MANAGEMENT FACTORS CONTRIBUTING TO DELAYS IN CANCER DRUG REGISTRATION IN SOUTH AFRICA

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DECLARATION

I, Mmatsela Lorraine Shai, declare that this research report is my work except as indicated in the references and acknowledgments. It is submitted in partial fulfillment of the requirements for the degree of Master of Business Administration at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination in this or any other university.

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CERTIFICATION

I undersigned certifies that I have read and hereby recommends for acceptance by the University of Witwatersrand, A Research entitled Leadership and Management factors contributing to delays in cancer drug registration in South Africa, in fulfillment of the requirements for the award of Master of Business Administration.

Name:

Signature: _____ Date _____

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DEDICATION

This research study is dedicated to God Almighty first for his grace and mercy throughout the journey from beginning to end. I would also like to dedicate the study to family and friends who unfortunately are not with us today due to cancer, may their souls rest in eternal peace.

Lastly, I dedicate this study to my two late aunts' Mokgadi Elaine Mokgawa and Elizabeth Mathakga Botha who were very dear and special people in my heart. They were the Masters of Education and today I am proud to have been not only a niece to them, but a student too. Their lessons will forever live on. They have always been a positive anchor and strength to me. May their beautiful souls rest in eternal peace.

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ABSTRACT

One of the leading causes of sickness and early death worldwide is cancer.The cancer mortality is especially high in low and middle-income countries (LMICs). The National Medicines Regulatory Authorities (NMRAs) play an important role to ensure that drugs meet the quality, safety, and efficacy requirements made available to patients. The National regulatory authorities are also accountable for enforcing regulatory demands promptly and ensuring that patients have timely access to drugs. Delays in the registration of cancer drugs will have an adverse impact on cancer patients such as poor quality of life and early death. Section 27 of the Constitution of South Africa guarantees the right to have access to health care service. The study aims to determine management factors that contribute to delays in the registration of cancer drugs. As a result, the research contributes to the theoretical body of knowledge. The study took a qualitative approach by sending out an interview schedule to 10 South African pharmaceutical companies for self-completion.

Several methods were considered in determining a suitable study strategy, study design, research approach, and self-administered interview questions. These methods were implemented in order to achieve the study's objectives. This served as a primary source of information. The interview questions were completed and uploaded for analysis using the Qualtrics XM tool. The information that was gathered showed that all of the participants have to deal with the problem of registration delays for cancer drugs. The findings could help to clarify the overall critical factors, their impact, and the relationship between the key factors and stakeholders involved in cancer drug registration. The uniqueness of this research lies in the results provided by different participants from the pharmaceutical industry and in evaluating their perspectives on these delays. The research adds significant value through its evidence based on the responses received.

KEYWORDS

Management factors, Delays, cancer, registration, drug application, regulators, and Pharmaceutical Companies.

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LIST OF ABBREVIATIONS

WHO	World Health Organization
USA	United States of America
EU	European Union
EMA	European Medicines Agency
GMP	Good Manufacturing Practice
TGA	Therapeutic Goods Administration
FDA	Food and Drug Administration
HC	Health Canada
SAHPRA	South African Health Products Regulatory Authority
MCC	Medicines Control Council
NCE	New Chemical Entity
NAS	New active substance
API	Active Pharmaceutical Ingredient
GRevPs	Good Review Practices
LMICs	Low- and middle-income countries
NMRAs	National Medicines Regulatory Authority
QoS	Quality of Decision-Making Orientation Scheme
ZaZiBoNa	Zambia, Zimbabwe, Botswana, Namibia

CHAPTER ONE: INTRODUCTION

1.1 Introduction and Background

One of the leading cause of sickness and early death worldwide is cancer (Cortes et al., 2020). Globally, one in five people will have cancer in their lifetime and one in ten will die from the disease (Ferlay et al., 2021)..The cancer mortality is especially high in low and middle income countries (LMICs) such as sub-Saharan Africa (Kizub et al., 2022).It is predicted that in 2040 new cases of cancer will increase by 47% globally from the estimated 19.3 million cases in 2020 if the trends remain the same (Sung et al., 2021). The increasing disease burden and high risk of death especially in LMICs requires governments to put efficient infrastructure and measures in place for cancer prevention and management (Chitha et al., 2022). One such measure is access to cancer drugs that are vital in pain management for cancer patients and in some malignancies, can cure the cancer (Ruff et al., 2016). The cancer drugs therefore provide extended life and improved quality of life for cancer patients (Davis et al., 2017).

Before drugs can be made available to the market and for use by patients, National Medicines Regulatory Authorities (NMRAs) assess them to ensure that the drugs meet the quality, safety, and efficacy standards (Broojerdi et al., 2020). Regulatory authorities therefore contribute to the public health of any country (Sithole et al., 2020). The key question is therefore whether these NMRAs are managed efficiently to provide a timely service to register the much-needed drugs for the benefit of public health. In South Africa, the South African Health Products Regulatory Authority (SAHPRA), formerly known as the Medicines Controls Council (SAHPRA, 2022), performs this regulatory function.

The approvals for the registration of drugs have been found to take three to five years in South Africa (Keyter et al., 2020). The approval of drugs for registration by regulatory authorities is directly linked to access of vital cancer drugs to patients (Cho & Han, 2022). Delays in the registration of generic cancer drugs has also been identified by the Department of Health (2017) as one of the barriers to medicine access. These delays have been found to be caused by regulatory processes that are slow, complicated and lack transparency

(Barrios et al., 2022). Similar challenges were found within the Southern African Development Community (SADC) collaborative medicines registration initiative called ZaZiBoNa where drug registration delays were attributed to high number of applications, significant backlogs, insufficient technical staff/assessors, budgetary constraints, and inadequate capacity to assess highly technical product dossiers (Ncube et al., 2022). These regulatory process challenges relate to management because management is generally defined from a process perspective as the achievement of organizational goals through effective and efficient planning, leading, organizing and controlling (Tomaževič et al., 2015).

Management theory is therefore pivotal in the way complex organizations are managed and most 21st century organizations operate efficiently by applying principles such as those of the Scientific Management theory (Kumar, 2017). SAHPRA as a public institution is by its nature bureaucratic and slow, hierarchical and process-based management (Drechsler, 2020) characterizes bureaucracies. Some proposed solutions for timely access to essential medicines have been found to include the improvement of turnaround time of drug registration processes and systems as well the development of requisite technical capacity (Roth et al., 2018). These solutions are aligned to some of the Classical Management theory's principles such as Scientific management that emphasize the need to appoint appropriately skills staff for efficiency, effectiveness and productivity (Kitana, 2016); and the Modern Management theory such as the Systems theory that emphasizes an integrated approach that focuses on systems and addressing complex problems using complex management strategies (Sridhar, 2017; Hussain et al., 2019).

The pharmaceutical industry plays a key role in any health system as they develop, manufacture and market new drugs to deal with the disease burden (Tawfik et al., 2021). This study aims to determine management factors that contribute to delays in cancer drug registration in South Africa from the pharmaceuticals' perspective. Section 27 of the Constitution of South Africa guarantees the right to have access to health care service (Republic of South Africa, 1996). This study is important because drug registration delays affect access to vital lifesaving or life extension drugs by cancer patients; a basic human

right guaranteed by the Constitution. Furthermore, there are risks associated with NMRAs that are not efficient in the regulation and registration of drugs such as citizens being exposed to medical products that are potentially unsafe; creation of an environment fertile for the distribution of “substandard, spurious, falsely labelled, falsified and counterfeit” (SSFFC) medical products; and precludes the coherent use of medical products (Ndomondo-Sigonda et al., 2017). This study contribute to the body of knowledge that address identified risks associated with delays in the registration of cancer medications.

