Barriers that Restrict Patient Involvement in Drug Development: An Industrial Perspective

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

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"Barriers that Restrict Patient Involvement in Drug Development: An Industrial Perspective" submitted for MSc in Pharmaceutical Business and Technology is the result of my own work and that where reference is made to work of others, due acknowledgment is given.

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LIST OF ABBREVIATIONS

ARHQ	-	Agency for Healthcare Research and Quality
CFF	-	Cystic Fibrosis Foundation
CHMP	-	Committee for Medicinal Products for Human Use
COA	-	Clinical Outcome Assessments
CTTI	-	Clinical Trial Transformation Initiative
DART	-	Dystrophy Annihilation Research Trust
EMA	-	European Medicine's Agency
EPF	-	European Patients Forum
EUPATI	-	European Patients Academy on Therapeutic Innovation
EURORDIS	-	European Organisation for Rare Diseases
FDA	-	Food and Drug Administration
GDPR	-	General Data Protection Regulation
GSK	-	Glaxo Smith Klein
ICF	-	Informed Consent Form
IT	-	Information Technology
NIH	-	National Institute of Health
NORD	-	National Organisation for Rare Diseases
PCORI	-	Patient-Centered Outcome Research Institute
PCWP	-	Patients' and Consumers' Working Party
PDUFA	-	Prescription Drug User Fee Act
PED	-	Patient Experience Data
PFDD	-	Patient Focussed Drug Development
PIDD	-	Patient Involvement in Drug Development
PIL	-	Patient Information Leaflet
PLC	-	Patient Leadership Council
PPI	-	Patient and Public Involvement
PRO	-	Patient Reported Outcomes
R&D	-	Research and Development
SOP	-	Standard Operating Procedures

Abstract

Objective: To explore the barriers restricting the implementation of patient involvement in drug development (PIDD) from an industrial perspective and to get insights on knowledge and awareness of pharmaceutical employees around PIDD and its various facets.

Methods: A questionnaire-based survey (n=51) was conducted among the pharmaceutical employees currently working in Research and Development, to seek information regarding barriers pertaining to patient involvement in drug development. The study participants were evaluated for their understanding and awareness around the subject to get insights on the persisting knowledge gaps. The data was analysed descriptively and interpretatively, based on the type of responses obtained.

Results: In the study, 74% of the respondents considered lack of dedicated groups as a likely factor hurdling the execution of PIDD. In addition, a total of 62% of the employees corresponded lack of industrial confidence in patient knowledge and skills to hinder the effective industrial implementation of the concept, while 16% of the participants considered proper representation of patient population for PIDD activities unlikely to cause hurdles. Insights on participant's knowledge and awareness on PIDD and its support organisation, revealed it to be average, considering their close associations with drug development activities. Recommendations for improving the current state of patient involvement in drug development were primarily directed towards enhancing knowledge base around the topic, reforming the current industrial practices to better involve patients and strengthening regulations around PIDD.

Conclusion: Despite increasing efforts from patient organisations in promoting PIDD within industrial practices by empowering patients through trainings and by coming up with recommendations to recognize patients as equal partners in the venture, there still exists barriers that hinder its practicality. Bridging the gap between the conceptual theories and functionalism is necessary and requires identifying the factors posing challenges and overcoming them by establishing means to improve patient involvement. Assessing the value of methods offered for PIDD execution, expanding the population range and utilising information from regulatory database to gain insights on the state of PIDD, allows for further research.

Keywords: patient involvement, drug development, decision making, barriers, patient organisation, patient advocacy groups, patient centered, product lifecycle, regulatory bodies, outcome measures, stakeholders, industrial perspective, clinical research.

CHAPTER 1: INTRODUCTION

1.1 Overview

"It is more important to know what sort of person has a disease than to know what sort of disease a person has."

- Hippocrates

Drug development is the road to offering patients effective healthcare options by reimagining medicine. Meeting the needs and expectations of end users is the sole purpose of every industry, which is also true for pharmaceutical business. Prioritising developmental strategies at an early stage helps in better decision making and developing functional study designs, thereby preventing late stage failures. Drug development, being a rigorous and time consuming process, needs to be conducted methodically, meeting the required regulatory standards, to deliver high quality, effective products. (Hoos *et al.*, 2015) The increasing complexities of the process, with regards to regulatory stringency, manifests the need for ensuring product safety, efficacy and quality across all stages of the lifecycle. (Lansdowne, 2020)

The product lifecycle mainly comprises of five stages as shown in Figure 1, namely, drug discovery, preclinical, clinical, regulatory review and post approval. Clinical trials consume the maximum time in the drug development process and is itself comprised of four phases. While phase 1 determines safety in a small population, phase 2 is utilised for conducting extended safety studies in a comparatively larger population and acquiring efficacy data. The findings from phase 3 ensure product effectiveness in comparison to the pre-existing treatment options for a particular disease. Larger population group allows for the identification of rare observations such as unexpected adverse effects. Phase 4 of the trial assesses trends in the long term drug effects, after it is on the market.

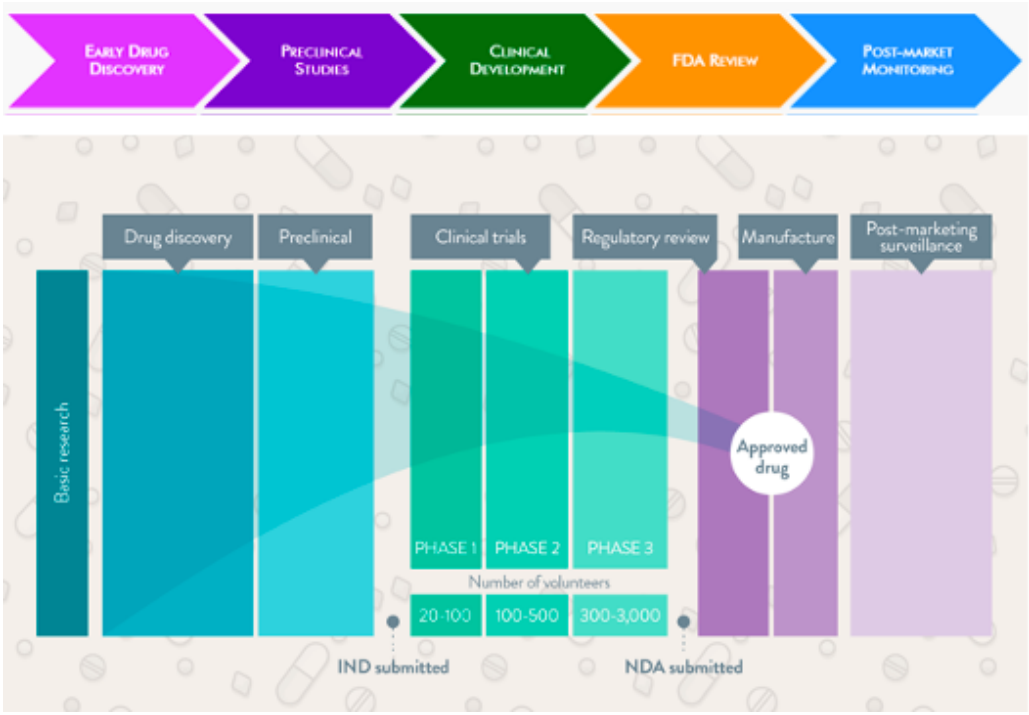

Figure 1: Stages of Drug Development (Lansdowne, 2020)

The predominant culture of research incorporates patients only as trial subjects and considers them a source of data, by conducting clinical investigations on them, rather than with them. (Sacristán *et al.*, 2016) However, the recent shift in pharmaceutical practice in considering patients as protagonists in the process, requisites their active involvement in research activities. The industry is entrusted with developing transformative medicines to improve patients quality of life and satisfy all the stakeholders involved in the process, while adhering to the regulatory standards. In addition, the burden of increased cost and time exhausted, due to stricter regulations, gives a more so reason for the industry to outperform in the area by changing the practise of medicine to a more favourable and sustainable method in order to remain profitable and competitive.

The concept of patient involvement in drug development (PIDD) aims to amplify patient voices and address their needs, through collaborations between various stakeholders in product lifecycle and patients, to create newer treatment options. This idea was originated post HIV/AIDS epidemic in 1980s, as a result of a protest by

affected patients to reflect their disappointment at their unmet medical needs. This lead to the formation of disease-specific patient advocacy groups. The trend then followed for cystic fibrosis, where the funding and development of innovative treatment for the disease was in collaboration with a patient advocacy group, namely Cystic Fibrosis Foundation (CFF). (Getz, 2019)

Recent years have seen growing support for patient involvement in drug development, from business sponsors and regulatory agencies by their actions of developing newer frameworks and initiatives. In the United States, the mandates for patient-reported outcomes for clinical end point measurement to solicit patient inputs marked the inception of approaches to patient centricity. While Patient-centred Outcome Research Institute's (PCORI's) guidance tools and Patient Focussed Drug Development's (PFDD's) contributions to risk-benefit assessments through interpretations of patient inputs, are adding to the momentum of changing healthcare practises in the US, the European regulations has other ongoing plans to enhance patient involvement, one such being Patients' and Consumers' Working Party's (PCWP's) platform for patients to put forward their real time experiences and suggestions regarding regulatory decisions for pipeline and marketed drugs. TransCelerate-Biopharma, a consortium of 19 pharmaceutical companies, is a great example of the most recent industrial effort towards encouraging, integrating and managing the concept of patient involvement in drug development.

The concept of patient involvement in drug development is based around three core principles: relevance of data obtained from people living with a condition, control given to them through transparency and convenience in concept implementation without any added burden. It unprecedently collaborates all the stakeholders in drug development process – sponsors, patients, advocacy groups, payers, investors, regulatory bodies – towards the realisation and mobilisation of the concept to be a mutual responsibility.

Previous studies describe the various industrial initiatives towards incorporating patient inputs that have been planned and piloted, through the establishment of patient advisory boards, telemedicine, conducting interviews, feedbacks and virtual communications, in order to better understand the unmet medical needs, jointly set the plan of action for research, and ensure support for financial requirements associated with these initiatives. (Getz, 2019)

Thus, the growing interest of healthcare stakeholders towards incorporating patient inputs in drug development as a step in improving the practise of scientific research with the establishment of systemic tools, strategies, frameworks and guidelines to positively impact patient health outcomes is encouraging. However, considering the fact that with more than 70 initiatives currently in place, the overall reflection of its potential benefits and utilisation is still not satisfactorily justified in regards to patient involvement in the industrial setup. (Lowe *et al.*, 2016) Therefore, identifying knowledge gaps and barriers posing hurdles in the effective execution and progress of the area is key in tackling the underlying issue.

1.2 Research Purpose

This study was undertaken with the aim of identifying various barriers restricting patient involvement in drug development and exploring the industrial mindset on the subject by obtaining insights on the knowledge and awareness of pharmaceutical employees to improve the practicality of the concept. Risk of unmet medical needs, rise in drug prices, regulatory stringency and time constraints, all contribute to an added development burden. For the pharmaceutical industry to remain profitable and competitive, while adhering to regulations, providing value adding services is key so as to improve the relevance and quality of scientific research by aligning to patient needs. Patient involvement in drug development is one such approach capable of

improving patient lives, regardless of having to make additional efforts, rather utilising the most underused resource in scientific research.

Though the outcomes of involving patients in drug development is thought to be promising by various patient organisations and regulatory bodies, there still remains a gap in the system that prevents its complete inclusion in the industrial setup. The author thus carried out this study to address the reality of knowledge and awareness around PIDD and the cause of its stunted growth within the pharmaceutical world.

1.3 Significance of the study

The cultural shift observed in the healthcare system of keeping patients at the centre of research, demands companies to allow end users define value of service provided. Therefore, understanding patient needs and expectations is vital in aligning all facets of drug development to patient preferences. Incorporation of patient inputs in health technology assessments as a step taken in Europe and the United States, towards value creation demonstrates efforts apropos maximisation of concept utilisation across industrial practice, however, the vastness of the healthcare system offers larger scope for improvement.

Surveying pharmaceutical employees in identifying barriers restricting patient involvement in drug development should give an insight on the industrial perspective. Even though some studies have been previously conducted among pharmaceutical leaders, the targeted number was comparatively smaller. Representing a larger group of participants from various businesses with varied levels of experience is believed to provide more uniform viewpoint on the subject. Literatures on evaluation of the current state of PIDD also demonstrated a major gap in establishing subject knowledge from an industrial perspective. Regardless of the fact that there are innumerable sources of information available on patient involvement in drug development,

understanding the level of knowledge and awareness regarding the same, is important in evaluating if the information is translated adequately. Even though several patient organisations, specifically, European Patients Academy on Therapeutic Innovation (EUPATI) and Clinical Trial Transformation Initiative (CTTI) are vigorously working towards empowering patients in developing their scientific knowledge base, lack of industrial confidence in patient skills was observed to be a factor posing challenge in the implementation of the concept. In addition, getting insights on the knowledge and awareness of pharmaceutical employees in relation to their understanding of the subject and its potential benefits in drug development, will help in comprehending the extent of its correlation with industrial reluctance as a barrier in drug development.

1.4 Research Objectives

1. To identify the barriers restricting patient involvement drug development by collecting responses from employees of pharmaceutical companies.
2. To understand the industrial mindset towards patient involvement in drug development and its various facets, by getting insights on the knowledge and awareness of pharmaceutical employees.
3. To collate recommendations from industrial employees regarding ways to improve patient involvement in drug development.

1.4.1 *Research Questions:*

1. How aware are the industrial R&D employees about the concept of patient involvement in drug development?
2. What are the barriers that restrict patient involvement in decisions relating drug development within the pharmaceutical industry?
3. What recommendations would help to improve involvement of patient in drug development?

1.5 Structure of the study

The research was carried out using a questionnaire, which involved both open and closed questions to collect qualitative and quantitative data respectively. The questionnaire was administered to pharmaceutical employees working in research and development division.

The questionnaire was divided into five sections:

1. First section sought information on demographics including employment details and level of experience.
2. Second section sought information on awareness of Patient Involvement in Drug Development and its various facets.
3. Third section sought information on knowledge around Patient Involvement in Drug Development.
4. Fourth section sought information on barriers to the implementation of Patient Involvement in Drug Development.
5. Fifth section sought recommendation on ways to improve Patient Involvement in Drug Development.

While the qualitative questions were used to contemplate results so as to form better conclusions by effective interpretation of collated data, quantitative questions explored the study population and described its characteristics in regard to patient involvement in drug development.

1.6 Conclusion

There are constant efforts on behalf of several organisations and regulatory bodies to support and facilitate the practise of patient involvement in drug development and its related aspects, by building a solid base for its industrial implementation. Understanding the barriers restricting incorporation of patient inputs within the process of drug development, from a pharmaceutical employees' perspective, will help in getting industrial insights, further assisting in framing solutions specific to industrial practise, so as to improve the quality of products delivered.

CHAPTER 2: LITERATURE REVIEW

2.1 Introduction

The pharmaceutical Industry is a business licensed for research, development, manufacture and marketing of medicinal products, including biopharmaceuticals, for human use. The current trend in the economic development of the world is based around information and knowledge. As of today, healthcare economy is the major contributor, after IT industry, in the technology sector. (Dorocki, 2014) Unlike many other sectors of the economy, pharmaceutical industry is highly regulated and requires its products to be safe for use and of high quality. There are several other legislative aspects, such as patent rights, copyright and trademark, to it as well. (Agarwal and Karwa, 2018) The emergence of newer technologies, discovery of newer molecules, novel business and product strategies are adding to the overall expansion of the industry, making it one of the fastest growing sectors within the economy. (Dorocki, 2014) – See Figure 2.

