOCUMENT CHECKLIST

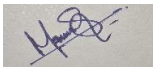
NOTE: Applicants must attach the following documents in electronic format to the appendix.

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

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

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

For Student:

STUDENT SIGNATURE: 

DATE: 07/07/2025

Survey questionnaire

1. What is your professional role?

o Physician

o Pharmacist

o Hospital administrator

o Payer/Policy maker

o Other (please specify)

2. How many years of experience do you have in your current field?

o Less than 5 years

o 5–10 years

o 11–20 years

o More than 20 years

3. Do you think that national regulations to biosimilar vary so much compared with that of EU?

o Strongly Agree

o Agree

o Neutral

o Disagree

o Strongly Disagree

4. Have you any experience of delay in the use of biosimilar adalimumab because of the regulatory processes of use in your country?

o Yes

o No

5. Does non-harmonised policy on substitution and interchangeability influence your readiness to prescribe/ dispense bio-similar products?

o Yes

o No

6. Does your institution have transparent and inclusive procedures of procurement or tendering to biosimilar suppliers?

o Strongly Agree

o Agree

o Neutral

o Disagree

o Strongly Disagree

7. Are you keen that the existing pricing policy promotes a sustainable competition between the producers of biosimilars and original manufacturers?

o Yes

o No

8. Has your facility developed shortages or instability on biosimilar adalimumab?

Q

o Yes

o No

9. Are you satisfied with the level of safety and efficacy of adalimumab biosimilar information?

o Yes

o No

10. Does a fear of immunogenicity or adverse effects present a significant obstacle to prescribing biosimilar adalimumab practice?

o Strongly Agree

o Agree

o Neutral

o Disagree

o Strongly Disagree

11. Do you think that patients under your care are adequately informed concerning biosimilars to make informed choices?

o Strongly Agree

o Agree

o Neutral

o Disagree

o Strongly Disagree

R

12. Have you noticed how patients have not wanted to change to biosimilar adalimumab when they had originator?

o Yes

o No

13. Has your institution/healthcare system realised any cost savings by the introduction of adalimumab biosimilars?

o Strongly Agree

o Agree

o Neutral

o Disagree

o Strongly Disagree

14. In your environment, is the savings of biosimilar adoption used to better access or services to the patients?

o Strongly Agree

o Agree

o Neutral

o Disagree

o Strongly Disagree

15. Would aligned EU-wide approaches on the authorisation of biosimilars, their substitution and the procurement of adalimumab biosimilars enhance uptake and access of biosimilar adalimumab?

S

o Yes

o No

Sample Size Calculations

Cochranes Formula

$N = Z^2 \times P \times (1-P)/E^2$

- N = Sample Size
- Z = Z-score for Confidence Level (1.96 for 95%)
- P = Estimated Population Proportion
- E = Margin of Error (0.05 for 5%)

Given Parameters

- Desired Sample Size (N): 100

Calculation

$n0 = (1.96)^2 \times 0.10 \times 0.90/(0.06)^2$

$= 3.8416 \times 0.09/0.0036$

$= 0.345744/0.0036$

≈ 96.04

Result

A sample size of approximately 96 is required. Rounding up, would use N = 100 for survey.

T