1.2 Problem Statement

Cancer is the second leading cause of death worldwide, after heart disease. It is responsible for one out of every six deaths (Ritchie, 2018). The cancer epidemiology trend in Low and Middle Income Countries (LMICs) is particularly concerning. Even though LMICs have a lower cancer incidence than high-income countries, overall cancer-related mortality is much greater in LMICs (Shah et al., 2019). One critical success factor of managing burdens of diseases in countries is the availability of safe and efficacious medicines (Narsa et al., 2021). Godman et al. (2018), new drugs 'capacity to meet patients' medical demands is still a challenge in different nations, particularly for cancer therapies.

Several studies have found that one of the causes of delays in the introduction of efficacious medicines in South Africa is drug registration delays at the South African Health Products Regulatory Authority (SAHPRA) (Masini et al., 2018; Leng et al., 2016);.These registration delays have been found to be caused by poor planning and monitoring of key timelines within the application review process (Keyter et al., 2020); and regulatory processes that are slow, complicated and lack transparency (Barrios et al., 2022); high staff turnover, insufficient technical staff/assessors, budgetary constraints, and inadequate capacity to assess highly technical product dossiers (Ncube et al., 2022). These weaknesses relate to the management of the drug registration process. The impact of drug registration delays prevent patients from having timely access to new innovative, efficacious and cost-effective drugs and therefore will lead to poor health outcomes such a poor quality of life and early death (Leng et al., 2016; Cho & Han, 2022). Other negative impacts of delays in the drug

registration are patients being exposed to medical products that are not safe; increased distribution of “substandard, spurious, falsely labelled, falsified and counterfeit” (SSFFC) medical products because of the gap created by the delays; and inconsistent and incoherent use of medicines (Ndomondo-Sigonda et al., 2017). It is therefore critical that NMRAs improve their management skills and operational efficiency to improve regulatory performance levels (Pejović et al., 2016).

1.3 Objectives of the study

The primary objective of this research is to investigate management factors that contribute to the delays in the registration of cancer drugs in South Africa.

The secondary objective is to determine management strategies that could be implemented to address delays in the registration of cancer drugs in South Africa.

1.3 Research questions

The research questions for this study are:

- What are the management factors that contribute to the delays in the registration of cancer drugs in South Africa?
- What management strategies can be implemented to address the delays in the registration of cancer drugs in South Africa?

To answer these questions, the three auxiliary questions below are asked**:**

- To what extent does the application process contribute to the registration process delays of the cancer drugs in South Africa?
- To what extent does review process contribute to the delay of the cancer drug registration South Africa?
- What is the impact of drug registration delays on the patient access to cancer drugs?

1.5 Significance of the study

This study will be significant for the following stakeholders:

1.5.1 SAHPRA

Findings from the study will be beneficial to SAHPRA, as it will provide inputs into SAHPRA's registration process as received from the pharmaceutical companies. These inputs will assist SAHPRA to improve their registration process and systems.

1.5.2 Patients

Management strategies that the study findings will provide in addressing drug registration delays will also benefit patients as the improved drug registration timelines will ensure that they have access to needed medicines for better health outcomes. This will also protect them from being exposed to unsafe medicines being distributed because of the gap created by the registration delays.

1.5.2 Pharmaceutical Companies

This study will give the pharmaceutical companies a voice in providing inputs to SAHPRA as a client of the organization. Improvements made a SAHPRA will also benefit pharmaceutical companies in terms of profits and improved service to the clients, being the patients.

1.6 The scope of the study

The study was restricted to the ten (10) pharmaceutical companies located in Gauteng, South Africa that could potentially be experiencing delays in cancer drug registration. The rationale for selecting Gauteng-based pharmaceutical companies is that the researcher lives in Gauteng and therefore it is convenient and cost-effective to have access to participants in these pharmaceutical companies. Data was collected by means of interview schedules distributed online completed in writing, instead face-to-face interviews because of Covid-19 restrictions.

1.7 Delimitation

This study is limited to participants who are Pharmacists by profession, responsible for submissions of drug registration applications to the regulators, as stakeholders. The study does not include participants from SAHPRA because the focus is on external and independent voices outside of the organization. Previous studies have focused on collecting data from within the organization at Medicines Control Council recently called SAHPRA. The focus of the study will be on cancer drugs and not any other drugs.

1.8 Limitations of the study

During the study, the researcher should expect to encounter the following limitations:

i. Due to a potentially large number of participants in the study, the sample involved was only focused on participants who work in pharmaceutical companies specifically in the Drug Regulatory Departments in Gauteng, South Africa.
ii. The use of the non-probability convenience sampling method has its limitation in that the sample is not truly representative and therefore results cannot be generalized.
iii. The study was also limited to having only one regulator in South Africa, called SAHPRA of which research studies has already been conducted on by several researchers.
iv. The study was limited to secondary data collection regarding access to patients' perspectives on the delays in cancer drug registration and timeous treatment due to confidentiality reasons.
v. Some participants could be uninterested in participating in the study, resulting in poor cooperation and non-completion of the interview questions.

1.9 Assumptions

The study assumptions are that participants are truthful and honest in their responses.

1.10 Definition of Terms

1.10.1 Management

Management, according to Das & Mishra (2019), is "the task of planning, coordinating, inspiring, and regulating the work of people toward a certain goal." Fayol defines management as planning, organizing, staffing, directing, coordinating, reporting and budgeting" and has led to the popularity of the acronym POSDCORB (Nhema, 2015). According to Hall (2019), submitting a new drug application is a significant operation that necessitates a large staff, several tools, and a swerve of sub procedures all working in unison for a good outcome. Researcher further mentions that allowing any of these to be left to chance will almost certainly result in missed timelines and excessive "crunch time."

1.10.2 Cancer drugs

Anti-neoplastic drugs are drugs that are used to treat cancer, according to Health (2017-2022). Anticancer, chemotherapy, chemo, cytotoxic, or hazardous drugs are some of the alternative names for these drugs, as stated by Health (2017-2022). Early care for malnutrition, according to Molina-Garrido (2020), can improve drug tolerance and improve health-related quality of life in individuals.

1.10.3 Management factors contributing to delays in cancer drugs registration

It is important to understand the context of management elements that contribute to cancer drug registration delays to comprehend the factors that could influence the 'delayed' outcomes. These include planning, organizing, staffing, directing, coordinating, reporting and budgeting within the regulatory authority and how efficiently they are implemented to ensure that they achieve their objectives, including registration of drugs.

1.11 Organization of the Study

Chapter one has provided an introduction and orientation to the purpose of the study. It also represents the background of the study, statement of the problem, objectives, research questions, significance, limitations, and the definition of significant terms as used in the study. The rest of this study is structured as follows: Chapter two outlines the theoretical and

empirical literature review, which will include management theories, management factors contributing to drug delays, the impact of drug registration delays on patients, and the role of stakeholders. Chapter three will include the research design, target population, sampling procedure, data collection procedures, data collection instruments, instrument reliability, validity, and data analysis. Chapter four will represent the analysis of the results. Chapter five will conclude the research study with a conclusion and recommendations for future work. References and Appendix are the last part of this document.

1.12 Conclusion

This first chapter has provided an introduction and orientation to the study. The background-included literature on the cancer disease burden, drug registration and management challenges that contribute to the delays in the drug registration. Implications of these delayed were also outlined together with the importance of the study. The chapter also provided the problem statement for the study, research objectives and research questions. The next chapter provides results of collected literature pertaining to the answers to the research questions and achieving the research objectives.

CHAPTER TWO: LITERATURE REVIEW

2.1 Introduction

The previous chapter has introduced the project and given the overview of the research. This chapter discusses the researcher's review of the literature on delays in registering cancer drugs in South Africa. The literature review begins with looking at theoretical literature on management relevant to the identified problem, then empirical literature review on causes of drug registration delays and the impact of registration delays on patients, globally and in South Africa. The chapter will also include a research gap analysis and an examination of emerging themes from the empirical literature. Lastly, a conceptual framework will be developed from the emerging themes from the literature review and chapter summary.