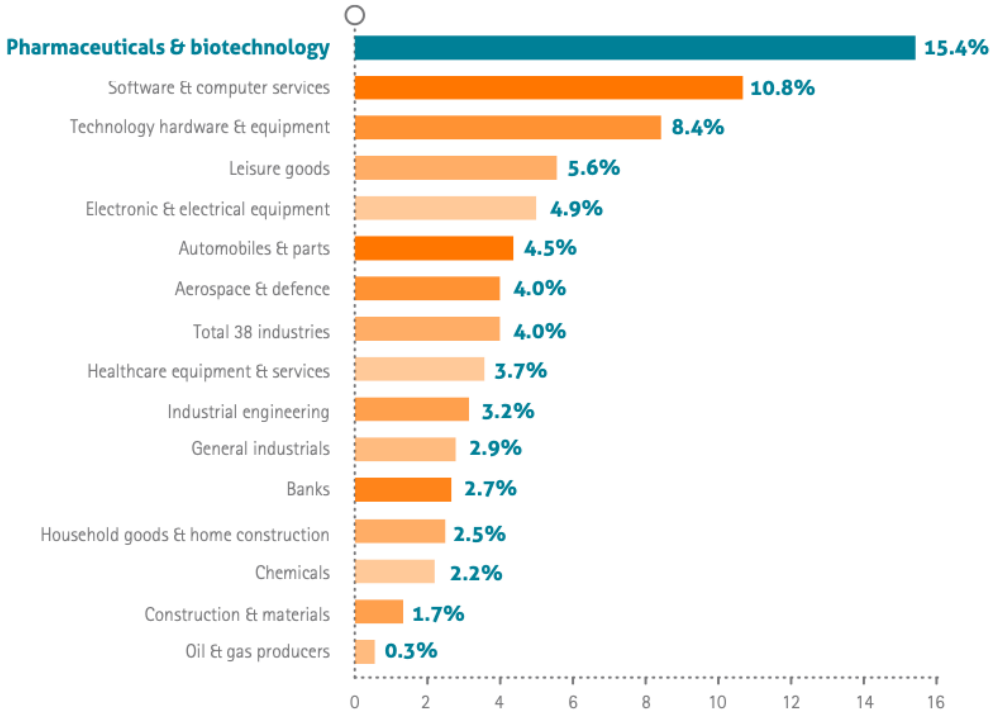

Figure 2: Ranking of Various Sectors of Economy (EFPIA, 2021)

Research and Development (R&D) is a key business activity of the pharmaceutical industry. Not to mention that other activities such as regulatory submissions and approvals, investments and sales & marketing are also important. However, to withstand industrial competition, pharmaceutical companies must have a strong R&D base. It is by increasing total income and optimising expenditure that pharmaceutical companies achieve competitive advantage over its competitors. This is brought about by consistent innovation (newer drug molecules) and higher production. (Teramae *et al.*, 2020)

R&D covers majority of the overall business timeline (approximately 12-14 years), of which clinical trials take up about half the time. The stringency by the regulatory authorities, with regards to clinical trials is the biggest challenge faced by pharmaceutical companies recently, as it has drastically impacted the success rate of newer molecules. This decline has resulted in an increase in the expenditure of approved drugs. (Teramae *et al.*, 2020) Therefore, keeping up with the increasing consumer demand, regulatory expectations and sustaining the pharmaceutical market by competing with a large number of players, is challenging for the industry. (Dorocki, 2014)

Even though, there have been challenges, the pharmaceutical industry has seen tremendous growth in the recent past (Figure 3). The strive to strengthen its scientific base by implementing innovative technologies and reimagining medicine, has helped the industry handle these challenges in a better way. Improved access to healthcare has considerably boosted global market sales in the recent years with an yearly exponential growth rate of 7.8% (PWC, 2020). The global statistics indicate that the revenue generated by the pharmaceutical industry in 2019 totaled to 1.25 trillion US dollars (Matej Mikulic, 2020), which is significantly high when compared to the numbers in 2001 (390 billion).

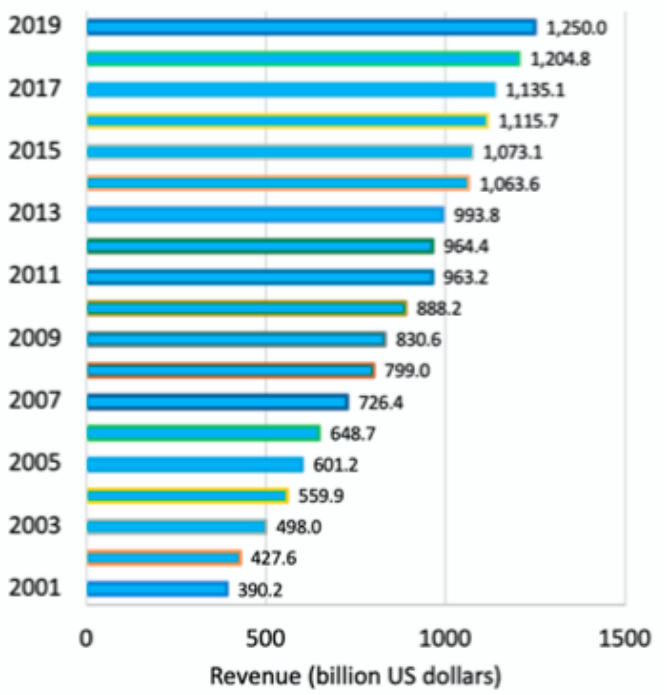

Figure 3: Revenue generated by Pharmaceuticals globally from 2001 to 2019 (Peña, Zavala and Ruelas, 2021)

Apart from technological advancements, the industry is also witnessing a shift in its approach to healthcare as a result of increased pressure from the regulators to develop products that are in the best interest of individual patients. Therefore, partnering with patients and utilising their experience and knowledge of the disease should be emphasised in industrial practice so as to empower them and recognise their importance in drug development. (du Plessis *et al.*, 2017)

2.2 Patient Involvement in Drug Development (PIDD) and its current state in the Pharmaceutical Industry

The concept of Patient Involvement in Drug Development (PIDD) involves purposefully incorporating patient's ideas, opinions, expectations, needs and experiences into the process of drug development. This is achieved by systematically collecting real life inputs from patients and identifying ways to enhance treatment options by utilising the information to assess potential risks and benefits involved. (CDER, 2020)

In the recent years, individualised treatment options have paved way for patient centric approaches to medicine. Even though this is prevalent within medical practice, there is not much encouragement and implementation of the same within the industrial setup. Societal Perception that pharmaceutical industrial activities do not have as much of a direct impact on people's lives as medical care, is one of the reasons for its poor industrial acceptance and implementation.(Sacristán *et al.*, 2016)

Traditionally, patients have only been utilised as trial subjects, however, lately, this is questioned because even though patients are the end users, they still remain the most underused resource in the healthcare system. This problem is identified to be majorly associated with regulatory restrictions. It is high time that clinical trials be carried out with patients instead of, on them. Some pharma companies, such as Novo Nordisk, are taking steps to break this monotony by establishing a patient advisory board within the organisation, however, this practice is restricted to just a few companies. Understanding the reason for reluctance will help in bringing solutions for the problem. (Hansen, Nørgaard and Hallgreen, 2019) Another example of practical implementation of patient involvement in drug development is at Astra Zeneca. The company, in collaboration with PatientsLikeMe, is connecting 30000 patients from various disease specific areas, for its research purposes. It has also formed patient network groups to encourage organisation's product lifecycle team to develop product solutions collaboratively. (du Plessis *et al.*, 2017)

With advancements in science & technology, there is much information available online, which has increased public knowledge and awareness, especially among patient groups. However, information regarding realistic patient experiences is still lacking. Connecting with patients to gather these real time data, knowing their perspective about a disease and extracting their needs and expectations from a product, will help in efficient decision making by getting a holistic view for developing efficient treatment options.

Self-injection devices are a route of administration that has faced several challenges related to injection phobias, misleading treatment assumptions and incorrect administration. Patient involvement in the form of feedbacks, has helped some pharma companies in combating issues related to these challenges, majorly adherence. Such feedbacks are helping companies to come up with various innovative administration options such as prefilled syringes, pens etc. Offering a range of products, aids in choosing the most appropriate device for individual use by patients. (Bemt *et al.*, 2019)

Even though, there have been some companies that have attempted to involve patients in research other than just as trial subjects, there is still a greater scope for improvement. It not just helps with easier decision making, but also aids in better understanding of patient needs. Patients are the ones who closely experience a drug reaction or device related challenges. Therefore, utilising their real time experience to create and develop newer products or devices, with an aim of combating existing product/device related issue, not only saves time but offers better value to patients. Such an approach would aid in minimising cost and creating value.

Various pharmaceutical companies have engaged themselves in outreach programs that involve creating awareness about their products, however, such initiatives are generally part of the marketing strategy and patient education, which are majorly beneficial for the company and its product. However, involving patients in drug development related decision making, not just helps the company in better understanding the customer demand, but also helps the customers by offering better value adding products, that are capable of improving patient lives. (Lowe *et al.*, 2016)

In a study conducted in Germany that assessed patient and researchers' expectations from patient and public involvement in developing drugs for urinary tract infection (UTI), patients put forward their concerns about their present roles in decision making

relating drug development and their desire to be able to openly express themselves, their experiences and expectations, so as to have an impact in the current drug development strategies. On the other hand, researchers expressed their concerns regarding setting up agendas and clarity of individual roles. These conflicting motives can serve to better anticipate any hinderance in the implementation of idea. (Schilling *et al.*, 2019)

2.3 Initiatives by Regulatory Bodies and Patient Advocacy Groups towards PIDD

Stakeholders involved in drug development believe that there is a greater scope for effectively implementing and encouraging patient involvement in drug development (PIDD). Despite the increasing demand for realistic evidence generation, patient centricity and individualised treatment options, there lacks a proper functional framework for engaging patients in drug development. Involving patients in stages of product lifecycle will help eliminate systemic loopholes of scientific research, such as high cost, lack of effective treatment options and lack of adequate and reliable evidence, to a subsequent level. It is true that deeply understanding their disease condition in terms of the challenges they face on a regular basis, adverse events, problems with drug administration and dosing frequency, meeting their expectations and providing implementable solutions to these problems is key in serving patients and improving their quality of life, to the maximum efficiency. It is believed that patient organisations, such as European Patients Forum (EPF), European Organisation for Rare Diseases (EURORDIS) and National Organisation for Rare Diseases (NORD), that are enriched with a diverse pool of information and real time evidence gathered from patients, have immense potential to contribute to the upcoming revolutionary changes in the future. (Hoos *et al.*, 2015)

In Europe, the European Patient's Academy on Therapeutic Innovation (EUPATI) initiative encourages patient participation and involvement in drug development activities. Being a multi-stakeholder organisation, it helps in bringing together inputs from expert minds and patients in order to enrich the quality of evidence generated. As part of the initiative, guidance documents are formulated that describe where and how patients and their inputs can be integrated within the 4 major areas of drug development process: Research & Development, Ethics Committee, Regulatory Authorities and Health Technology Assessments. (Haerry *et al.*, 2018) EUPATI also provides patients with adequate training via access to online libraries and toolboxes so as to enhance their capabilities to advise on the various aspects of drug development such as pharmacovigilance, risk-benefit assessments and clinical trials. (Hoos *et al.*, 2015)

As far as enhancing patient involvement in clinical trials is concerned, 'Clinical Trials Transformation Initiative' (CTTI) is a public-private partnership between FDA and Duke University that is working towards formulating patient centric practices and frameworks for clinical trials. Despite the fact that the concept of patient centricity is widely talked about, there are only a handful of organisations that practice and implement it, especially in clinical trials. (Hoos *et al.*, 2015) In order to recognize patients as equal partners in the venture and promote their involvement in translational research, CTTI has come up with recommendations for all stakeholders, specifically sponsors and patient groups. Following are the key points from the recommendations: (CTTI, 2015) – See Table 1.

Organisation/ Body	Recommendations
All Stakeholders	• Engagement of patients at the early stage of drug development i.e., at the planning phase. • Formulating a clear plan, defining expectations and distinguishing individual roles and responsibilities. • Building trust and maintaining transparency. • Collaboration among multiple partners to promote pipeline enrichment. • Establishing effective policies to manage conflicts of interest.
Sponsors	• Integrating patient involvement strategies into ongoing projects in pipeline and creating awareness about the impact of patient inputs in drug development within the organisations. • Aligning the expertise of patients and patient groups as per the requirements of ongoing projects. • Ensuring equal partnership of patient groups throughout the product lifecycle. • Establishing effective collaboration, consistency and communication between the sponsor and patient group. • Assessing the impact of PIDD. • Establishing and maintaining ongoing relationships.
Patient Groups	• Taking charge of representing patient's opinions and inputs to stakeholders on relevant research interests. • Proving and expressing one's value and expertise by actively taking part in relevant research activities and forums. • Delivering valuable inputs to stakeholders who align to similar goals.

Table 1: CTTI's Recommendations for PIDD

CTTI's Patient Leadership Council (PLC) is a group of leaders from various patient organisations engaged in activities relating various therapeutic indications. (Hoos *et al.*, 2015) CTTI in conjunction with its Patient Leadership Council (PLC) also published a prioritization tool for identifying key areas that offered opportunity for patient groups and sponsors to collaborate. (*Patient Group Engagement*, 2016) The tool is also used to assess how impactful patient involvement in an area of research is by estimating its financial value based on key drivers such as cost, risk, time and money. (Levitan *et al.*, 2018)

Inputs from patients are considered important as they improve the relevance of data. Developing a clear understanding of the desired health outcomes at an earlier stage of drug design ensures better likeliness of achieving the target goals and expectations. The Patient-Centered Reported Outcome Research Institute (PCORI) is one such organisation that is focusing on enhancing evidence generation as an initiative to help the stakeholders with effective and informed decision making. The organisation also supports innovative researches, specifically comparative effective researches, by funding it to build relevant databases. (Hoos *et al.*, 2015) It also organises workshops and challenges as part of brainstorming among universities to extract innovative ideas with regard to the concept of patient centricity. There are many research funders and federal agencies within the business such as National Institute of Health (NIH) and Agency for Healthcare Research and Quality (ARHQ), however its preeminent intent of purposefully involving patients across all the aspects of research is what distinguishes it from other funders. (Barksdale, Newhouse and Miller, 2014)

Industry is witnessing encouragement from regulators in the form of schemes and initiatives in support of patient involvement in drug development. FDA's initiative towards patient focused drug development is in alignment with the Prescription Drug User Fee Act (PDUFA), to incorporate patient inputs on their real-life experience with

a disease, its impact and opinions on the available treatment options, so as to expedite drug approvals. (Hoos *et al.*, 2015) In June 2017, the agency included sections in the New Drugs and Biologics license applications for Patient Experience Data, as an initiative to embrace the concept of patient involvement in drug development. (Schultz-Knudsen *et al.*, 2021)

As part of the Cures Act and Reauthorisation Act of 2017, Title 1, FDA has taken steps to promote patient focused drug development (PFDD) by formulating a series of guidance documents that provide a systematic procedure to facilitate the process by addressing issues relating to patient reporting, data collection, outcome assessment development and its incorporation into endpoints. It discusses sampling methods, eliciting disease related information, extracting key clinical outcomes and its method of analysis. The agency has even developed grants and awards to encourage the use of patient inputs in identifying correlation between clinical outcomes and its endpoints. (CDER, 2021)

As far as European Regulations are concerned, the European Medicines Agency's (EMA's) Patients' and Consumers' Working Party has facilitated interaction between patients, consumers and the agency. It has formulated guidance in regard to involving patients in its advisory groups and committees, with the aim of better understanding patient's perspective on a disease. EMA has practically involved patients in a pilot study to assess risk-benefits associated with drugs in September 2014. The study was launched in Committee for Medicinal Products for Human Use (CHMP), where patient opinions and recommendations were invited on areas such as product licensing and unmet medical needs. (Hoos *et al.*, 2015)

Following are some regulatory initiatives undertaken to support patient involvement in drug development: (Schultz-Knudsen *et al.*, 2021) – See Table 2.