2.2 Management theories

A good definition of management has been conceptualized by Drucker in 1963 where he defines management as “the product of effectiveness and efficiency where ‘doing things right’ is regarded as efficiency while ‘doing the right things’ is considered as effectiveness (Hussain, Haquee & Baloch, 2019: p. 157). Another definition of management from the process perspective is by Fayol who defines it as planning, organizing, staffing, directing, coordinating, reporting and budgeting” and has led to the popularity of the acronym POSDCORB (Nhema, 2015). This study will adopt Fayol’s definition due to it focus on processes, which are key in the registration of cancer drugs.

2.2.1 Scientific Management Theory

The Scientific Management theory was developed by Frederick Taylor (1856 - 1915) and focused on “time and motion” which emphasized finding ways to “improve productivity, efficiency and effectiveness of workers along with their performance” (Kitana, 2016: p. 18); and was meant to be a solution for labor challenges (Sulieman, 2019).Scientific management theory views money as the major motivation for employees (Husain et al., 2019). The four principles underpinning the scientific management theory are:

i. The development of a science of work, which replaced the old rule-of-thumb methods. This principle is used in today's human resources management language as performance/job analysis, work-study and work design (Turan, 2015).
ii. The selection of workers with appropriate skills. This principle is based on the notion that if the right people are recruited in an organization, there will be higher levels of productivity this is the fundamental principle in human resource management today.
iii. Scientific training and development of workers.
iv. Cordial co-operation and division of work between workers and the management

(Kwok, 2014; Ferdous, 2016)

The Scientific Management theory is relevant to the improvement of drug registration process particularly the aspect of selecting appropriate skills for improved productivity and scientific training and development of workers. The evaluation and assessment of drug application is a technical process and requires technically skilled personnel to ensure timely drug registration (Ncube et al., 2022). The study by Roth et al. (2018) has also highlighted the need for requisite technical capacity and staff development to improve the timeliness and efficiency of the drug registration process. NRAs have also been found to have high staff turnover due to budgetary constraints to offer market-related salaries or provide continuous staff training and capacity development programmes (Ncube et al., 2022). Taylor's focus on financial incentives to drive performance is relevant in addressing the above staff turnover challenges at the Regulatory Authority that contribute to delays in drug registrations.

2.2.2 The Administrative Management Theory

The original proponent of the Administrative Management theory is Henri Fayol (1841-1915). The theory focus on the ways managers can manage an organization as a whole to increase organizational performance (Sulieman, 2019).

Fayol's process-oriented definition of management that focuses on planning, organizing, staffing, directing, coordinating, reporting and budgeting is relevant to addressing drug

registration delays. Some of the weaknesses found at SAHPRA was poor planning, monitoring and enforcement of key milestones for the review process (Keyter et al., 2020); staffing challenges and budgetary constraints (Ncube et al., 2022).

2.2.3 Human Relations Theory

Elton Mayo is the proponent of Human Relations theory the asserts the value of employees in an organization and that satisfied employees will result in higher productivity. High staff turnover has been identified as one of the factors that contributes to the delays in the registration of drugs at NMRAs. The human relations theory is therefore relevant in addressing the challenges as it provides an environment that values employees as asserts.

2.2.4 Systems Theory

The Systems theory discourages managers from viewing the organization from individual departments but should consider the completely internal and external elements that affect the organization (Kitana, 2016). The theory focuses on relationship between parts within an organization and how they work together to achieve efficiency and productivity (Sridar, 2016). This theory is relevant in dealing with delays in the registration of cancer drugs because the cooperation between stakeholders and systems within and external to the organization will improve efficiency.

2.3 Key factors contributing to delays in cancer drug registration

Empirical research shows that there are several factors that contribute to delays in drug registration. Themes that emerged from the literature include:

1. Slow process of evaluating drug applications
2. Poor planning and monitoring of key milestones within the application review process
3. Poor staff retention,
4. Inadequate technical capacity
5. Budgetary constraints,
6. Poor drug application submissions.

The below information provides a better understanding of the identified factors contributing to causes of delays in cancer drug registration.

2.3.1 Slow process of evaluating drug applications

The time it takes to review a drug application is a lengthy process however can be minimized if certain processes are adopted and adapted by the regulator. For example, Sithole et al. (2021) has highlighted that the Southern African Development Community collaborative medicines registration initiative has resulted in significant time and resource savings in other countries. However, issues mentioned include a lack of clear information about the participating nations' registration procedures and requirements, including extensive registration timelines. If the regulators can iron out the above-mentioned challenges, this will overall have an improvement in timeous access to drugs for their treatments.

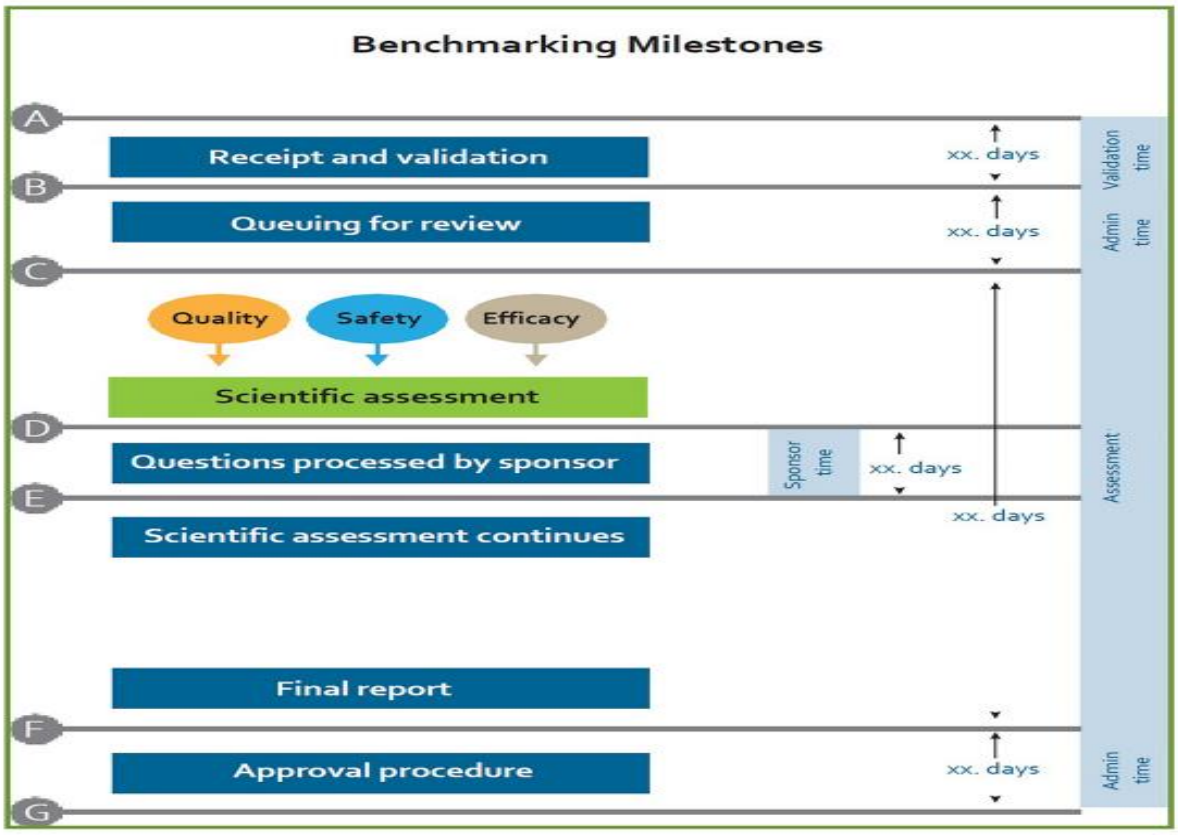
According to Keyter et al. (2019), timely access to innovative drugs can be addressed by improving registration efficiencies and periods in South Africa. From the contributions made by several researchers thus far, this could be achieved by building value-added registration processes, resources, and structures. In addition, according to Keyter (2019), lengthy delays in drug evaluation and registration might be ascribed to inefficient operational processes, resource constraints, and increased volume of registration applications.
All newly discovered drugs, according to Chorniy, Bailey, Civan, and Maloney (2021), go through a lengthy review process. Many suppliers complain about the registration procedure and regulators lose their drug applications frequently, which slows the review process even further (Chorniy et al., 2021).