Country	Regulatory Body	PIDD Initiatives
United States (US)	Food and Drug Administration	Patient-Focused Drug Development (PFDD)
Europe	European Medicines Agency (EMA)	Regulatory Science Strategy to 2025
Japan	Pharmaceutical and Medical Device Agency	Patient's First

Table 2: Regulatory Initiatives in support of PIDD

2.4 Barriers restricting Patient Involvement in Drug Development

Despite the fact that the concept of patient centricity and patient involvement in drug development is getting recognition within industrial practice, there still lies a huge scope for its expansion across pharmaceutical business activities.

A research article titled 'Increasing Patient Involvement in Drug Development' conducted among 14 industrial leaders of different domains (healthcare, patient group and advocacy groups) was aimed at better understanding the current state of patient involvement in drug development, through interviews. Even though the interviewees of the study believed that involving patient inputs and opinions into drug development is a positive approach to research, they also expressed some concerns associated with the same. They identified five key areas of concerns: time and investment, regulatory challenges, organisational reluctance, lack of confidence about patient knowledge and concerns related to its incorporation within existing practice. Leaders in the study are of the opinion that involving patients in drug development, will not only add to the burden of providing extra support but will also prolong the time taken for the completion of development process. The study also highlights barriers associated with identifying adequate number of patient representation and

reducing related uncertainties, patient's ability in scientific reasoning, complexities with regulatory requirements in adverse event reporting, and its efficiency in protocol optimisation. The research findings are in favor of establishing a well-structured framework to involve patients more efficiently in drug development, so as to create value by developing and offering better products to patients. According to the authors, in spite of the barriers, there is eagerness among patient population to be represented and involved in the process of drug development. (Lowe *et al.*, 2016)

As per the findings from a review article, even if patients show willingness to be involved in drug development, some barriers such as patient's wellbeing, health status, language, embarrassment, family pressure and availability, still impede the process. Preconceived notions by people of their role as an inferior is another factor that can potentially hold back their involvement in healthcare. (Ocloo *et al.*, 2021)

A recent study on patient and public involvement (PPI) in antimicrobial medicine development determined that the major reason for poor patient involvement in antimicrobial research is because of unawareness of its potential benefits. The study was conducted in USA, UK, mainland Europe and Vietnam. It involved telephonically interviewing principal investigators with previous experience in leading trials with patient and public involvement, or who were keen on the concept of PPI. The study highlights the importance of framing a system to measure outcomes of patient involvement in translational research by clearly defining its objectives and methodology. There are numerous evidences of the positive impact of PPI in scientific research however, there are not many established frameworks to facilitate its implementation within the system. Apart from systemic concerns, the study also identified barriers related to the nature of research. Acute antimicrobial infections, allowed lesser time for researchers to establish working relations with patients, substantially limiting patient involvement. Therefore, time constraint was one of the major barriers identified. As per the authors, laboratory-oriented researches have

lesser scope of involving patient inputs as compared to applied health sciences research. (Gibson *et al.*, 2019) On the contrary, a research conducted by Epstein decades ago, was aimed at establishing a correlation between AIDS activists with AIDS research. (Epstein, 1995)

In 2017, a publication summarised key points from The Renaissance Europe Patient Centricity meeting held in London. It highlighted some challenges that need to be addressed for better adoption of patient centricity in industrial practice. The challenges associated with involving patients in drug development were identified as doubtfulness with regards to its ability to generate profits, maintaining process standardisation, adhering to regulatory compliance, lack of sufficient knowledge about scientific research, establishing and aligning to a common vision and conflict of interests. According to the author, the barriers restricting patient involvement in drug development affects the industry holistically and overcoming them requires collaborative effort. (du Plessis *et al.*, 2017)

2.5 Recommendations for Improving Patient Involvement in Drug Development

A study published in 2016 proposed a framework for increasing Patient Involvement in Drug Development. The principles outlined in the framework talk about defining and acknowledging the concept, understanding its importance, reviewing current trends and identifying areas of patient inclusion, transparency and making deliberate efforts for improving the current status of patient involvement, trusting and educating patients, encouraging and continuously engaging patients, treating patients with respect and giving them equal partnership, knowledge sharing and addressing lessons learnt, owning up to responsibilities, initiating change and collaboration. (Lowe *et al.*, 2016)

The study also identified key areas in the drug development processes where patients can be better utilised. The five major focus areas considered are: product strategy, clinical trials, evidence generation, patient reported outcomes (PRO) and particpation in meetings. It is believed that collecting patient experiences and inputs consistently aids in formulating effective product strategies. From a clinical trial's perspective, involving patients in equal partnerships, helps in gaining their confidence and interest. Considering their viewpoints and leveraging their real-life experiences will facilitate management of clinical trials. Partnering with patients for the development of PRO tools to assist them in self managing their disease conditions, will not only empower patients but will also improve their quality of life. Data collected from patients can also be used to develop research tools and establish economic models. Proper training and knowledge building programs will enable patients to effectively deliver their viewpoints in scientific meetings. (Lowe *et al.*, 2016)

Establishing Patient Advisory groups to gather patient inputs on matters concerning unmet medical needs, interpretation of collected data, risk mitigation and outcome measures will result in improved decision making, real time evidence for regulatory submissions, reduced completion times and wider product ranges. It is important that the industry collaboratively standardises the practices of involving patients within its business activities, if its aim is to establish patient centric approaches. (du Plessis *et al.*, 2017)

Involving patients at the earlier stages of drug development, not only helps in formulating a patient centric design but also saves time by easing the recruitment process and developing interest among patients, assuring their commitment towards clinical trials. In order to ensure regulatory compliance, pharmaceutical companies can create forums or platforms for exchanging ideas and practicing effective communication with the regulators on a regular basis. Such initiatives will help identify and mitigate potential risks. Managing challenges related to conceptual framework is

key in the implementation of the concept. This is achieved by recognizing patients and respecting the time and effort they put in. Creating tools that measure value adding elements and generating evidences depicting the impact of their involvement in the process can act as a motivation. Acknowledging and treating patients as equal partners in business will not only boost their confidence but will also result in their active participation. In order to build trust, maintaining transparency among all the stakeholders is a must. Clearly defining and effectively communicating individual roles and responsibilities within business adds onto the overall process integrity. It is also important not to underestimate their knowledge solely on their ability to provide scientific reasoning. Rather embracing their inputs and making deliberate efforts to collaborate and extract maximum information relevant to the subject must be practiced. To enhance the validity of patient representation, pharmaceutical companies can develop a set of pre-determined patient characteristics depending upon what the situation calls for at that moment of time. This approach will facilitate the process of patient selection by providing categorical dissemination of the available data. Identifying key personality traits of patients, such as confidence, knowledge and assertiveness, helps in assigning individual roles. (Lowe *et al.*, 2016)

A study conducted in 2015, proposed a rationale to formulate a strategic framework by consolidating existing initiatives. The five steps towards building the framework include, identifying time points in the product lifecycle, assigning patients roles based on time points, developing methodologies for patient involvement, identifying loopholes and duplications in existing initiatives, formulation and implementation of the developed strategic framework. (Hoos *et al.*, 2015)

As for the steps, pharmaceutical companies can take to involve patients in drug development from an organisational level, there are recommendations provided by Patients Included charter that can be beneficial. These recommend encouragement from leadership team, establishment of patient councils representing individual key

disease areas, tasking them with standard operating procedure (SOP) generation for assimilating patient inputs into decision making, backing the council with resources to collaboratively come up with patient solutions and including yearly patient contributions in annual reports. (Lowe *et al.*, 2016)

Parkinson's Foundation formulated a framework describing the scope of patient involvement in drug development. It stagewise segregates different patient roles. According to the framework, patients can be involved across all stages of drug development, from discovery and preclinical to post approval. In the Discovery phase, patient can contribute by elaborating on disease specific aspects such as disease progression and clinical outcomes. Whereas in the conduct phase, patient inputs will help in clinical assessments such as risk-benefit ratios and study setup activities such as protocol generation and structuring informed consent. Patients are identified to have role in regulatory activities as well especially with regard to decisions regarding rare diseases. Once a drug is marketed, patients can support the sponsor by propagating study results and participating in post marketing surveillance activities, such as assessing safety reports. (Feeney *et al.*, 2020)

Authors	Study Description, Publication Year	Sample Size	Key Points	Conclusion
Maria M. Lowe et al	Study on the current state of patient involvement in drug development, 2016	14 interviews of healthcare leaders (8), patient leaders (5), patient advocacy group (1)	The current models are not sufficient enough to support and encourage patient involvement in drug development.	Encouragement from leadership team and overcoming cultural and logistical barriers are vital in the implementation of PIDD.
Danie du Plessis et al	Summary of key points regarding patient centricity, discussed in the Renaissance Europe Patient Centricity meeting, 2017	Review article	Patient centric approaches create value and credibility with partners.	For better incorporation of the concept in industrial practise, there must be acceptance to change, collaboration and knowledge sharing.

Anton Hoos et al	Study on the impact of partnering with patients in the process of Drug Development, 2015	Review Article	Framework for the implementation of PIDD must be based on inclusivity, transparency, credibility and honesty. Patients to be considered equal partners. Their difference in perspective from other stakeholders can support efficient decision making.	Patient Involvement enables better product lifecycle development and management. A systematic framework for patient involvement must be in place to improve drug development.
Josephine Ocloo et al	Exploration of theories, barriers and enablers for patient involvement in healthcare and social welfare, 2021	Review Article of 42 publications	Out of 42 articles, 22 mentioned theory, 31 mentioned equality and diversity and 19 talked about barriers and enablers.	Implementing PPI is a collaborative and a holistic effort. It requires considering the enablers and addressing disparity among various groups.
Andy Gibson et al	Exploring the barriers and enablers of PIDD in antimicrobial medicine development, 2019	9 interviews of experienced principal investigators	Responses conveyed doubt regarding the impact of PPI in antimicrobial medicines development however in other medical researches, PIDD was considered beneficial.	Implementation of PPI was found to have minimal impact on laboratory based research such as antimicrobial medicine development. However, further exploration of this field can discover potential benefits.
Marianne Botoft Hansen et al	Perspectives of Pharmaceutical, regulatory and patient organisations on Involving Patients in Drug Development, 2019	12 interviews of people from Pharmaceutical industry (4), patient organisations (6) and regulatory authorities (2)	3 perceptions identified: ways to improve quality of life, avoid business losses and encourage speedy drug development process. Factors associated with effective collaboration were identified as trust, transparency and openness.	The 3 stakeholders were found to be unaware of the concept, which explains the hesitance observed. However, among the 3, pharmaceutical industry was found to be the most influential with regard to PIDD.

Katrine Schultz-Knudsen et al	Study on the evaluation of Patient Experience Data in FDA drug approval packages and product labels, 2020	48 FDA Approved drugs of 2019	81.3% of the approved drugs incorporated PED, of which Clinical outcome assessments (COA) was the most prominent. PED data was not observed in any of the qualitative studies.	There is a larger scope of incorporating PED, apart from COM, if there is better awareness, transparency and a strategic framework to facilitate its industrial application.

Table 3: Summary of Publications from Literature Review

2.6 Conclusion

After a thorough review of literatures on topics relating patient involvement in drug development, it is evident that in spite of the numerous benefits associated with incorporating patient inputs in drug development such as value generation, improved credibility among stakeholders and better products, the pharmaceutical industry is still skeptical about its impact on the overall development process. The review findings identified lack of awareness as a predominant factor for the existing situation. In order to streamline patient involvement, the pharmaceutical industry must change the mindset, build trust, maintain transparency, encourage knowledge sharing and collaborate with patients. This shift from conventional method of research, where patients were only considered end-users, to a patient centric approach, utilising the real time patient experiences and suggestions to develop a product or device, requires support and encouragement from the organisational leadership team. Utilising existing patient organisations as a base, to formulate frameworks will not only assist filling existing gaps but will also balance stakeholder representation.

Even though this review highlights a shared interest in improving the current state of patient involvement in drug development among the stakeholders, there are several challenges that need to be overcome before its practical inclusion as part of the normal process of drug development. The main hurdles to wider acceptance to PIDD appear to be time, budget, methodologies, organisational reluctance and doubts with regard to patient knowledge and scientific skills.

CHAPTER 3: RESEARCH METHODOLOGY

3.1 Overview

Section. No	Primary Data	Details
3.2	Approach	Qualitative and Quantitative analysis
3.3	Philosophy	Interpretivism and Positivism
3.4	Strategy/Source	Online Questionnaire: Created and Distributed through Google Forms
3.5	Structure	Five sections comprising of 20 questions
3.6	Participants	Employees of Pharmaceutical Industry's R&D Department

Table 4: Overview of the Research Methodology

3.2 Research Approach

To understand the industrial mindset in relation to patient involvement in drug development (PIDD) and to determine the barriers associated with it in decisions relating to drug development, the author took a mixture of qualitative and quantitative research approaches, through use of a survey.

The survey was generated and distributed online to employees of the pharmaceutical industry currently employed in Research and Development. The platform used was Google Forms, which is a web-based application. This allowed for effective data collection and analysis. The questionnaire was structured in a way to translate industrial outlooks towards PIDD and obtain insights on the knowledge and awareness of pharmaceutical employees about current patient-centric approaches and initiatives. Ascertaining this information helped the author identify gaps in the existing system.

People's opinions on ways to improve the current state of PIDD was gathered by a qualitative approach using open-ended questions. It aided in acquiring a better understanding of what people thought was lacking in the contemporary practice of research and identifying areas of potential improvement.

The data collected by utilising qualitative and quantitative approach, in conjunction with the understanding developed from reviewing existing literatures, was used by the researcher to draw conclusions on the objectives of the study.

3.3 Research Philosophy

The research was based on the philosophy of positivism and interpretivism. It was applied to assess the measurable factors obtained by collecting data from research participants. The quantifiable factors were analysed based on the concepts of deduction by inferring the hypothesis through logical reasoning. The data was collected impartially from research participants by indirectly administering the questionnaires to pharmaceutical employees through a web-based application, ensuring maximum objectivity and minimum risk of bias. The participants were free to complete or withdraw from the survey without any sort of interference from the author.

The philosophy of interpretivism was applied to the qualitative approach, where participants' opinions and suggestions were gathered to shape the basis of primary research. The reliability of these data were unclear as it was based on respondents' honest thoughts and ideas. However, its validity was ensured by the depth of knowledge portrayed in the responses provided by the study participants.

3.4 Research Strategy

A timeline for the research plan was created using a Gantt Chart to assist in scheduling research activities – See Figure 4.

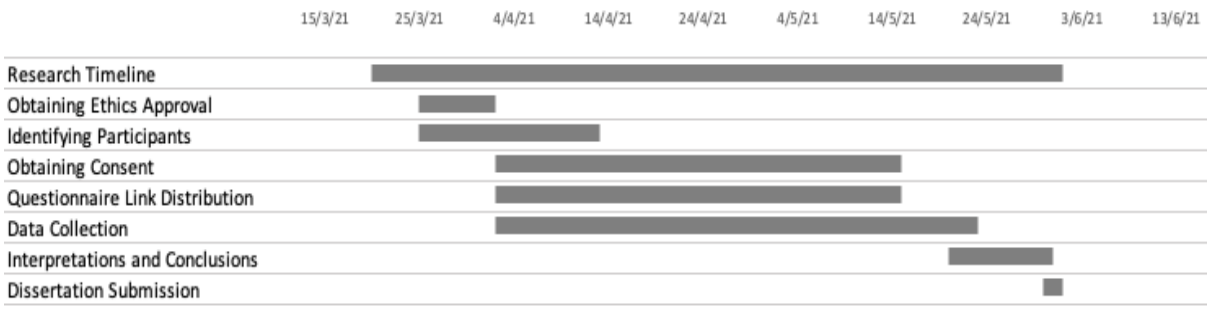

Figure 4: Research Timeline

The strategy of this research was to understand the industrial mindset regarding PIDD and to identify the barriers that restrict its implementation within business practices, by obtaining insights on their knowledge, awareness and opinions about the same. It is evident from the literature review that even though there have been studies that have explored the concept of PIDD by conducting research among the industrial leaders, not many have considered to get the employee standpoint, which gave scope to this research.

The research participants were informed of the purpose of the study and that this research was as part of the author's dissertation work for MSc in Pharmaceutical Business and Technology. The language used in the questionnaire was such that it was easy to understand and respond to. It comprised of open- ended and closed questions to capture facts and their opinions on the topic. It was administered to nearly 90 people currently working in the pharmaceutical industry's Research and Development (R&D) sector.

The questionnaire was divided into five sections and consisted a total of 20 questions. It included a shortened version of the patient information leaflet (PIL) which stated the purpose of the research and asked participants to tick the first box to demonstrate that they understood the reasons for the study. The questionnaire also contained a section from the informed consent form (ICF) explaining to participants that if they ticked the second box, they were permitting the author to use their responses for the purpose of the study. This agreement was a mandate before the participants could further proceed onto the survey. Participants were assured of the protection of their anonymity and confidentiality, and that the handling of data was in line with the current general data protection regulation (GDPR).

3.5 Primary Data Collection

The sole tool for data collection in the research was a questionnaire, generated and distributed online to the pharmaceutical employees in the drug development sector. The questionnaire was structured in a way that gathered information required to meet the objectives of the study – See Appendix A and Table 5.

Section Number	Section Title	Number of Questions per section
Participant Consent and Introductory Letter		
1	Demographics	7
2	Awareness of Patient Involvement in Drug Development	4
3	Knowledge around Patient Involvement in Drug Development	4
4	Barriers to Patient Involvement	2
5	Ways to Improve Patient Involvement in Drug Development	3
Total number of Questions		20

Table 5: Summary of Questionnaire Structure

Section 1 on demographics contained seven questions that gathered information on respondents' gender, age, geographical zone of employment, level of experience and company details particularly the name, department and line function they worked in. These questions helped the author ensure respondents met the inclusion criteria of the study.

Section 2 on awareness of Patient Involvement in Drug Development (PIDD) consisted of four questions aimed at assessing the extent to which the respondents were familiar with concepts of PIDD and its current practice in the industrial setup. This section covered questions on patient involvement in drug development and its various supporting organisations. A question on respondent's understanding of drug development was also included as a measure to ensure correct sampling.

Section 3 on knowledge around PIDD aimed at collating information on how well the respondents knew about the fundamentals of this initiative. This section included a mixture of open- and close-ended questions to allow gathering respondent's opinions on ways of incorporating patient inputs in drug development in an industrial setup.

Section 4 on barriers restricting patient involvement aimed at understanding respondent's perspective of the potential factors related to limited involvement of patient and their inputs in medicines research. This involved questioning their individual choice of supporting the concept by a close ended question. A 3-point Likert scale was included to comprehend the degree of probability related to ineffective implementation of PIDD, from an employee's perspective.

Section 5 comprised of questions aimed at obtaining respondent's opinions and suggestions on ways to improve the current state of PIDD. This included questions on their preferred choice of therapeutic areas and drug developmental activities, that would most benefit from adopting patient inputs.

3.6 Participants

The questionnaire was created and distributed to the study cohort, comprising of a group of pharmaceutical employees, currently working in the R&D Department via an online Google Form application. A total of 51 valid responses were obtained. Using Microsoft Excel, the author further assessed the data and represented the results graphically, in the form of graphs and pie charts. The elaborate responses were used to generate interpretations and recommendations for improving the current state of patient involvement in drug development.

LinkedIn profiles of Pharmaceutical employees currently working in the Research and Development sector were reviewed to identify people who matched the inclusion criteria of the study. The author then reached out to the recognized people, where she explained the research topic and asked them for their interest in participation. On receiving positive feedback, the online survey was sent to them through a link.

3.6.1 *Inclusion Criteria*

Apart from the requirement of study participants to have knowledge, understanding and experience in drug development, there were no other specific inclusion criteria, considered by the author for study participation.

3.6.2 *Exclusion Criteria*

People who refused to voluntarily participate in the survey were excluded from the study. If participants showed disinterest after sending the questionnaire, they were encouraged to disregard the link.

3.7 Access and Ethical Issues

All the identified employees of the pharmaceutical Research and Development sector who participated in the survey were duly and clearly briefed about the study and the reason for its conduct, which was as part of the academic requirements in the fulfilment of her master's thesis. The data gathered was used only for the purpose of this research titled 'Barriers that restrict patient involvement in Drug Development: An Industrial Perspective'.

While designing the questionnaire, care was taken to only include questions that were in relation to this research and aligned to its objectives. The respondents were free to share their opinion without any form of pressure or manipulation from the author. Respondents' agreement to the participation consent at the start of the survey ensured their voluntary participation in the research. Only responses from participants who met the inclusion criteria were considered for data analysis.

Special attention was paid to not question the respondents on any sensitive information that breached the conflict of interest. Questions that invaded personal space and those that were irrelevant to the research, were also excluded such as name of the respondent. As the age ranges were a measure of ensuring diversity in the study population and had no other significance, they were grouped broadly.

In order to get ethical approval, the following forms and documents were completed and signed according to Innopharma and Griffith College's ethics policies - see Appendix B.

- Ethical Approval Application Form
- Informed Consent Form (ICF)
- Participant Information Letter (PIL)
- Ethics Declaration Form

3.9 Conclusion

The study utilised qualitative and quantitative approaches to explore the truths about the barriers restricting patient involvement in drug development and assess awareness and knowledge around the topic among pharmaceutical employees. The philosophy of positivism and interpretivism was used to better understand and interpret the facts obtained.

While the study was conducted in adherence to the institutional ethical guidelines, with full assurance to patient confidentiality and anonymity, the data was handled in line with the current general data protection regulation. The collected data was analysed and interpreted in comparison to the findings from the literature review and is presented in the following chapter.

CHAPTER 4: FINDINGS AND ANALYSIS

4.1 Overview

This chapter illustrates findings obtained from the analysis of data collected from study participants, which formed the basis of conclusions of this research.

4.2 Demographic Data

This section gathered general information about respondents to ensure their qualification in the study and to get a better understanding of their characteristics.

4.2.1 *Response Rate:*

The questionnaire was distributed to 90 pharmaceutical employees, out of which a total of 51 acceptable responses from 29 females (56.9%) and 22 males (43.1%) were obtained, constituting a response rate of 56.6%. Reminders sent via text messages on timely intervals contributed to a noticeably improved response rate.

4.2.2 *Age Group:*

Out of the 51 respondents, 26 of them were predominantly young adults aged between 18-30 years (51%), while 25 of them fell under the age group between 31-50 years (49%). There were no respondents aged above 50 years of age.

4.2.3 *Geographical Distribution:*

The majority (96.1%) of the respondents who completed the questionnaire were Asians with just one respondent from each of Europe and America.

4.2.4 *Employment and Level of Experience:*

All of the respondents qualified for the study, worked in Pharmaceutical Industries, majorly in Novartis (46%). However there was participation from employees of other pharma companies as well who weren't keen on disclosing their organisation name and comprised of 27% of the total respondents. Employees of Pfizer, GSK, Eli Lilly, Bioclinica, Roche, Covance and Iqvia, comprised the rest of the cohort (27%).

Respondents working in Global Drug Development Department (35.3%) and Data Management Function (64.7%) were in majority, however, respondents from various other departments (pharmacovigilance, data operations, research and development, global regulatory affairs, centre of excellence and life sciences) and line functions (Drug Safety, clinical coding, data standards and digital) also participated in the study constituting rest of the cohort (64.7% and 35.3% respectively).

Respondents who participated in the study were observed to have varied levels of experience. Majority (52.9%) of the them had 1-5 years of experience followed by people with experience of over 10 years (23.5%), 6-10 years (13.7%) and less than a year (9.8%).

Geographical Distribution				**Years of Experience**				**Age (Years)**			**Gender**		**Total Number of Respondents**	**Response Rate**
A	**E**	**AU**	**AM**	**<1**	**1 - 5**	**6 - 10**	**>10**	**18-30**	**31-50**	**>50**	**M**	**F**		
49	1	0	1	5	27	7	12	26	25	0	22	29	51 out of 90	56.6%

*Key: A=Asia; E=Europe; AU=Australia; AM=America; M=Male; F=Female

Table 6: Demographics

4.3 Awareness of Patient Involvement in Drug Development (Questions 1 – 4)

The responses gathered from this section were promising and presented varied and improved awareness of patient involvement in drug development among the respondents.

Question 1:

The analysis of respondent's familiarity with drug development process illustrated that all the respondents who participated in the survey were well aware of it. This confirms the eligibility of the respondents who took part in the survey - see Figure 5.

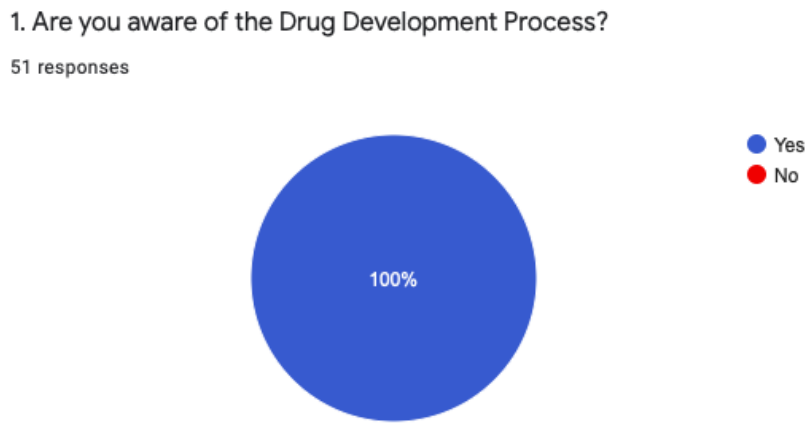

Figure 5: Awareness among Pharmaceutical Employees of the process of Drug Development

Question 2:

In the analysis of respondents' familiarity with the concept of patient involvement in drug development, 9 (17.6%) out of 51 respondents admitted to have not heard about the concept, whereas 42 (82.4%) respondents were aware of it – see Figure 6.

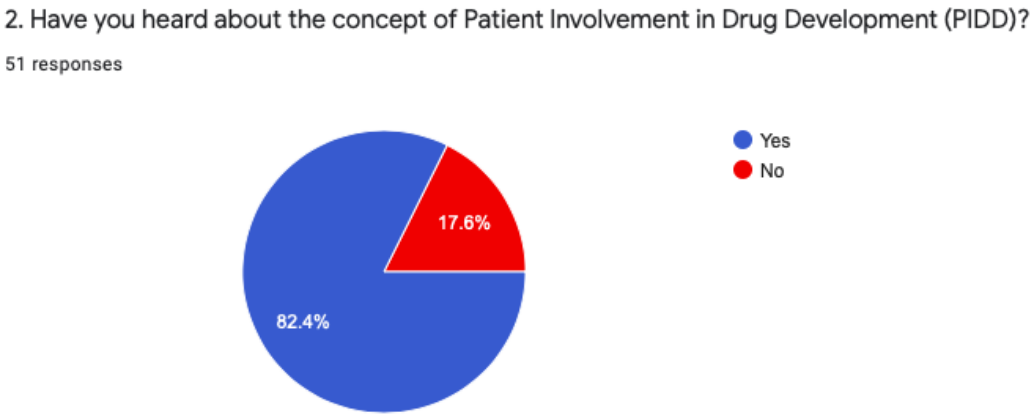

Figure 6: Familiarity of pharmaceutical employees with the concept of Patient Involvement in Drug Development

This confirms that there is scope within the pharmaceutical industry to create awareness amongst its employees towards the concept of patient involvement in drug development (PIDD) in order to facilitate its implementation.

Question 2a:

As a follow-up to the above question, this asked about the sources from which they had heard about patient involvement in drug development. For this question, 16% of the respondents did not answer. However, from those who answered, the majority (59.5%: 25 employees) stated to have heard about patient involvement in drug development from organisational internal communications. As per the analysis, professional journals and verbal communication with colleagues were the next major sources, both contributing to 54.8% (23 employees), followed by internet (52.4%: 22 employees) and news (47.6%: 20 employees). Apart from the predefined choices of enlisted sources, one respondent admitted to have heard about PIDD from a Pfizer project – see Figure 7.

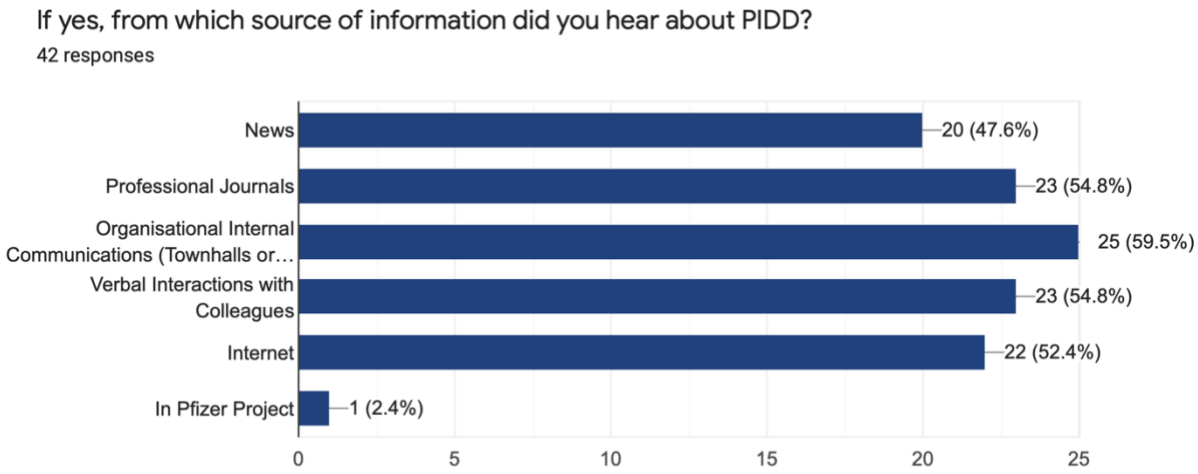

Figure 7: Sources that informed the pharmaceutical employees of PIDD

This is indicative of the concept being talked about and encouraged at the industrial and organisational level. Interestingly, from the responses gathered, Pfizer came out to be the only organisation that was specifically mentioned with regard to incorporation of PIDD within internal projects, suggesting a larger scope of improvement.

Question 3:

Out of 51 respondents, only 16 (31.4%) were aware of organisations supporting PIDD, whereas majority (68.6%: 35 employees) were unaware of any – see Figure 8.