2.3.2 Poor planning and monitoring of key milestones

SAHPRA has been found to have challenges in the develop and monitoring of key milestones within the review process (Keyter et al., 2021). These milestones include the overall approval time, dossier validation and queue time, scientific assessment time, applicant time when the regulator was waiting for a response or data from the applicant, and other regulatory authority timelines (Keyter et al., 2021)

Keyter et al. (2018) provide an analysis of benchmarking milestones currently utilized by regulatory authorities for drug registration as illustrated in Figure 1 below.

Figure 1 Benchmarking milestones currently utilized by regulatory authorities



Source: Keyter et al. (2018)

Figure 1 above shows that the approach has no target timeline for important review milestones. Allison (2020) further mentions that the total approval time and major review milestones must be established, formalized into policy and guidelines, and then recorded, measured, and monitored. Figure 1 above shows a general diagram of individual landmarks used by other regulatory agencies and could be explored for use by SAHPRA enhanced.

Allison (2020) mentions that appropriate processes and resources must be implemented to track overall approval time for cancer drug registration accurately. Research highlights that the time it takes for both the administrative and technical screening, queuing before review,

and final reviews must be recorded and tracked. Additionally, the metrics-gathering procedure must be enhanced to facilitate monitoring and improvement of SAHPRA regulatory performance.

2.3.3 Poor staff retention

NMRAs in Africa have been found to not have adequate resource to provide competitive salaries leading to staff turnover (Ncube et al., 2022). Lack of career-pathing and unattractive incentives in the NMRAs have been found to contribute to the poor staff retention (Ndomondo-Sigonda et al., 2017). Naturally, this brain drain from the NMRAs attributes to the reduced technical skills required for their efficiency.

2.3.4 Inadequate technical capacity

The poor staff retention discussed above plays a significant role in reducing the technical capacity at the NMRAs in Africa. Several studies have found that there are capacity constraints related to technical skills such as assessors (Leng et al., 2016; Ncube et al., 2022). This is evident in the findings that showed that the majority (90%) of NMRAs in Africa have “minimal-to-no capacity” while only 7% of NRAs in Africa have established average capacity to fulfil their regulatory functions (Ncube et al., 2021). The technical nature of the evaluation of drug registration applications requires constant supply of skilled workforce for operational efficiency.

2.3.5 Budgetary constraints

NMRAs in Africa have been found to have significant budgetary constraints that hamper their operational efficiency and are not able to pay competitive salaries for their employees. Majority of the regulatory authorities depend on Treasuries for financial support Ncube et al., 2022). These budgetary constraints will natural have an impact on the registration of drugs.

2.3.6 Poor drug application submissions to the regulators

According to Parascandola (2021), each pharmaceutical company's role in regulatory affairs is to provide a strategy and knowledge needed to ensure that practices are carried out

following regulatory bodies like the FDA (US Food and Drug Administration) and EMA (European Medicines Agency). Parascandola (2021) further mentions that the regulation is critical in ensuring that pharmaceuticals and therapies manufactured for patients are safe, effective, and of high quality. Research further stated that the pharmaceutical companies' primary role is to prepare and assemble regulatory submissions as well as direct interaction with the regulator.

Carino and Hadid (2018) confirms that regardless of the company size or phase of product development, regulatory submissions can be challenging. The process for registration involves numerous steps and potential opportunities for missteps. However, Carino & Hadid (2018) further state that businesses can control these challenges. Researcher continues to add that this can be achieved if project managers experienced with regulatory submissions can help anticipate, avoid, mitigate, and overcome these challenges. Carino and Hadid (2018) highlights some of the challenges faced by pharmaceutical companies below:

2.3.6.1 Changing regulatory requirements:

Managing different country-specific submission requirements, like the US, Europe, and Japan, can be difficult. Corporations must keep a close eye on global rules since they frequently change, and these changes may have an impact on product submission requirements. A seamless and successful submission outcome requires keeping a careful watch on the ever-changing regulatory landscape.

2.3.6.2 Unclear regulatory strategy:

Organizations that will be submitting applications for cancer drug registrations must define the right regulatory approach upfront to the regulators. They could and undertake a pre-submission meeting with the target regulatory body to help drive product development and identify required data to submit with the application.

2.3.6.3 Lack of submission experience:

Recognizing, obtaining, and maintaining experienced regulatory resources to manage submissions is a common difficulty for businesses. Adapting to product changes requires proactively identifying regulatory growth possibilities and providing enough chances for continuing education.

2.3.6.4 Lack of ownership

At the start of the project, the company must establish an overall owner of the submission. The submission leader oversees fostering internal communication and achieving team cohesion to assure responsibility. The goal of a successful submission that results in product registration is to assist patients by enhancing their quality of life or potentially saving their lives. Parascandola (2021) also highlights some of the challenges that are faced by pharmaceutical companies when submitting drug applications to the regulators:

2.3.6.5 Lack of regulatory strategies:

Also supported by Carino & Hadid (2018) manufacturers are advised to develop the right plan of time and meet with regulators for guidance and clarification on required data during pre-submission discussions.

2.3.6.6 Inconsistent data

The FDA and other regulatory agencies have discovered that pharmaceutical companies frequently fail to appropriately define the background of their products. Different subject matter experts, resulting in conflicting submissions, may write various components of the proposal

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2.4 Impact of Cancer drugs registration delays on patients

The themes emerging from the literature relating to the impact of delays of cancer drug registration on patient access are:

1. Delayed access to Cancer Treatment
2. Exposure to unsafe Drugs

3. Poor quality of life
4. Early Death

2.4.1 Delayed access to Cancer Treatment

According to Javier et al. (2020), access to cancer drugs remains a critical concern, particularly in poor and emerging economies. Godman, et al., (2018) states that new drugs 'capacity to meet patients' medical demands is still a challenge in different nations, particularly for cancer therapies. According to Hanna et al. (2020), the impact of delayed cancer therapy on patients is a global issue.

2.4.2 Exposure to unsafe drugs

Delays in the registration of drugs have been found to expose patients to medical products that are not safe and increased distribution of “substandard, spurious, falsely labelled, falsified and counterfeit” (SSFFC) medical products because of the gap created by the delays (Ndomondo-Sigonda et al., 2017). Statistics show that Africa contributes 42% of cases of fake and substandard medical products (WHO, 2017).

2.4.3 Poor quality of life

Eevidence shows that cancer patients need quick access to treatment because patients who get treatment quickly have better outcomes, such as a higher quality of life and a higher chance of living Lindhorst (2021).

2.4.3 Early death

Researchers Hanna et al.,(2020) mention that the impact due to the delays can be observed, for example, a four-week delay in cancer treatment, increases mortality. Monthly delays in cancer treatment, according to BMJ (2020), can raise the risk of death by 10%. The longer it takes therapy to begin, the greater the dangers and fatalities. Helsper, Van Erp, Peeters, & De Wit (2017) contributes to the researchers’ findings by stating that, despite increasing treatment outcomes, one of the major challenges with cancer is the high morbidity and mortality rates around the world.

According to Helwick (2015), many lives are lost because of effective treatments not being approved on time. Researcher Helwick (2015) further highlights that thousands of people die each year because of delays in the approval of anti-cancer drugs around the world. BMJ (2020) also affirms that researchers in Canada and the United Kingdom discovered that delaying treatment has a substantial impact on a person's death. According to BMJ (2020), cancer treatment delays are an issue in health systems around the world, and commonly known that such delays can have negative effects on a patient's outcome.

Researcher BMJ (2020) premeditated those delays of up to eight weeks and twelve weeks further increased the risk of death. Furthermore, an example an eight-week delay in breast cancer surgery would increase the risk of death by 17%, and a 12-week delay would increase the risk by 26%. A surgical delay of 12 weeks for all patients with breast cancer for a year (for example during COVID-19 lockdown and recovery) would lead to 1,400 excess deaths in the UK, 6,100 in the United State of America, 700 in Canada, and 500 in Australia.

2.5 Roles of Stakeholders

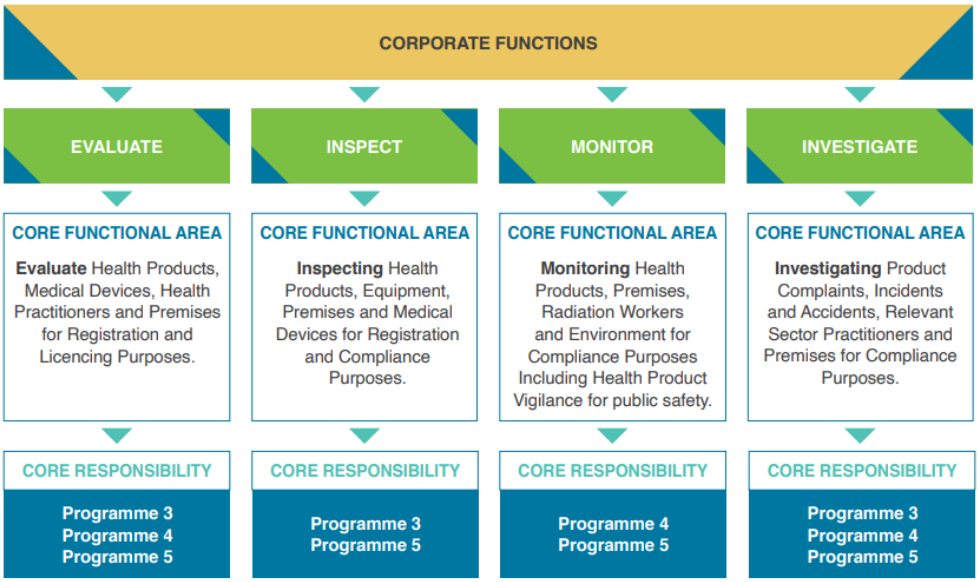
2.5.1 Regulators Globally

Broojerdi et al., (2020) posit that the NRAs are the gatekeepers of the supply chain of drug products. They are responsible for ensuring the excellence, safety, and efficacy of medications, vaccines, blood and blood products, medical devices (including diagnostics), and traditional or herbal remedies. According to Broojerdi et al. (2020), regulators act in a legal framework and a set of regulatory functions that cover the lifecycle of a drug product. These include scientific trial oversight, product marketing authorization, registration, licensing establishments, regulatory inspections, product testing, post-marketing surveillance, and observance operations are all part of this process (Broojerdi et al., 2020). Drugs can only be placed on the market if they have gained registration clearance from the European Commission or competent national authorities, according to Kawalec, et al., (2017). The EU European Union (EU) legislation offers uniform rules for drug approval. Kawalec, et al0, (2017) highlights that all EU member state has implemented their

respective regulatory policies at the same time. States (2019) mentions that regulatory policy in the European Union has evolved under the better Regulation Agenda and has played a critical role in shaping present regulatory processes.

2.5.2 Regulators in South Africa

Figure 2: SAHPRA's Operational framework



Source: Strategic Plan (SAHPRA, 2022-2024)

Figure 2 above illustrates the function of the South African regulator SAHPRA, which is mandated by the Medicines and Related Substances Act, 1965 (Act No. 101 of 1965) to provide for the monitoring, evaluation, regulation, investigation, inspection, registration, and control of medicines, scheduled substances, clinical trials, and medical devices and related matters in the public interest." Dohmen et al. (2021) state that SAHPRA is responsible for screening and approving or refusing applications for registration of drugs and related substances for sale in South Africa.

According to Reddy & Reddy (2017), regulatory organizations have been established in a variety of industries around the world and play a vital role in ensuring that the legal requirements for a country's drug development process are followed. Reddy & Reddy (2017)

highlight that regulators are also responsible for ensuring that the drugs are safe, effective, of good quality, accurate and that the public has access to relevant information.

2.5.3 Pharmaceutical companies

Laenen (2021) mentioned the below about the role of pharmaceutical companies and drug application to the regulator:

The applicant, who is referred to as the pharmaceutical company, must carefully consider all logistical and regulatory issues before submission of a cancer drug application. A key source for input and implementation throughout the decision-making process will be from the regulatory affairs team within the pharmaceutical company. An estimation for the approval of the application would need to be made by the team depending on the type of pathway for the application of cancer drugs. Different pathways may be used which can either be a full review, an expedited review or an abridged review of which all have different guidelines on how and what is required for the application.

Furthermore, Laenen (2021) also mentions that the regulatory affairs unit plays an important role throughout the product lifecycle from the application until approval of the drug. Laenen (2021) also states that the lifecycle management of the drug will start early at the beginning of the discovery and Research and Development phase and will continue until the patent expiry of a product. Researcher Laenen (2021) also notes that after a successful clinical phase, the expectations from applicants to obtain regulatory registration for the drug product immediately. However, the regulatory approval processes from the regulator are still lengthy, time-consuming, and naturally unpredictable.

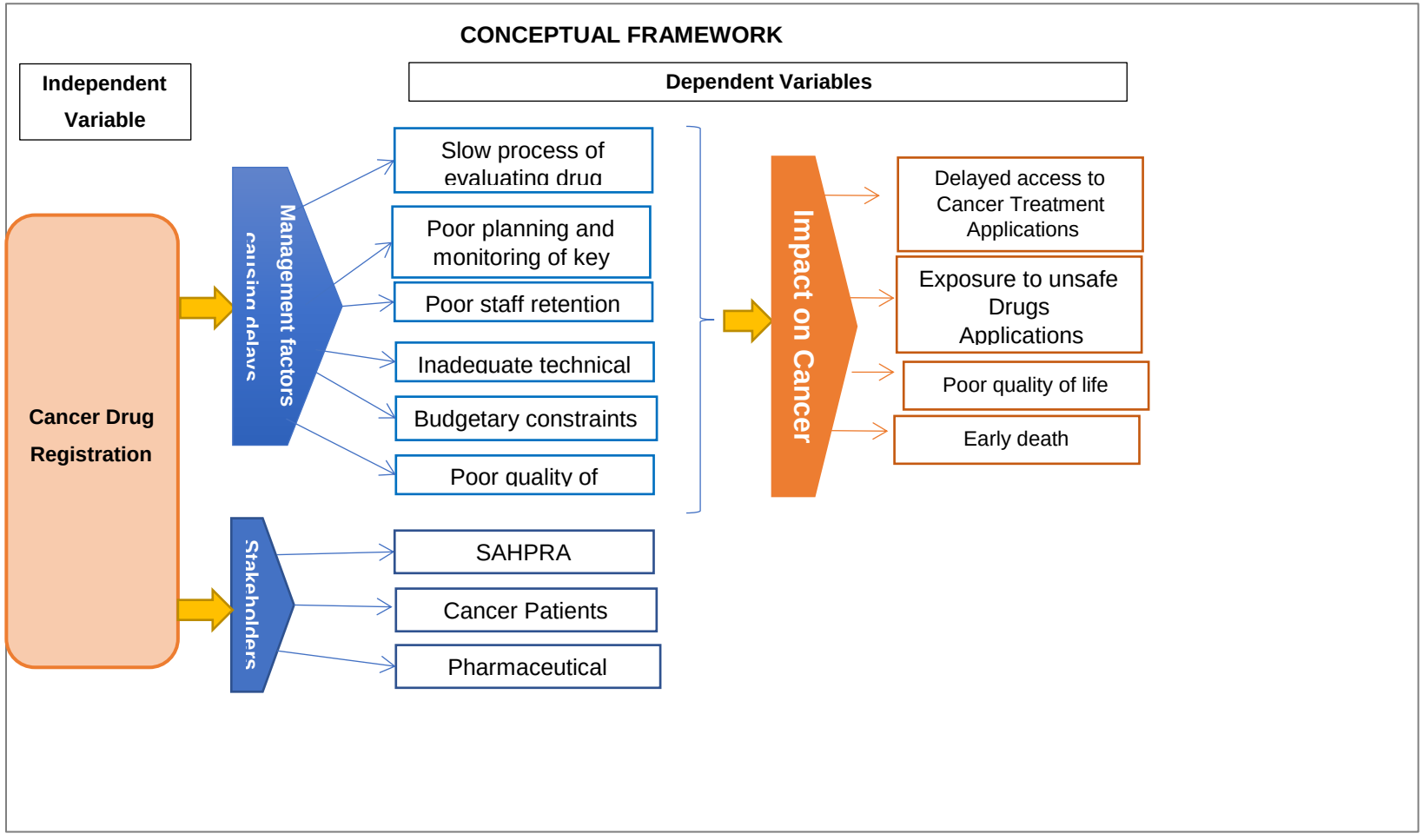
2.6 Research gap

Previous studies have focused on collecting data from within the organization at Medicines Control Council and recently at SAHPRA (Leng et al., 2015; Leng et al., 2016; Keyter et al., 2018; Keyter et al., 2020; Keyter et al., 2021). There is need to understand the management factors that contribute to these drug registration delays from the pharmaceutical companies' perspective as SAHPRA's clients.