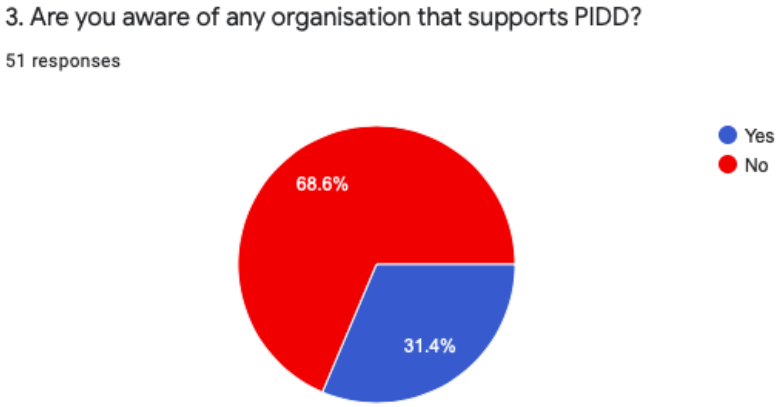

Figure 8: Awareness of pharmaceutical employees on PIDD support organisations

Even though there have been various sources imparting information on PIDD, an underwhelming level of awareness was observed from the responses collected regarding organisations supporting PIDD. Interestingly, from the responses to question 2, the majority of the pharmaceutical employees who took part in the survey had heard about the concept, but this aspect of organisations supporting PIDD has grabbed less attention.

Question 3a:

As an addendum to Question 3, for those respondents (31.4%: 16 employees) who knew about organisations supporting PIDD , respondents were asked the names of such companies. There were a variety of responses given ranging from pharmaceutical organisations (Novartis (32%), Pfizer (32%)), regulatory bodies (FDA (5%)), patient organisations (National Organisation for Rare Diseases (NORD) (11%)), European Patients Forum (EPF) (5%)), and initiatives (Clinical Trials Transformative Initiative (CTTI) 5%), TransCelerate (5%), Innovative Medicines Initiative (5%), European Patient's academy on Therapeutic Innovation (EUPATI) (5%)) – see Figure 9.

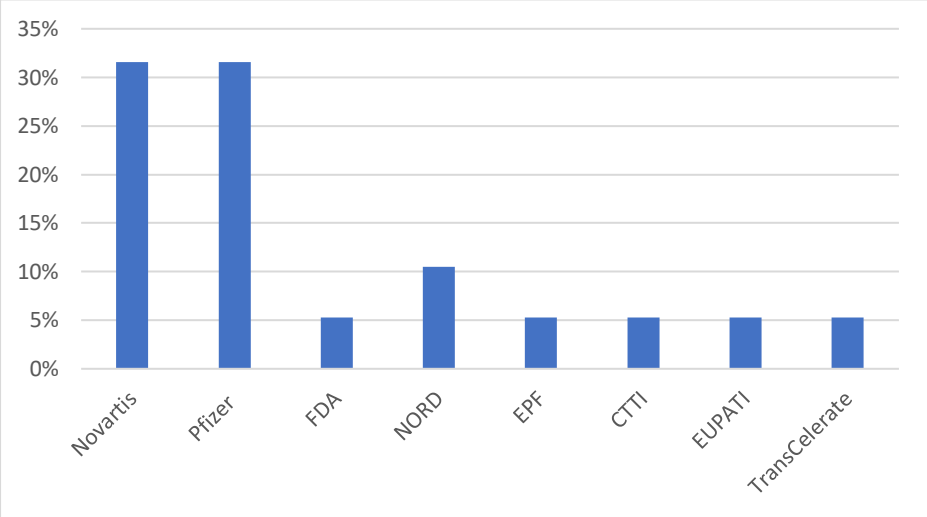

Figure 9: Names of supportive organisations named by pharmaceutical employees

From the varied responses obtained from this question, it is confirmed that, out of the respondents who knew about the organisations in favour of PIDD, all of them exhibited remarkable awareness, as they correctly identified the organisations and related initiatives.

Question 4:

In the analysis of respondents' familiarity with organisations in support of PIDD, 52.9% (27 employees) of respondents had heard of PCORI, followed by CTTI's PLC (41.2%: 21 employees), EUPATI (37.3%: 19 employees) and DART (7.8%: 4 employees) – see Figure 10.

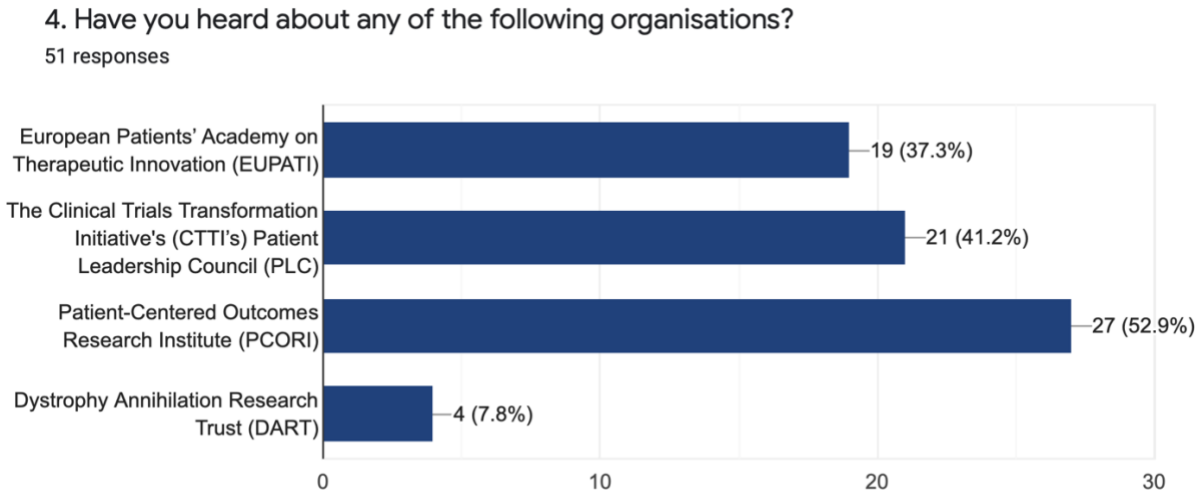

Figure 10: Familiarity of pharmaceutical employees on the enlisted organisations

Interestingly, responses from question 3 indicated that the majority of the respondents had not heard of any organisation which was in support of PIDD. On the contrary, when asked about the organisations by names, it was noted that the respondents had at least heard of one of the four organisations. This clearly confirms respondents lack of awareness regarding the purpose of the above-mentioned organisations.

4.4 Knowledge around Patient Involvement in Drug Development (Questions 5-8)

Question 5:

In order to determine the knowledge of what stages of drug development patients can be involved in, majority (30%: 15 employees) of the respondents opted for Phases 1, 2, 3 and post-approval. Even though only four (8%) of the total respondents selected the correct response of all stages from discovery to post approval, the author noticed scepticism towards involving patients in discovery (19.6%: 10 employees) and preclinical (21.6%: 11 employees) phases when compared to rest of the phases of drug development. Only one (2%) person said there was no scope for patient involvement in any stage of drug development – see Figure 11.

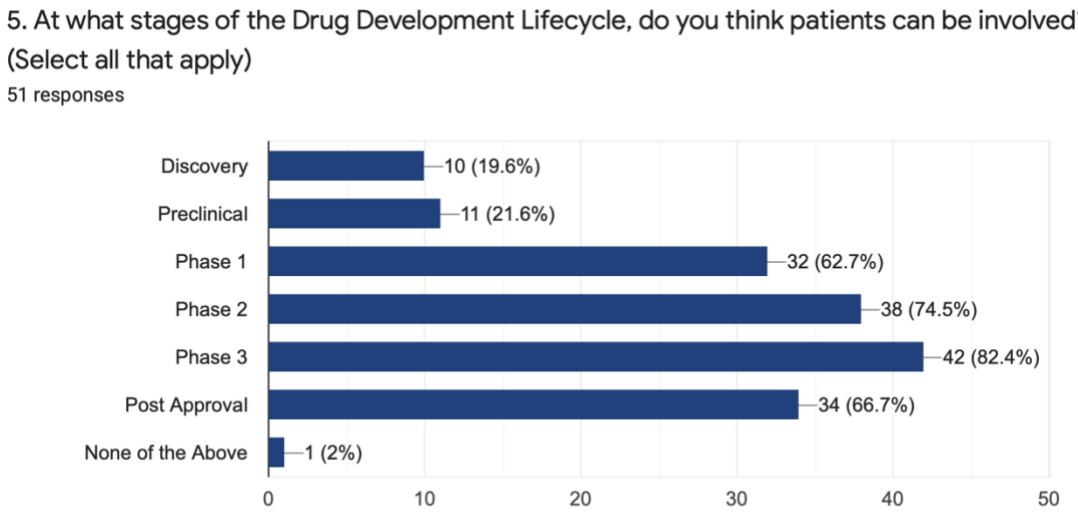

Figure 11: Knowledge of pharmaceutical employees about the scope of patient involvement in the various stages of drug development

As observed from the responses gathered, only a few of the respondents correctly recognised patients to be involved across all stages of drug development. This shows a lack of knowledge among pharmaceutical employees of the benefits associated with incorporating patient inputs and experiences at individual stages of drug lifecycle. The fact that respondents considered Phases 1-3 to have more scope for patient

involvement could potentially be due to their poor understanding of the term ‘patient involvement’ and it being confused with ‘patient participation’ as trial subjects.

Question 6:

In ascertaining the stakeholders responsible for implementing PIDD, an overwhelming 54% (27 employees) correctly recognised all three (patient organisations, pharmaceutical industry and regulatory agencies) to be the stakeholders, out of which patient organisations were individually perceived to be more accountable in the conceptual implementation, closely followed by pharmaceutical industry (82.4%: 42 employees) and regulatory agencies (68.6%: 35 employees). Only one respondent (2%) did not consider any of the options to be the stakeholder in PIDD – see Figure 12.

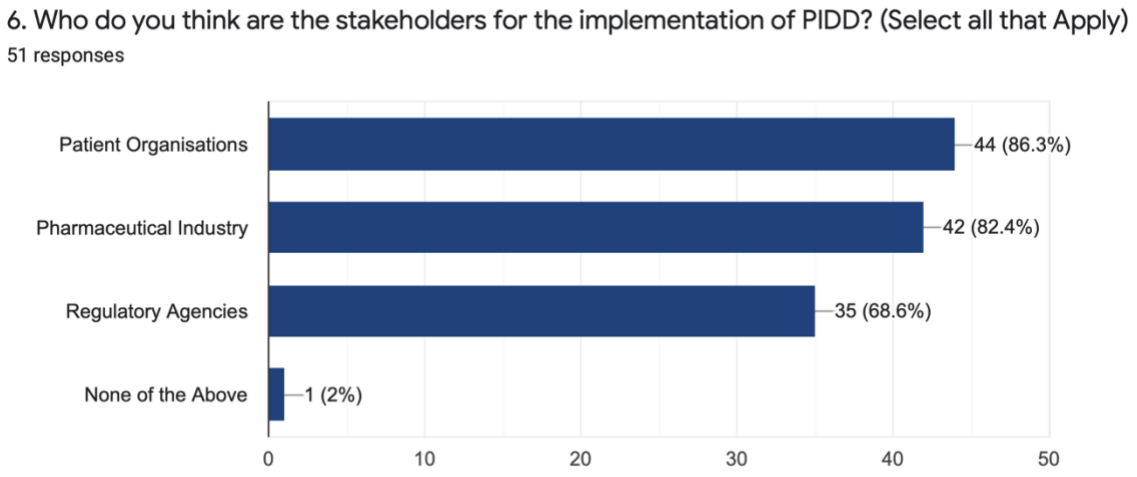

Figure 12: Knowledge of pharmaceutical employees on the stakeholders for the implementation of PIDD

This demonstrates adequate knowledge among pharmaceutical employees of the stakeholders in PIDD. However, respondents’ perception about patient organisations being the most keen about PIDD, is indicative of an inadequate awareness of PIDD’s implementation and encouragement from an industrial and regulatory standpoint in regard to the efforts and steps taken by them towards addressing patient needs.

Question 13:

An overwhelming 96.1% (49 employees) of the respondents who participated in the study believed that involving patients and their disease experiences would benefit the drug development process, whereas only one respondent disregarded patient involvement as being of any benefit to product lifecycle – see Figure 13.

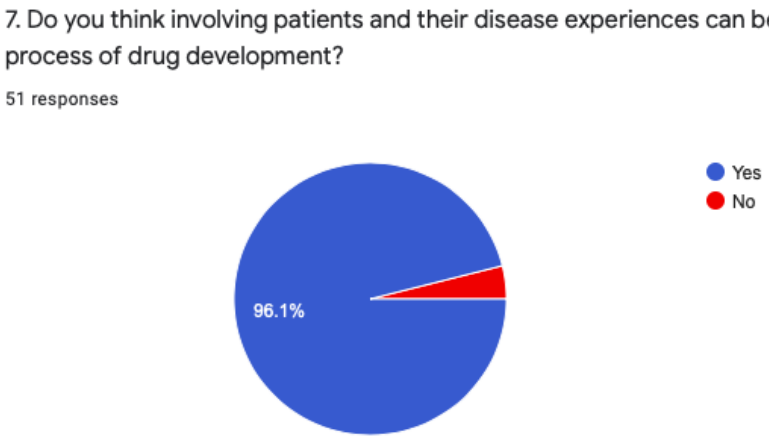

Figure 13: Viewpoint of pharmaceutical employees on the benefits of PIDD

The responses strengthen the fact that employees have some knowledge about the concept of PIDD, however, there is lack of in-depth understanding which requires further investigation.

Question 7a:

On asking the respondents reasons for their response to the preceding question about the benefits of involving patients in drug development, they came up with several benefits and risks associated with the implementation of PIDD, which are collated and outlined by the author in Table 7.

Benefits	
Early Phase	• Better decision making • Better target identification enhancing the process of molecule development. • Identification of focus areas. • Improved prioritisation of early treatment options that result in better research outcomes. • Support in Risk-benefit assessments.
Conduct Phase	• Better understanding of disease pathology, drug interactions and safety profiles of existing drugs to improve trial design. • Insights on protocol design and expected patient outcomes. • Improved access of clinical trials to larger population. • Development of novel products by collecting real time data to better understand the challenges associated with existing treatment options. • Enhanced patient retention and recruitment by generating interest. • Better understanding of potential Adverse Events and drug effects especially in case of related comorbidities. • Better parametric analysis of the varying Pharmacodynamic and Pharmacokinetic properties to better understand the pros and cons of existing drugs. • Ensures better meaningfulness of endpoint measures. • Better resource allocation
Post Approval	• Better product planning. • Demonstrates value of label claims and market value discussions. • Insights on unknown Suspected Unexpected Serious Adverse Reaction (SUSAR) reports.

Risks	
Bias	• Associated with patients and their interests.
Improper measurability	• Different people perceive feelings differently, resulting in exaggeration or understated measures of symptoms or pain.

Table 7: Benefits and Risks associated with the implementation of PIDD

The author noticed a positive attitude among respondents towards PIDD as they highlighted various aspects associated with its implementation. As per the collated responses, it was observed that they understood the impact and importance of exceptional efforts within the industrial setup so as to accelerate the overall drug development. Broadening the understanding and studying the exact mechanisms and drug effects, by utilising patient experiences without solely limiting to endpoint measurement, was perceived as a positive approach to translational research. Getting deeper insights on disease pathologies, quality of life and patient responses to existing treatment options and using them to improve clinical study designs, was regarded as a step towards patient centricity.

Question 8:

The interpretations generated from the collated responses identified ways in which patients can be better involved in drug development. Varied ideas on ways to facilitate PIDD in industrial setup were identified which, when practically implemented, had the potential to improve the current state of PIDD.

Table 8 collates the key points in relation to potential areas of PIDD, as described by the pharmaceutical employees who participated in this study.