2.7 Conceptual framework

The themes that have emerged from the empirical literature review have led to the development of the conceptual framework. The conceptual framework as illustrated in Figure 3 below explains the link between the independent and dependent variables.

Figure 3: Conceptual framework



Source: Researcher, (2022)

2.8 Chapter summary

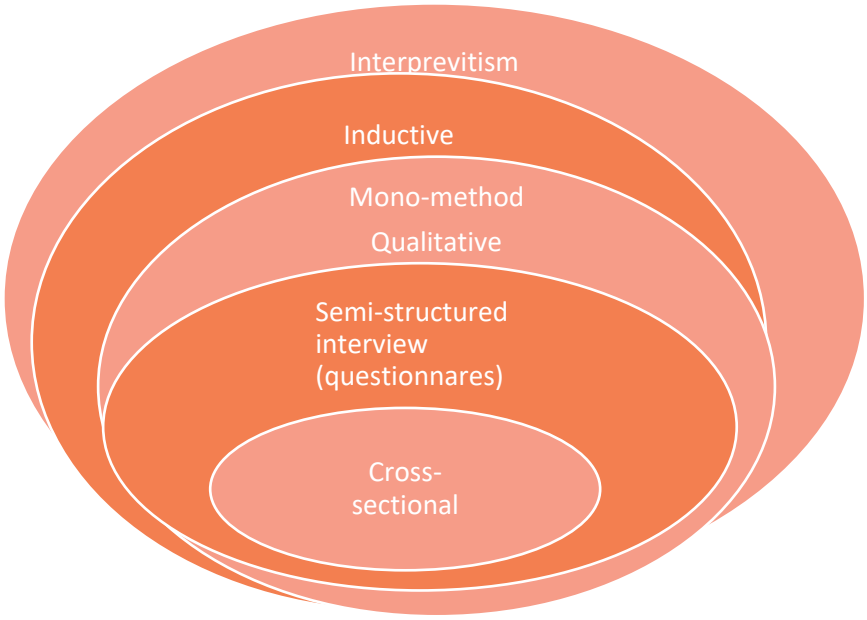
This chapter has explored the literature pertaining to management theories relevant to the study, management factors that contribute to delay in cancer drug registration and the impact of the delays on cancer patients, with the focus on the research objectives that was set. Management theories that are applicable to problem identified in the study include Scientific Management Theory, Administrative Management Theory, Human Relations Theory and Systems Theory. Themes that emerged from the empirical literature on management factors contributing to delays in the registration of cancer drugs are slow process of evaluating drug applications, poor planning and monitoring of key milestones with the application review process, poor staff retention, inadequate technical capacity, budgetary constraints and poor drug application submissions. These drug registration delays have an impact on cancer patients such as delayed access to cancer treatment, exposure to unsafe drugs, poor quality of life and early death. Various stakeholders were also identified who are key in the drug registration process. Lastly, s conceptual framework was developed based on the themes that emerged from the empirical literature review. The next chapter outlines the research strategy, design and methodology that was used in conducting this research.

CHAPTER THREE: RESEARCH STRATEGY, DESIGN, AND METHODOLOGY

3.1 Introduction

The previous chapter provided an exposition of previous literature and studies relating to the study's research objectives and problem statement. In this chapter, the research methodology used to provide answers to the research questions is discussed. Figure 4 below reflects the research methodology in the context of the 'research onion'. This chapter will cover the research approach, research design and techniques, population and sampling techniques, data collection methods, data analysis methods, trustworthiness of the research instruments and approach, ethical considerations, and lastly the chapter summary. To summarize the methodological approach undertaken for this study, based on the "Research Onion" a figure has been depicted by the researcher and is shown in Figure 4 below.

Figure 4: Research onion



Source: Researcher, (2022) adapted from Saunders & Lewis (2018)

The above research onion shows that the research philosophy that has been selected is interpretivism with an inductive approach instead of positivism and deductive approach because of the qualitative nature of the research. The selected approach is based on subjectivist ontological assumptions that entities are constituted of discourse, and aims to provide an insight not a prediction (Melnikovas, 2018). This study will not develop a hypothesis that will predict the results but formulates research objectives and questions that will be answered from the interview data from pharmaceutical companies. A mono-method has been selected instead of the multi-method or mixed-method. The data collection technique will be in the form of semi-structured interviews as they provide in-depth information relating to participants' experiences and viewpoints of a particular topic (Edwards & Holland, 2013). In this study, the experiences and viewpoints of pharmaceutical companies on the management factors that contribute to delays in drug registration were explored. The study will be cross-sectional and not longitudinal because the data will be collected once at a specific period.

3.2 Area of study

This research was carried out in Gauteng, South Africa. This location was chosen because it is very known and accessible to the researcher, and it was convenient to obtain the information required for data collection.

3.3 Research approach

There are generally three approaches to conducting research, namely, the quantitative, qualitative or mixed approach (Goundar, 2012). Bahari (2010) asserts that the difference between qualitative and quantitative research strategies. Quantitative approach is selected to answer research questions that require mathematical data; while a qualitative approach is selected to answer research questions that require descriptive data, mainly in the form of words; and a mixed method approach answers research questions that require both mathematical and descriptive information. Mohajan (2018) asserts that qualitative research is typically associated with the use of an interpretivism approach that incorporates human interest, while there are other choices. Qualitative research explores people's experience,

beliefs and meaning of a situation from their perspective. This study seeks to identify the contributing factors to delays in cancer drug registration in South Africa. The research is based on the perceptions of the professionals within the industry who have had prior experience and therefore will contribute with their interpretation of the subject. A qualitative study is therefore appropriate, as the participants will describe their experiences when registering new drugs and therefore descriptive data will be provided in the form of words. The delays in the drug registration are also being assessed from their perspective. The study does not involve numbers but rather experiences or perceptions. The quantitative approach will therefore not be appropriate.

3.4 Research design

The research design aims to ensure that the data collection will be correctly collected, and the research questions will be addressed appropriately. Different types of study designs may be used. Either the cross-sectional or the longitudinal design. Lewis (2018) states that the cross-sectional design allows the researcher to collect data from participants at once or over one period, often called a ‘snapshot. Lauren (2020) that in a longitudinal study, researchers repeatedly examine the same individuals to detect any changes that might occur over some time this may take several months to years to conclude the study. The research design selected for this study is cross-sectional because it focused on collecting data at once from participants from the pharmaceutical companies working in Gauteng, South Africa.

3.5 Sampling strategy

sampling is a systematic selection of a relatively smaller number of representative items or individuals from a predefined population to serve as subjects for observation or experimentation in line with research objectives (Sharma, 2017). There are generally two types of sampling techniques namely, probability and non-probability sampling. Probability sampling is a technique where every item in the population has an equal chance of being included in the sample; while in a non-probability technique, a sample of participants or cases does not need to be representative, or random, but a clear rationale is needed for the inclusion of some cases or individuals rather than others (Tahedoorst, 2016). Probability sampling

strategies include simple random sampling, systematic random sampling, stratified random sampling, cluster sampling and multi-stage sampling; while non-probability sampling strategies include convenience sampling, snowball sampling, quota sampling and judge mental or purposive sampling (Rahi, 2017).

This study employed a non-probability convenience sampling technique to select the 10 pharmaceutical companies in Gauteng. This sampling strategy is appropriate because the researcher lives in Gauteng and therefore it was convenient and cost-effective to have access to participants in these pharmaceutical companies.

3.6 Target population

Bell, Bryman and Harley (2019: p. 594) define population as “the universe of units from which a sample is to be selected.” The target population of this study is 188 registered pharmaceutical companies located in Gauteng, South Africa.

3.7 Sample Frame

McCombes (2019) defines a sample as a subset of that group from which the researcher will gather data. In this study, the sampling frame consisted of pharmaceutical companies in Gauteng, South Africa particularly professionals working in the regulatory units.

3.8 Sample size

Kabir (2016) describes a sample as part of the population that represents the characteristics of the population. Appropriate and adequate sample sizes influence the quality and accuracy of research. Based on the study, a sample size of 10 pharmaceutical companies was selected for the study with 24 participants selected to respond to the online interview schedule.

3.9 Data collection methods

The selected research approach for this study is qualitative in nature and therefore qualitative data collection instruments were appropriate. Trigueros (2017) identifies the most

used qualitative instruments as interviews, observation and focus groups. There are mainly three types of interviews in qualitative research: structured interviews, semi-structured interviews and unstructured interviews, and can be administered face-to-face, by telephone or other electronic devices (Kabir, 2016). Bell et al. (2019: p. 451) identifies two types of online interviews: synchronous online interviews "where communication takes place in real time" in that questions are answered almost immediately; and asynchronous online interviews where "exchanges are not in real time" in that questions are responded to over a period based on the participant's convenience.

In this study, online asynchronous semi-structured interviews were used to collect data from participants administered electronically through Qualtrics XM. Choosing the online interviews was ideal versus face-to-face due to the current new world we are living in of COVID 19 pandemic. Several advantages and disadvantages should be considered when using online interview schedules to collect data. These are highlighted in Table 1 below.

Table 1: Advantages and disadvantages of using asynchronous online interviews

Advantages	**Disadvantages**
Ability to collect a large amount of data in a relatively short period. Time saved from non-traveling.	The participant is more likely to drop out of the study because the completion of the interview schedule depends on him/her making time for it.
Saving of paper printing-based interview schedules by sending via emails/electronically.	Not all the online interview schedules may reach the relevant participants for completion of the study.
Participants to give their honest opinions or perspectives versus face-to-face interviews, which might have limited or restricted participants in being honest as possible.	The researcher is not able to pose probing or clarifying questions as the interaction is not in real time.
Easy to collect data from participants online	Not easy to verify and validate information/feedback provided by participants.

Source: Researcher, (2022)

3.10 Interview Schedule

The study has focused on getting the views, perspectives, opinions, and insights on pharmaceutical company personnel's experiences when applying for new drug registration with drug registration health authority in South Africa. Interview schedules were used to collect primary data. The interview schedule was divided into the following two sections namely:

I. Section A: General information with close-ended questions, and
II. Section B: Information about drug registration and causes for delays, with open-ended questions.

Qualtrics XM was used to produce the interview schedule that was distributed through email with a set deadline completion. Martin (2021) as a software platform that puts a highlight on a customer's experience defines Qualtrics experience management (XM).

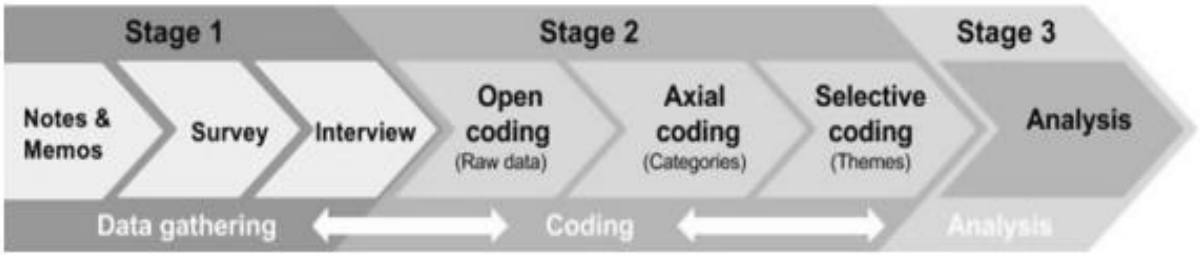
3.11 Secondary data

Secondary data were acquired from a variety of sources, including books; journal articles research reports, dissertations, and seminar/conference reports.

3.12 Data analysis technique

There are different techniques to analyzing qualitative data. Bell et al. (2019) contend that coding is the most common starting point to qualitative data analysis. Allen (2017) describes data coding as the process of converting obtained data or observations into a collection of meaningful, cohesive categories. Petty, Gongwer and Schnabel (2018) provide a three-stage coding framework that starts with data gathering, coding and then analysis, as illustrated in Figure 6 below.

Figure 5: Dynamic stages and fundamental components of coding



Source: Petty, Gongwer & Schnabel (2018)

In this study, the three stages of Petty et al. (2018) data analysis framework was adopted as follows:

- Stage 1 (data gathering) - data analysis involved collection of the raw data through online interviews distributed through Qualtrics XM and entered into spreadsheet tables.
- Stage 2 and 3 (Data coding and Analysis) - the raw data was entered into a spreadsheet table and was analysed through open coding. Axial coding by analysing key words and expressions to determine associations and relationships that were then grouped into categories, and finally these categories were analyzed to develop themes and sub-themes through selective coding.

3.13 Trustworthiness

Instead of validity and reliability, trustworthiness is the best tool to implement rigour in qualitative research (Wagner, Kawulich and Garner, 2012). Trustworthiness is defined as "the systematic rigor of the research design, the credibility of the researcher, the believability of the findings, and applicability of the research methods" (Rose and Johnson, 2020: p. 434). Trustworthiness comprises of four components, credibility, dependability, confirmability, and transferability (Korstjens & Moser, 2018), and these are discussed below.

3.13.1 Credibility of the results and findings

Credibility is "the confidence that can be placed in the truth of the research findings and it establishes whether the research findings represent plausible information drawn from the participants' original data and is a correct interpretation of the participants' original views"

(Korstjens & Moser, 2018: p.121). In this study, credibility was maintained by using accredited and peer-review sources such as Journals as well as textbooks. The pre-testing of the instrument through the pilot study helped determine the suitability of the interview questions/schedule. The researcher also used data triangulation to gather information from a variety of sources, including primary and secondary sources. The use of more than one method to collect data is made easier by methodological triangulation (online interviews and document reviews).

3.13.2 Transferability of the findings

Moss (2017: p. 12) asserts that transferability is the extent to which the result of qualitative research are used in a wide range of situations. In essence, qualitative generalization oversees transferability. In this study, a detailed description of the research process and participants was provided to enable other researchers to assess whether the findings are transferable to their own setting/context.

3.13.3 Dependability

Dependability refers to “the stability of the data over time and over the conditions of the study” (Connelly, 2016: p. 435). The dependability of this study was maintained through an audit trail of process logs and notes. The research also ensured that interview questions are clear and relevant to the research objectives ensure rigour of data and results.

3.13.4 Confirmability

This gauges how impartial and unbiased the study's findings are (Taherdoost, 2016, p. 152). Korstjens and Moser (2018: p.121) posit that confirmability is concerned with establishing that data and interpretations of the findings are not figments of the inquirer’s imagination, but clearly derived from the data. . The results of this study are based on the participants' stories and words rather than the researcher's biases. The researcher maintained audit trail and flexibility procedures to guarantee the study's objectivity.