Focus Areas	Ways to incorporate patients
Development of Patient Reported Outcomes	Collating inputs on patient experiences, quality of life and health status by conducting interviews or through surveys by administering questionnaires.
Pharmacovigilance activities	Gathering reports on adverse events and monitoring side effects through virtual communications for risk benefit assessments.
Natural history Study	Collecting data on medical histories, allergies, reactions to drug interactions and comorbidities to form the basis for further research and investigations.
Regulatory Review	Participating in regulatory meetings as patient representatives from the sponsor's end and voicing opinions with regard to decisions relating patient welfare and safety by providing information on potential risks and benefits associated with disease area, based on their real time experience.
Concept Elicitation	Collecting epidemiological data in the form of surveys and interviews to conceptualise healthcare systems.
Facilitated Discussions	• Involving in discussions drug effectiveness and safety so as to provide patient perspective on those topics, which is otherwise disregarded. • Patient participation in organisational internal meetings by forming patient advocacy groups and councils, representing patients and their views in decisions relating product lifecycle, also facilitates patient centricity.
Trial Conduct	• Gathering patient specific information about the ongoing treatments from Patient Diaries.

	• Involving patients in protocol designing by providing information on the barriers to participation and endpoint measures. • Involving in formulating eligibility criteria and informed consent for research.
Post Marketing Surveillance	• Engaging in developing product strategies by addressing real time day-to-day challenges associated with product administration, storage and handling. • Collaborating in post marketing surveillance by supporting tracking of drugs.

Table 8: Ways to incorporate patients in drug development

4.5 Barriers to Patient Involvement (Questions 9 and 10):

Question 9:

An overwhelming 98% (49 employees) of the respondents who took part in the survey were in support of PIDD, whereas only one respondent (2%) was against the concept – see Figure 14.

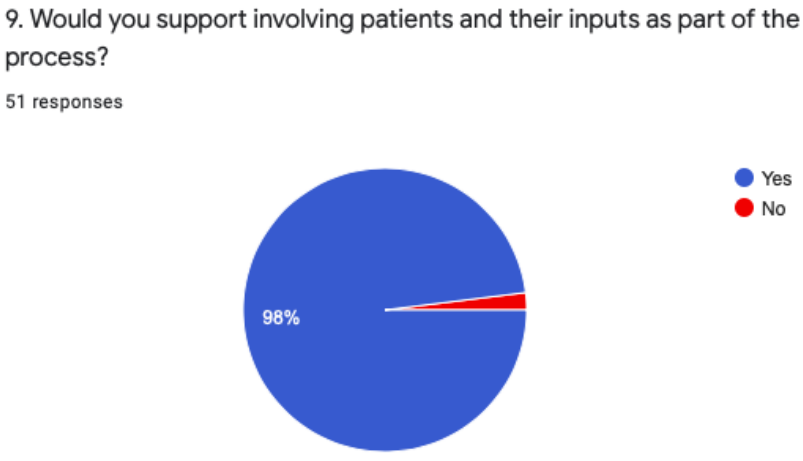

Figure 14: Employee support towards PIDD

This revealed optimism among pharmaceutical employees regarding incorporation of patient inputs into translational research and as a result rules out employee attitude, as a barrier to patient involvement in drug development.

Question 10:

In the analysis of identifying barriers restricting patient involvement in drug development, the respondents were provided with a scale to determine their likelihood levels on the factors restricting the implementation of PIDD in the industrial setup. Respondents were asked to choose from a range of factors that the author identified as posing challenges towards industrial application of PIDD – See figure 15.

74% of the respondents considered lack of dedicated groups, committees and personnel to conduct PIDD activities were likely to be a factor, 18% of the respondents remained neutral and 8% of the respondents thought of it to be an unlikely cause.

Interestingly, over half (52%) of the respondents thought regulatory and legal constraints were most likely to be the cause of inadequate adoption of PIDD and its related activities within the pharmaceutical industry. 40% of the respondents remained neutral, whereas 8% of respondents considered it unlikely.

62% of the respondents believed lack of industrial confidence in patient knowledge and skills to be a likely factor in the poor acceptance of PIDD in industrial setup. 32% of the respondents remained neutral, whereas 6% of respondents disregarded it to be a factor and considered it unlikely.

Concerns regarding added financial requirements and support was considered likely to be a barrier to PIDD by 63% of the respondents, 24% of the respondents remained neutral and 14% of respondents thought it to be unlikely.

Over half (56%) of the respondents considered difficulty in choosing proper representation of patient population to be a likely factor restricting patient involvement in drug development, 28% of the respondents remained neutral whereas 16% considered it to be unlikely factor.

Interestingly, 60% of the respondents were of the opinion that lack of interest from patient population was likely to be a factor restricting the implementation of PIDD in industrial practice. 28% of the respondents remained neutral while 12% of respondents conceived it to be unlikely.

Lack of opportunities for patients to be involved in drug development was regarded a likely barrier to PIDD in the industrial practice by 64% of the respondents. 22% of respondents remained neutral, whereas 14% of respondents thought of it to be an unlikely factor.

Interestingly, fear of patient bias was attributed by 64% of the respondents as a likely factor restricting patient involvement in drug development. 30% of the total respondents remained neutral while 6% of respondents considered it to be an unlikely cause.

Surprisingly, 42% of the respondents considered reluctance from the organisation to be a likely factor restricting the maximisation of patient involvement in translational research. Though, 44% of respondents remained neutral, 14% of respondents disregarded it as an unlikely factor.

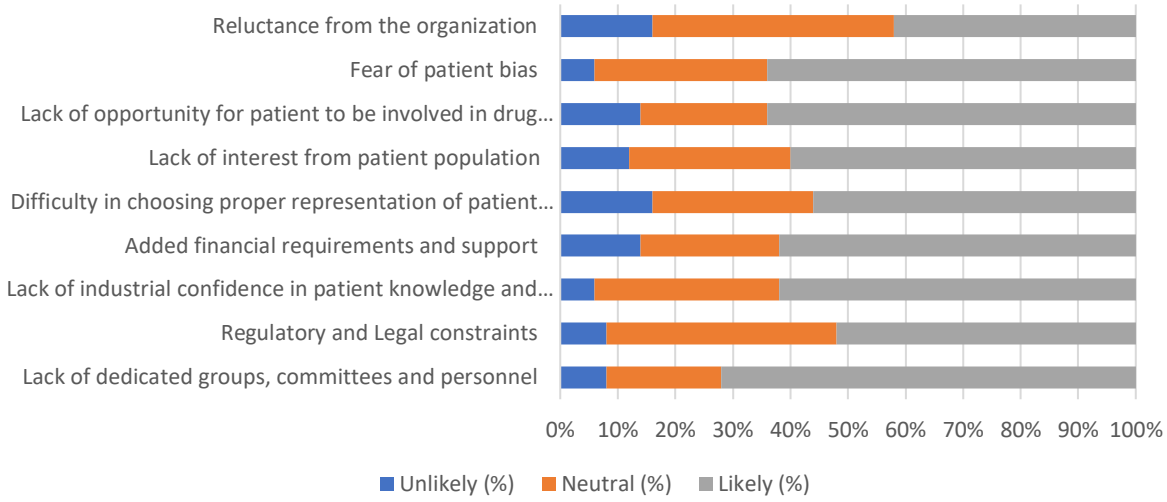

Figure 15: Barriers restricting patient involvement in drug development

Apart from the predefined items on the Likert scale, 10% of the respondents associated a few other factors to restrict patient involvement in drug development. Respondents were of the opinion that patient involvement could lead to extended research, resulting in delays in project deliverables. This was considered one of the reasons for organisational reluctance. In addition, interpretation of patient inputs and opinions was considered a challenge by respondents for the industry, as inaccurate interpretations could completely alter the context, further misleading the process.

4.6 Ways to improve patient involvement (Questions 11-13)

Question 11:

In the analysis of which drug development activities would benefit from the implementation of patient involvement, respondents were given a choice of selecting all the options they thought were apt. Majority (98%) of the respondents opted for clinical trials as one of the options in their responses. Pharmacovigilance and evidence generation were considered the next crucial drug development activities by 66% and 44% of the respondents respectively, where patients and their inputs could be

incorporated. 28% and 30% respondents out of the total participants were of the opinion that involving patient ideas and experiences could benefit in policy generation and product strategy respectively. As per the findings, respondents preferred patient involvement in regulatory meetings (20%) over funding (16%). Only one (2%) person mentioned observational studies to be a focus area for PIDD – see Figure 16.

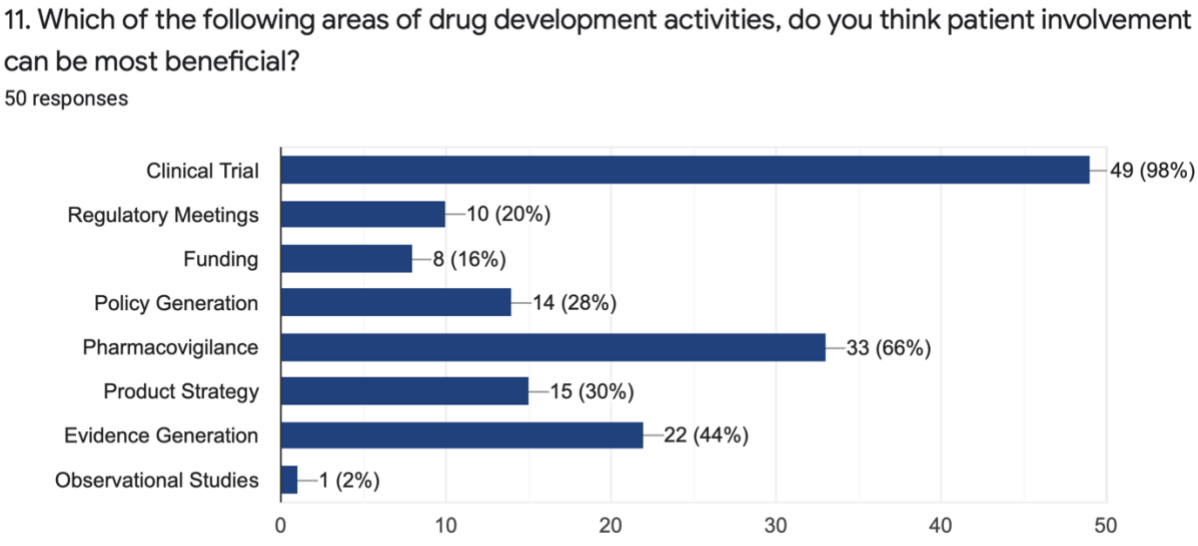

Figure 16: Preferred choice of drug development activities for PIDD

The received responses demonstrate respondents inclination towards the existing areas of patient engagement. Lack of awareness and clarity on the term 'patient involvement' and its related benefits in different stages of drug development, could possibly be the reason for respondents to opt for clinical trials to have maximum benefit from patient involvement in drug development.

Question 12:

In identifying the preferred therapeutic area among the respondents for PIDD, the respondents were asked to select all the predefined therapy areas they considered relevant, practical and useful for incorporating patient inputs. The most widely chosen therapeutic area was oncology (84%), followed by cardiovascular (78%) followed by

rare diseases (72%) and respiratory (66%). Neurology, on the other hand was opted the least number of times by the respondents (44%) among all the predefined choices of therapy areas. Only one respondent did not consider PIDD in any of the therapeutic areas – see Figure 17.

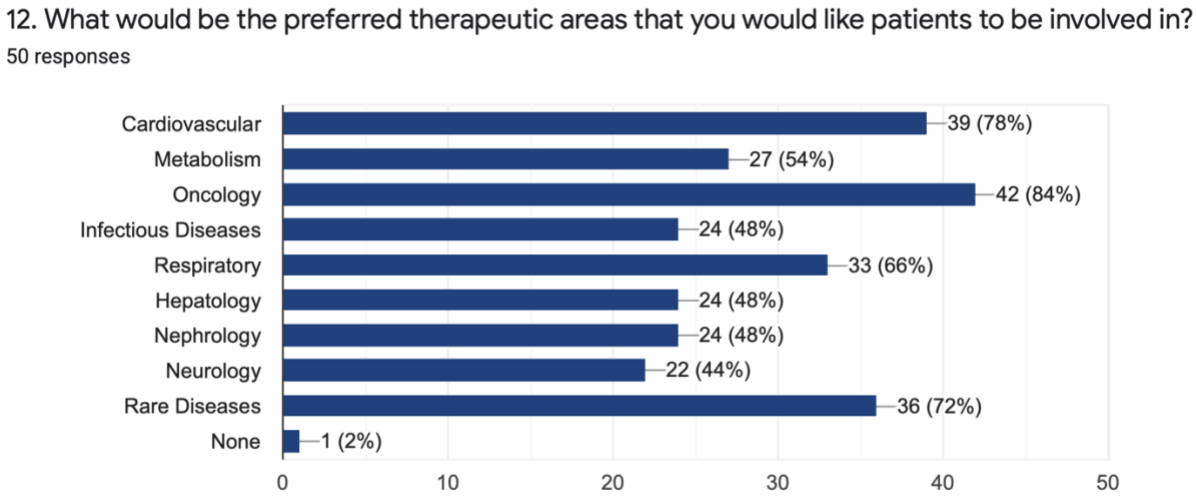

Figure 17: Preferred choice of therapeutic area for PIDD

Question 13:

In the exploration of respondents perception on ways to improve patient involvement in existing industrial setup, the author observed a pattern among the responses gathered which emphasised improving patient awareness and knowledge of clinical trials by providing adequate training to improve their ability to correlate real experiences with industrial practicalities. They also highlighted the importance of enlightening patients of their roles in drug development and its associated benefits in the advancement of healthcare systems. Spreading awareness of the opportunities available for patients in relevant phases of drug development so as to bring out better and novel treatment options was considered effective in improving patient and public interest in medical research.

Respondents also felt the need for companies to take the initiative in promoting involvement of patients in drug development by improving patient access to scientific research by engaging them in clinical trial discussions and internal decision making throughout all stages of pharmaceutical product lifecycle as and when needed to enhance the existing approaches to medicine. In addition, they believed that understanding patient concerns and considering their experiences through collecting feedbacks and conducting surveys by administering questionnaires, will help in formulating better methods of administration and processes of execution, to improve patients quality of life by delivering better quality products.

Regarding the suggested solutions for reforms in existing industrial practices, an overwhelming majority of respondents favoured the establishment of an institutional patient advisory board, to include patients as equal partners in the process of drug development. The responses indicated cultural change, amendments in organisational functionalities and openness to adoption of concept, with the support of organisational leaders, as initial steps towards a positive change in the practise of drug development. Responses also indicated that empowering patients by providing sufficient resources to strengthen their knowledge base would facilitate exchange of ideas. Maintaining specific patient databases was suggested in the responses so as to capture patient-related information. The importance of transparency in building trust between the organisation and patient, was perceived as the foundation of collaboration. Engaging in cross-industry fora, was regarded as a practical approach to infer and formulate frameworks for patient engagement. Respondents also believed that collaborations with organisations such as NGOs and hospitals (closely connected to patients) had the potential to broaden patient involvement.

Respondents suggested considering therapeutic areas in deciding the level of involvement by patients and their inputs by using gene therapy as an example. Reviewing existing projects in the pipeline and identifying possibilities for incorporating patient inputs was one of the positive suggestions from a respondent.

Few of the respondents believed that strengthening regulations around patient involvement in drug development by implementing proper funding strategies and adding relevant references could elevate the standards of drug development. Industrial engagement with regulators to better understand, how best to include PIDD in Heath Authority interactions was also highlighted in the responses obtained.

4.7 Conclusion

The findings from the results reinforce the fact that most of the pharmaceutical employees in the study have heard of the term 'Patient Involvement in Drug Development' but their awareness and knowledge about the subject and its related aspects specifically in terms of organisations that support it, is unsatisfactory. This was confirmed when the employees who admitted their familiarity with the names of support organisations (EUPATI, CTTI's PLC, PICORI and DART) listed in the questionnaire, contradicted themselves in another question (Have you heard of any organisation that supports PIDD?) by providing 'No' as the response. Interestingly, all the employees who admitted knowing about PIDD, ascertained their awareness by correctly enlisting names of the supporting organisations.

The study reveals that even though there has been immense encouragement from patient organisations in support of PIDD, in the form of patient training, funds and recommendations, they have not been successful in fulfilling their responsibility of creating awareness among patients and the pharmaceutical industry. Most of the employees still have the perception that patient involvement is best benefited in

clinical trials as supposed to any other drug development activity, which is possibly due to their unawareness of the potential benefits of patient inputs in other areas of scientific research.

Surprisingly, most of the pharmaceutical employees demonstrated adequate knowledge on all of the three stakeholders (patient organisations, pharmaceutical industry and regulatory authorities) responsible for the implementation of patient involvement in drug development within the pharmaceutical industry.

It is evident from the findings that the pharmaceutical industry is creating awareness among its employees through internal communications and organisational townhalls, however, it still lags behind on blending the concept into its existing practices. Needless to say that there are organisations, namely Pfizer and Novartis (according to the collated responses), currently incorporating patient inputs at various stages of its drug development, but there still remains a larger scope for its implementation across all the organisations within the industry.

The pharmaceutical employees expressed a positive attitude towards the industrial application of PIDD. Majority of them considered it to benefit in effective target identification, risk-benefit assessment, better understanding of disease pathology, drug interactions and drug safety profiles, resulting in better decision making, providing valuable insights on protocol design, enhancing pharmaceutical innovation, effective pharmacovigilance, meaningful outcome measures and better product strategy. They also expressed concerns regarding patient bias and improper measurability criteria.

The findings revealed several ways of incorporating patient inputs in the process of drug development, which includes development of patient reported outcomes, concept elicitation, collaboration in post marketing activities, participation in

regulatory review meetings and organisational internal decision making, collation of natural history, obtaining adverse event reports for supporting pharmacovigilance activities, involvement in designing trial documents such as protocol and informed consent.

The results supported the study objectives by identifying several barriers to PIDD, out of which lack of dedicated groups to conduct PIDD activities was considered the most likely factor, which justifies the emphasis given to the formation of patient advocacy groups, as a recommendation on ways to improve the practise of PIDD. Respondent's positive attitude towards the incorporation of PIDD is believed to enable better execution of the programme, while improving their knowledge and awareness on the subject will maximise its utilisation.

The next chapter will include further conclusions based on comparisons from secondary research and will provide answers to the original posed research questions.

CHAPTER 5: CONCLUSIONS

5.1 Answering the research questions

Question 1: How aware are the industrial R&D employees about the concept of patient involvement in drug development?

As indicated from the responses obtained in the survey, it is evident that the level of awareness observed among pharmaceutical employees, is just average, considering the fact that they all work in research and development and are closely associated with drug development activities. This is mainly because of their lack of knowledge and training on the concept, which is apparent in the pattern of responses observed to be more inclined towards existing practices. Even though a remarkable knowledge and awareness of PIDD among pharmaceutical employees was portrayed, there still remains scope of ameliorating their awareness around the core concept and its related facets.

Despite the encouragement and efforts from patient organisations and regulatory bodies in empowering patients by creating an environment viable for the implementation of patient involvement in drug development, there still remains a gap with respect to its in-depth knowledge and awareness, that needs to be filled. Measures and initiatives taken by the Pharmaceutical industry to inform its employees about PIDD through internal communications further improves verbal communications among colleagues. This improves knowledge of PIDD, but not to the extent where they can clearly distinguish between the terms ‘patient involvement’ and ‘patient participation’. The study participants highlighted the importance of adequate training and improved access to clinical trials for patients to provide their inputs, as measures to improve awareness of patient involvement in drug development.

Question 2: What are the barriers that restrict patient involvement in decisions relating drug development within the pharmaceutical industry?

The findings make it apparent that the pharmaceutical employees find managing the additional efforts associated with the implementation of a new concept, to pose challenges to its adoption within companies. These include lack of dedicated groups to coordinate the activities of PIDD, delays in project deliverables and time constraints associated with extensive research.

Several patient and organisation related apprehensions also contribute to the under-utilisation of patients and their inputs in drug development due to fear of patient bias, organisational reluctance, lack of patient interest, scepticism in relation to patient knowledge and skills, doubts regarding available opportunities, budget constraints and adequate population delineation. According to the employees, regulatory and legal constraints add to the slowness of its progress and execution.

The study of the barriers restricting PIDD according to the pharmaceutical employees surveyed in this study helps to elucidate the detrimental effects it can have on the future advancements of healthcare practices.

Question 3: What recommendations would help to improve involvement of patient in drug development?

Since a lack of dedicated groups for handling PIDD activities is identified as the major factor in the reluctance towards its implementation, establishing a patient advisory group within organisations, committed to the scheme, will foster effective drug development practices. As per the suggestions from study participants, stakeholders must strive to create awareness among patients and avail opportunities within company's internal systems to effectively utilise patients and their inputs in promoting

better medical practices. They believe that pharmaceutical organisations should be more proactive towards promoting PIDD in organisational internal activities such as decision making and formulation of strategies. Considering patients as equal partners in the process of drug development is regarded as key in collaboratively working towards safeguarding patient health by delivering innovative medicines.

It is contemplated that understanding patient concerns and their day-to-day challenges with the existing treatment options through surveys, virtual communications and feedbacks, will give a profound insight into gaps in the healthcare system. Support from regulatory bodies in strengthening the practicality of the scheme, is considered important for understanding how best to include PIDD in health authority interactions and establishing policies for renumeration.

The answers, thus, reveal a strong knowledge base around the concept to be an enabler for the implementation of PIDD in industrial practise. It not only enhances problem solving capabilities but also generates interest and an easier acceptance to change.

5.2 Comparing results from Primary and Secondary Research

On comparing the primary research with the secondary research, it is observed that previous studies on PIDD are centred around identifying the barriers, enablers (Ocloo *et al.*, 2021) and perspectives (Hansen, Nørgaard and Hallgreen, 2019), whereas this study not just identified the challenges posing threat to the concept implementation but also gained insights on knowledge and awareness of pharmaceutical employees around the subject and its related aspects, specifically support organisations, stakeholders and target areas. These assessments assist in answering questions to why, even after constant efforts from various organisations such as EUPATI and CTTI in supporting the conceptual execution, there still is a hurdle in making progress.

Despite the fact that these patient organisations have established exceptional guidance, recommendations and tools for carrying out PIDD, observations on the unsatisfactory levels of awareness of their purpose, demonstrate their inefficiency in portraying and promoting themselves by grabbing organisational attention to inculcate proposed principles in medicine practice.

The barriers identified such as lack of dedicated patient groups, distrust in patient abilities, time and budget constraints and regulatory impediments are to a great extent similar to the ones observed in the previous studies (Lowe *et al.*, 2016), however, the risk of misinterpreting patient views and opinions was more strongly emphasised in this study. The majority of the studies on patient involvement in drug development have included multiple stakeholders, especially leaders representing various healthcare groups, while this study was aimed specifically at understanding the perspective of pharmaceutical employees on the subject. Unlike a study conducted on antimicrobial drug development (Gibson *et al.*, 2019), the recommendations collated in this study are predominantly targeted towards improvising drug development practices in general and are not specific to a particular field of medicine, keeping in line with the study objective of gathering an overall industrial insight.

5.3 Concluding thoughts

5.3.1 *Contributions and Limitations of the Research*

The study was conducted among 51 pharmaceutical employees across various divisions of research and development and was completed satisfactorily, considering the short span of time available for its completion. The findings and results were presented in both graphs and tables for better visualisation. Though the overall response rate was a bit less than expected, the data is believed to present a fair and honest presentation of participant perceptions, knowledge and awareness on the

subject of patient involvement in drug development. Unlike previous studies, with focus on collecting general data from a broad population group, this study utilised a specific group to generate elaborate interpretations on the subject so as to capture wholistic perspectives on the various aspects of PIDD.

The limitations of the study are based around the relatively smaller sample size. The opinions and responses collated from the survey could have possibly been impacted by factors such as personal bias and failure to recollect information. The administration of the questionnaire revealed a reluctance from employees about disclosing their company names, which was only intended to ensure their relevant background. In hindsight, this question could be reframed so as to avoid hesitancy.

Even though measures for effectively implementing the practise of PIDD are laid out by various initiatives of public and private partners, the lack of awareness and knowledge of them reduces their potential to make a significant impact. Thus, by assessing the collective consciousness, this study contributes to the unravelling of the main challenges hindering the maximal utilisation of PIDD outcomes. Apart from the lack of concept awareness and knowledge, study findings revealed the absence of dedicated groups in managing PIDD activities to be the most common barrier to patient involvement in drug development, for which establishing an organisational patient advisory group was recommended. The overall neutral responses to reluctance from the organisation being a barrier to PIDD limited complete understanding of employee perception, thereby providing room for future research.

5.3.2 *Recommendations for Effective Execution*

This study identified insufficient knowledge and awareness of both employees and patients as being the core problem in the underwhelming progress of patient involvement in drug development, leading to a chain of interconnected challenges.

While the employees considered patient's poor knowledge of scientific research and its affairs to be a factor in the lack of industrial confidence in PIDD, the study also found that respondents had an unsatisfactory degree of agreement on the concept. Even though the subject has been in the limelight recently and information is available online, in journals and moreover within the organisation in the form of internal communication and townhalls, the results were not satisfactory.

The author believes that addressing this core issue by providing adequate training to pharmaceutical employees will establish a stronger conceptual foundation that can help nurture innovative ideas and recommendations for better execution of patient involvement in drug development. It was also believed that enlightening patients will help in addressing challenges associated with individual interests and industrial trust.

Furthermore, industries should introduce a change in its culture so as to adopt newer methods and strategies. Establishing patient advocacy groups, building trust, creating opportunities, engaging patients in meetings and discussions, collecting feedback, experiences and opinions, maintaining transparency and developing knowledge sharing platforms are some of the key recommendations for effective execution of PIDD. Collaborations with health authorities and establishment of stronger regulations are also proposed to embrace the concept of patient involvement in drug development.

5.3.3 *Recommendations for Future Research*

The scope for future research could be centred on patients themselves, whereby surveys can seek to understand their perspective on being involved in drug development. Identifying barriers from patients' perspective will help in providing better optimised solutions and frameworks for battling the existing gaps in the system. Establishment of approaches involving patients requires their willingness and interest

in participation. Additionally, studies around identifying major sources of information about patient involvement in drug development, will help in evaluating the efficiency and impact of these informational tools in improving knowledge and awareness.

There is also scope for expanding this research by comparing the opinions and recommendations from employees of various divisions of R&D department. This will not only help in identifying unique and specific information perceived differently among various employee groups, but will also help spot key areas of improvement within each division.

In the pharmaceutical world, regulatory bodies can provide a range of information, which can give rise and also answer several research questions. Carrying out research in conjunction with regulatory bodies, to identify pharmaceutical companies that have included patient inputs as a mandate in their documentation for regulatory submissions will prove the worth of the concept. This will not only help in gathering evidence but will also build the PIDD database of the future.

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APPENDICES

Appendix A

Questionnaire

Barriers that Restrict Patient Involvement in Drug Development: An Industrial Perspective

Dear Respondent,

I am Dr. Ria Rose Roy, a post-graduate student at Griffith College Dublin, Ireland. For my dissertation in my degree in Masters in Pharmaceutical Business and Technology, I am carrying out this research on the barriers that restrict Patient Involvement in Drug Development. I am asking employees of Pharmaceutical companies to complete this survey in order to get an industrial perspective.

Patient Involvement, as per this research, is defined as consciously assimilating patients' opinions, ideas, needs, experiences and incorporating them into the process of drug development. Patients' contribution as trial subjects is outside the scope of this research topic.

The survey is divided into five sections, of which the first three sections are aimed at gathering information on the respondent's demographics, awareness and knowledge about the topic, whereas sections four and five are aimed at identifying barriers that restrict patient involvement in drug development and recommendations for improving the current state of the concept, respectively.

Participant privacy is highly assured. The responses collected will be anonymous, highly confidential and handled in compliance with the current General Data Protection Regulations (GDPR).

The survey will take approximately 6-8 minutes to be completed.

Thank you for your participation.

* Required

Participant Consent *

◯ I understand the purpose of this research. I voluntarily agree to participate in this study and have my responses used for the purpose of this research titled 'Barriers that Restrict Patient Involvement in Drug Development'.

Demographics

Gender *

- ○ Male
- ○ Female

Age *

- ○ 18-30 years
- ○ 31-50 years
- ○ Over 50 years

Which Geographical Zone do you belong to? *

- ○ Asia
- ○ Europe
- ○ Australia
- ○ America

Company Name *

Your answer

Department *

Your answer

Line Function *

Your answer

How many years of experience do you have in R&D? *

- ◯ Less than a year
- ◯ 1-5 years
- ◯ 6-10 years
- ◯ Over 10 years

Awareness of Patient Involvement in Drug Development

1. Are you aware of the Drug Development Process? *

- ◯ Yes
- ◯ No

2. Have you heard about the concept of Patient Involvement in Drug Development (PIDD)? *

- ◯ Yes
- ◯ No

If yes, from which source of information did you hear about PIDD?

- [ ] News
- [ ] Professional Journals
- [ ] Organisational Internal Communications (Townhalls or bulletins)
- [ ] Verbal Interactions with Colleagues
- [ ] Internet
- [ ] Other: _____

3. Are you aware of any organisation that supports PIDD? *

- ○ Yes
- ○ No

If 'Yes', then please name the organisation

Your answer

4. Have you heard about any of the following organisations? *

- [ ] European Patients' Academy on Therapeutic Innovation (EUPATI)
- [ ] The Clinical Trials Transformation Initiative's (CTTI's) Patient Leadership Council (PLC)
- [ ] Patient-Centered Outcomes Research Institute (PCORI)
- [ ] Dystrophy Annihilation Research Trust (DART)

Knowledge around Patient Involvement in Drug Development

5. At what stages of the Drug Development Lifecycle, do you think patients can be involved? (Select all that apply) *

- [ ] Discovery
- [ ] Preclinical
- [ ] Phase 1
- [ ] Phase 2
- [ ] Phase 3
- [ ] Post Approval
- [ ] None of the Above

6. Who do you think are the stakeholders for the implementation of PIDD? (Select all that Apply) *

- [ ] Patient Organisations
- [ ] Pharmaceutical Industry
- [ ] Regulatory Agencies
- [ ] None of the Above

7. Do you think involving patients and their disease experiences can be of any benefit to the process of drug development? *

- ◯ Yes
- ◯ No

Please provide the reason for choosing the above response *

Your answer

8. As per your opinion, what are the ways in which patients and their inputs can be involved within the drug development process? *

Your answer

Barriers to Patient Involvement

9. Would you support involving patients and their inputs as part of the drug development process? *

- ◯ Yes
- ◯ No

10. How likely do you think the following barriers could be restricting Patient Involvement in Drug Design? *

	Unlikely	Neutral	Likely
Lack of dedicated committees, groups and personnel to conduct Patient Involvement in Drug Development activities.	◯	◯	◯
Regulatory and Legal constraints	◯	◯	◯
Lack of industrial confidence in patient knowledge and skills	◯	◯	◯
Added financial requirements and support	◯	◯	◯
Difficulty in choosing proper representation of patient population.	◯	◯	◯

Difficulty in choosing proper representation of patient population.	○	○	○
Lack of interest from patient population.	○	○	○
Lack of opportunity for patient to be involved in drug development.	○	○	○
Fear of patient bias.	○	○	○
Reluctance from the organization.	○	○	○

If in your opinion, there are any other barriers that are not mentioned, then please specify

Your answer

Ways to Improve Patient Involvement

11. Which of the following areas of drug development activities, do you think patient involvement can be most beneficial? *

- [ ] Clinical Trial
- [ ] Regulatory Meetings
- [ ] Funding
- [ ] Policy Generation
- [ ] Pharmacovigilance
- [ ] Product Strategy
- [ ] Evidence Generation
- [ ] Other:

12. What would be the preferred therapeutic areas that you would like patients to be involved in? *

- [ ] Cardiovascular
- [ ] Metabolism
- [ ] Oncology
- [ ] Infectious Diseases
- [ ] Respiratory
- [ ] Hepatology
- [ ] Nephrology
- [ ] Neurology
- [ ] Rare Diseases
- [ ] Other: _____

13. According to you, what possible actions could be taken from an industrial standpoint to improve Patient Involvement in Drug Development? *

Your answer

Back Submit

APPENDIX B

I. Ethical Approval Forms – Application Form

SECTION 1: ETHICS APPLICATION DETAILS

1.1 PROJECT TITLE:

A Quantitative Exploration of the barriers that restrict patient involvement in drug development: An Industrial Perspective.

1.2 RESEARCHERS NAME:

Ria Rose Roy

1.3 PROGRAMME OF STUDY:

MSc. in Pharmaceutical Business and Technology

1.4 SUPERVISOR'S NAME:

Gillian McMahon

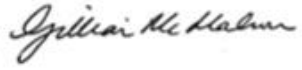
NOTE: Supervisors are responsible for ensuring that students fill in this form correctly and that all ethical areas have been considered.

1.5 DECLARATION: The information in this application form is accurate to the best of my knowledge. I undertake to abide by the ethical principles outlined by the Innopharma and Griffith College ethics policy. If this proposal is approved Griffith College Ethics Committee, I undertake to comply with any conditions required by the Committee. I confirm that this application is complete with all required documentation and signatures and that these are attached as appendices in an accompanied electronic document.

(Yes) No

STUDENT SIGNATURE :

DATE: 20.03.2021

SUPERVISOR SIGNATURE: 

DATE:1/4/21

SECTION 2: DESCRIPTION OF RESEARCH STUDY

2.1 Purpose of research (300 words maximum) –

The concept of Patient Centric Drug Development has been the talk of the town for the pharmaceutical industry in the recent years. Patients are only used as trial subjects in the drug development, however, it's high time that this practice is questioned. Even though patients are the end users, they still remain the most underused resource in the healthcare system. This is accounted to be because of the regulatory restrictions. Some pharma companies, such as Novo Nordisk, are taking steps to break this monotony by establishing a patient advisory board within the organization, however, this practice is restricted to just a few companies. Understanding the reason for reluctance will help in bringing solutions for the problem.

There have not been many studies that have looked over these barriers from an industrial perspective. This study will, therefore, fill this gap. There needs to be a shift from the conventional method of research, where patients were just considered the end-users, to a more patient centric approach, which utilizes the real time patient experiences and suggestions to develop a product or device. Such an approach would aid in minimizing cost and creating value. Various Pharmaceutical companies have engaged themselves in outreach programs that involve creating awareness about their products, however, such initiatives are generally part of the marketing strategy and patient education, which are majorly beneficial for the company and its product. However, involving patients in drug development related decision making, not just helps the company in better understanding the customer demand, but also helps the customers by offering better value adding products, that are capable of improving

patient lives. Therefore, understanding and identifying barriers would help in formulating better functional strategies, in the future, by taking all these factors into consideration.

2.2 Research methodology:

Study Design: The study is designed to collect qualitative data from the employees of research and development department of 2 Pharma companies, namely Pfizer and Novartis in India (as both the company's R&D departments are based in India). The data will be collected with the help of a questionnaire that will be provided to the respondents in the form of an online survey. The questionnaire will be designed so as to capture their attitude towards the involvement of patients in the drug development related decision-making.

Study Period and Population: The study period is estimated to be of 3 months (March 2021-May 2021), with a population size of 50-60 respondents. The study population will include employees of Novartis Healthcare and Pfizer (R&D department), particularly of the data management line function. This discretion is made in regard to the availability of the resources. The respondents will be contacted through LinkedIn. After obtaining their consent, they will be provided with online survey link, via email, so as to capture their individual responses, as part of data collection.

Data Collection: The data will be collected with the help of a previously designed questionnaire that aligns with the aim and objectives of this research and helps in capturing respondent's opinions regarding the possible barriers that restrict patient involvement in drug development. It will be designed based on previously conducted studies, their results and outcomes.

Data Analysis: The outcome variable in this research is respondent's opinion which will be analyzed using Likert Scale. The various levels of likeliness (very likely, likely, less likely and never) will be utilized to assess the opinion of industrial employees towards patient involvement and its associated barriers in drug development. The final research data will be represented graphically using pie charts and graphs.

2.3 Proposed questions for questionnaires and/or interviews **must be included**. You may attach a separate document as part of your appendices file if necessary.

The questionnaire design is based on the Likert scale so as to access the employee attitude and opinion about involving patients in drug development decision making, however, it is not restricted to Likert scale alone. The questionnaire will also include open ended questions so as to capture broader and uncommon perspectives and barriers which are not included in the preset selection options.

The questionnaire will be divided into 3 sections:

- **Section 1: Demographics** – This section will include details with regard to Company Name, Department and line function of the respondents.
- **Section 2: Barriers to Patient Involvement** – This section will include the main body of research wherein; the barriers would be identified, and opinions would be captured with the help of Likert scale and open-ended questions. It would include questions based on likeliness (very likely, likely, less likely and never). For example: How likely are the following barriers capable of restricting patient involvement in drug development?
    - Lack of dedicated committees, groups and personnel
    - Regulatory Constraints
    - Fragmented patient population
    - Lack of patient knowledge and skills
    - Lack of opportunities
    - Fear of Bias
    - Reluctance
    - Other (Open ended question)
- **Section 3**: **Involvement Improvement** – This section will be open ended and will be designed to capture respondent's opinion on how patient involvement could be improved in drug development. This section would provide an insight on the strategies, identified by the employees, that can be adopted so as to overcome the barriers.

SECTION 3: ETHICAL ISSUES

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

SUBJECT MATTER

Does the research proposal involve:

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

RESEARCH PROCEDURES

Does the research proposal involve:

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

PARTICIPANTS

Does the research proposal involve:

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

(Adult participants; Adults with psychological impairments; Adults with learning difficulties; Adults under the protection/control/influence of others (e.g. in care/prison); Relatives of ill people (e.g. parents of sick children); Hospital or GP participants recruited in medical facility; persons under the age of 18)

If you have answered NO to ALL questions, you do not need to complete Section 4. Please go to Section 5.

If you have answered YES to ANY question in SECTION 3, you must fill in SECTION 4.

SECTION 4: ETHICAL IMPLICATIONS

Only fill in this section if you answered YES to ANY of the questions in Section 3

4.1. If your ethics related to ***Subject Matter***, outline your action plan to deal with such sensitive issues.
4.2. If your ethics related to ***Research Procedures***, outline your action plan to deal with sensitive research procedures.
4.3. If your ethics related to ***Participants***, outline how you will protect vulnerable persons or those that do not have English as their first language.

SECTION 5: PARTICIPANTS

5.1. Outline your participant profile and why you have chosen them for this study

The participants of this study will be employees of 2 pharmaceutical companies, namely Novartis and Pfizer, of the Research and Development Department of the respective companies. It is necessary to get the data from people who are familiar with drug development, which is why the R&D employees are chosen as study participants.

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

The respondents will be contacted through LinkedIn and the online links to the survey will be sent to them. They will be clearly briefed about the aim and objective of the research, which would also include informing them about the data privacy policies, how the research data would be handled and what for the data will be used (which would state that the collected response/data will only be used for the purpose of this research, conducted as part of the Master's program in Griffith College, Dublin). The data would be used only for the purpose of this research titled 'A Quantitative Exploration of the barriers that restrict patient involvement in drug development: An Industrial Perspective'.

SECTION 6: INFORMATION, CONSENT AND CONFIDENTIALITY

6.1 **Information Letter for participants**

Please confirm below that your information letter covers:

Description of the research topic and method	(Yes) No
Details of what participation will involve	(Yes) No
Rights to anonymity	(Yes) No
Confidentiality	(Yes) No
Rights to withdraw from the research	(Yes) No
The contact details of the researcher and supervisor (if necessary)	(Yes) No

6.2 **Consent form for participants**

Please indicate below if your research requires a signed consent form by selecting the relevant option only:
Yes: my research requires signed consent and I have attached a completed consent form in the appendices of my application.
(**No**): my research study involves an online survey only and/or does not require signed consent. I will include boxes for participants to tick at the beginning of the survey to show they understand the research and agree to take part

SECTION 7: STORAGE OF MATERIALS

7.1. How do you propose to store the information & for how long? How will you manage data protection issues?

The data for this research will be stored for 2 years, in an electronic format, copy of which will also be sent to the college, as part of the dissertation submission. The file will be password protected, as part of data protection.

SECTION 8: DOCUMENT CHECKLIST

NOTE: Applicants must attach an electronic document to include all appendices.

Which documents are attached? Please tick N/A if not applicable:

8.1 Information letter for participant	(Yes) N/A
8.2 Consent form for participant	(Yes) N/A
8.3 Questions/survey for interviewees/focus groups etc *(i.e complete/close to complete)*	(Yes) N/A
8.4 Other document(s) - please specify below:	

GRIFFITH COLLEGE

Consent to take part in research

An Exploration of the barriers that restrict patient involvement in drug development: An Industrial Perspective

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

- I _____ voluntarily agree to participate in this research study.
- I understand that even if I agree to participate now, I can withdraw at any time or refuse to answer any question without any consequences of any kind.
- I understand that I can withdraw permission to use data from my survey within two weeks after submitting my responses, in which case the material will be deleted.
- I have had the purpose and nature of the study explained to me in writing and I have had the opportunity to ask questions about the study.
- I understand that participation involves answering the questions asked in the survey.
- I understand that I will not benefit directly from participating in this research.
- I understand that all information I provide for this study will be treated confidentially.
- I understand that in any report on the results of this research my identity will remain anonymous. This will be done by not collecting my name and disguising any details of my survey which may reveal my identity.
- I understand that disguised extracts from my survey may be quoted in the dissertation of the researcher and could potentially be made available in online e-journals.
- I understand that I will adhere to all of the codes of conduct and employee confidentiality for Novartis /Pfizer and there is no expectation to breach these by partaking in this research.
- I understand that if I inform the researcher that myself or someone else is at risk of harm, they may have to report this to the relevant authorities. They will discuss this with me first but may be required to report with or without my permission
- I understand that signed consent forms will be retained in an electronic format, with the researcher. The forms will be stored in a password protected file, with access to the researcher the exam board confirms the results of the researcher's dissertation.
- I understand that my responses for the survey will be retained for two years from the date of the exam board.

- I understand that under freedom of information legalisation I am entitled to access the information I have provided at any time while it is in storage as specified above.
- I understand that I am free to contact any of the people involved in the research to seek further clarification and information.

Researcher Details

Name: Ria Rose Roy

Degree Programme: M.Sc. in Pharmaceutical Business and Technology

College Details: Griffith College, Dublin

Contact number: 0892525560

Contact mail: riaroseroy@gmail.com

Signature of participant

[Full Name – Printed]

Signature of research participant

---------- ---------- Date

Signature of researcher

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

Ria Rose Roy 30 March 2021

GRIFFITH COLLEGE

Participant Information Letter

An Exploration of the barriers that restrict patient involvement in drug development: An Industrial Perspective.

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

WHO I AM AND WHAT THIS STUDY IS ABOUT

I, Ria Rose Roy, am a student at the Griffith College, Dublin, pursuing my Masters in Pharmaceutical Business and Technology. As part of my thesis work, I am conducting this online survey to identify the barriers restricting patient involvement in decisions relating drug development and to better understand the industrial mindset in relation to patient involvement in health research. The responses collected from this survey will only be used for the purpose of this research.

WHAT WOULD TAKING PART INVOLVE?

The participant will only need to answer the questions provided in the survey. The responses obtained by the participants will give the researcher, their perspective on the research topic, which is 'A Quantitative Exploration of the barriers that restrict patient involvement in drug development: An Industrial Perspective.'

WHY HAVE YOU BEEN INVITED TO TAKE PART?

The participant of this study is identified based on their job description and their company of work. This research involves identifying barriers associated with patient involvement in drug development from an industrial perspective, therefore as per the aim of the study, employees of the Research and Development Department of Novartis Pharmaceuticals and Pfizer are approached for taking part in the study. The R&D department is chosen so that the study population is well aware of the process of drug development.

The participants will be randomly identified via their LinkedIn profiles and on their consent, they will be sent the online survey form.

DO YOU HAVE TO TAKE PART?

The participation is completely voluntary with the participant having all rights to withdraw at any point of time without any consequence. It is the participant's choice if they want to completely answer the questionnaire or no. If the participant needs to withdraw, he/she may contact the researcher (Ria Rose Roy), details of whom are given below.

WHAT ARE THE POSSIBLE RISKS AND BENEFITS OF TAKING PART?

Possible risks:

- There are possibly no risks involved in taking part in the survey apart from data confidentiality, which is taken care of by keeping the responses anonymous (participant names are not collected) and confidential.

Possible Benefits:

- The responses can be help the researcher get a better understanding about the industrial perspective regarding the barriers that could potentially restrict patient involvement in drug development.
- The results of this study (which will be obtained through the responses given by the participant) can support future studies that intend to understand the concept of patient centric drug development.

WILL TAKING PART BE CONFIDENTIAL?

Taking part in the survey will be confidential as the access to the data is only restricted to myself and the college (as it is as part of my thesis submission). The data will be stored in a password protected file, access to which will only be granted to authorized personnel. The anonymity of the data will be maintained by not collecting names of the participants. Only the information required for the research is collected and information non relevant to the research will not be collected.

The collected response/data will only be used for the purpose of this research titled 'A Quantitative Exploration of the barriers that restrict patient involvement in drug development: An Industrial Perspective', conducted as part of the master's program in Griffith College, Dublin.

HOW WILL INFORMATION YOU PROVIDE BE STORED AND PROTECTED?

The data for this research will be stored as long as it is useful, in an electronic format, copy of which will also be sent to the college, as part of the dissertation submission. The file will be password protected, as part of data protection. Since this research is done as part of my thesis submission, the college and myself, will have access to the data, however, the confidentiality will not be harmed.

WHAT WILL HAPPEN TO THE RESULTS OF THE STUDY?

The results of the study and its content will be submitted to Griffith College, Dublin, as part of the thesis submission and will be made accessible in the college library and could potentially be made available in online e-journals.

WHO SHOULD YOU CONTACT FOR FURTHER INFORMATION?

For further details please contact the following:

Name: Ria Rose Roy

Contact Number: 0892525560

Email Address: riaroseroy@gmail.com

THANK YOU

IV. Ethical Approval Forms – Ethics Declaration Form

Innopharma education

Ethics Declaration Form

PROJECT TITLE:

A Quantitative Exploration of the barriers that restrict patient involvement in drug development: An Industrial Perspective.

RESEARCHERS NAME:

Ria Rose Roy

PROGRAMME OF STUDY:

MSc. in Pharmaceutical Business and Technology

SUPERVISOR'S NAME:

Dr. Gillian McMahon

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

DECLARATION: The information in application form is accurate to the best of my knowledge. I undertake to abide by the ethical principles outlined by Innopharma/Griffith College's ethics policy in my research project. I confirm that I have completed a full ethics assessment for my research project as per the college guidelines.

I confirm that the research contained within my research project proposal does not require Ethical review and/or subsequent approval by the GEC/Innopharma Ethics Committee.

STUDENT SIGNATURE : Ria

DATE: 1/4/2021

SUPERVISOR SIGNATURE: Gillian McMahon

DATE: 1/4/21