3.14 Ethical Considerations

Four potential transgressions are guarded against by ethical norms in social and business research: injury to participants, lack of informed consent, violation of privacy, and deception. The researcher needs to consider these because they are substantial (Bryman & Bell, 2014, p. 120)

3.14.1 Ensuring participants have given informed consent

In research, ethical considerations are values that affect how studies are designed and conducted. The option to participate in a research project is made available through informed consent. In other words, research participants choose to participate voluntarily rather than being forced to (Taherdoost, 2016). After being informed of the study's goals, research participants were given letters of consent attesting to their voluntary consent to participate. The online interview schedule also required participants to first consent to partaking in the study.

3.14.2 Ensuring no harm comes to participants

Participants should be physically and emotionally safe if the researcher takes the necessary safety steps (Cader, 2016). In this study, online interviews ensured that participants respond to the questions in a safe and comfortable space of their choosing. The researcher did not pose questions that embarrassing or humiliating to the participants and did not force participants to divulge information that could invoke anxiety or even fear.

3.14.3 Ensuring confidentiality and anonymity

Halej (2017: p. 4) states that anonymity means that there is no way to identify a person from the information provided. The study participants' information was kept private by storing it in a secure place, like a password-protected computer database, and in a locked facility that only authorized staff could enter, like a secure site. There was no need for participants to show any identification.

3.14.4 Ensuring that permission is granted

Singh and Wassenaar (2016: p. 42) indicate that researchers should seek permission and show “respect for autonomy” if their research is to be conducted in an institutional setting... Iin this study, the human resource department of the pharmaceutical companyis participating in the study approved the research to be conducted. An ethical clearance certificate from the ethics committee was received before the study could begin.

3.15 Chapter Summary

This chapter discussed the research methodology whereby online interviews were used as the instrument to collect data from participants in pharmaceutical companies. The sections of research techniques covered in this chapter are research design, population, sampling design, data collecting, research processes, and data analysis methods. The interview schedule was semi-structured and had open-ended questions to assist in collecting the data from participants. The next chapter provides an analysis and interpretation of the data collected from the online interview responses using coding and thematic analysis.

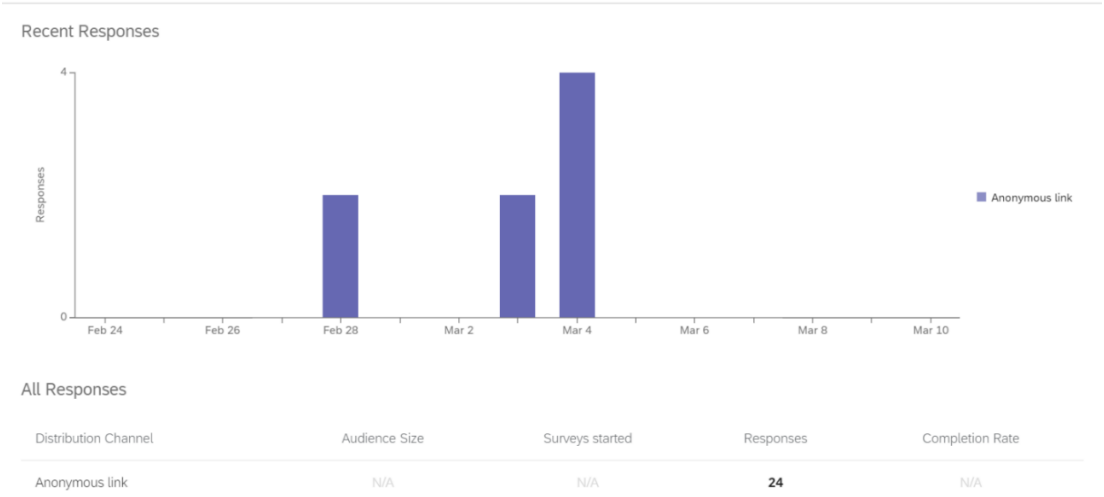
CHAPTER FOUR: DATA ANALYSIS, INTERPRETATION, AND DISCUSSION

4.1 Introduction

This chapter presents the results from data sourced from pharmaceutical companies based in Gauteng, South Africa. The data from the online interview responses are presented and analyzed based on research objectives presented in Chapter one.

Twenty-four (24) interview schedules were distributed to participants for online completion, to collect the data. Twenty (20) out of twenty-four (24) interview schedules distributed in South Africa, narrowed down to Gauteng were returned, resulting in a response rate of 83%. Participants are Pharmacists who are responsible for submissions of drug registration applications to the regulator. The results of the study show that 85% of participants (18 out of 21) experienced delays in the registration of drug with the Regulatory Authority, while only 15% (3 out of 21) did not experience any delays.

Figure 6: Distribution survey



Source: Qualtrics XM tool (2021)

4.2 Presentation of themes and sub-themes

The analysis of the data from online interview responses using Petty et al. (2018) three-stage coding framework the yielded the following themes and sub-themes per research objective as discussed in the next sections.

The first research objective relating to the factors that contribute to the drug registration delays yielded the following themes and sub-themes as presented on Table 2 below.

Table 2: Drug registration delays themes and sub-themes

THEMES	SUB-THEMES
1. Poor administrative Processes and systems	1.1 Slow and unclear processes. 1.2 Backlogs delaying new applications 1.3 Lost applications 1.4 Large information required unnecessarily 1.5 Pending Good Manufacturing Practices (GMPs)
2. Insufficient capacity	2.1 Inadequate technically qualified staff 2.2 Lack of accountability
3. Misalignment with other regulatory authorities	3.1 Does not align to EU and ZaZiBoNa processes.
4. Poor communication	4.1 Lack of feedback from relevant persons. 4.2 No information regarding causes of the backlog. 4.3 Lack of transparency on the processing time-lines.

The second research objective relating to proposed solutions to address the drug registration delays yielded the following themes and sub-themes as presented on Table 3 below.

Table 3: Proposed solutions themes and sub-themes

THEMES	SUB-THEMES
1. Improve internal systems and processes	1.1 Implementation of online registration platforms 1.2 Improve use of reliance model 1.3 Shorter Medicines review process for products already marketed in other markets that South Africa aligns with.
2. Increase capacity with qualified human resources	2.1 Dedicated and technically qualified staff f 2.2 Proper supervision of staff 2.3 Share work with other Health Authorities.
3. Align with other regulatory bodies	3.1 Reliance from other regulatory bodies 3.2 Automatic approval of ZAZIBONA approved applications
4. Quality applications from pharmaceuticals	4.1 Dossiers should comply with requirements
5. Improve Communication	5.1 Transparency regarding processing timelines

The following section discusses and interprets the results per theme and sub-theme as aligned to research objectives.

4.3 Objective 1: Factors contributing to drug registration delays

This study sought to determine management factors that contribute to the delays in cancer drug registration. Four themes were identified from the participants' responses namely: poor administrative processes and systems; insufficient resources; misalignment with other regulatory authorities and poor communication. These themes are discussed and interpreted in detail in the following sections.

4.3.1 Theme 1: Poor administrative processes and systems

The participants expressed their frustrations about the poor administrative system that included slow and unclear processes, application backlogs that delayed new applications,

applications that get lost and have to be resubmitted, requests large information that is not necessary for the registration process, and pending Good Manufacturing Practices (GMPs). The following are some of the participants' sentiments regarding the poor administrative processes and systems.

> "*SAHPRA is slow." - Participant* ***C***
> *"We are not sure of the SAHPRA process." -* ***Participant B***
> "*Too much information is at times required unnecessarily which contributes to the delays with the back and forth between the HA and the applicants." -* ***Participant G***
> *"There are backlogs at the Health Authority," -* ***Participant L***
> *"Registration of drugs took more than 5 years." -* ***Participant R***

The slow process and the amount of information that is required unnecessarily reflects on the Bureaucratic management approach used that has been criticized in the literature for its "excessive red tapism and paperwork" that take time, affecting operational efficiency and smooth running of an organization. (Kitana, 2016: p. 19). The findings of this study confirm that of Sithole et al., 2021 regarding lack of clear registration processes, information about the participating nations and the lengthy registration periods for evaluation and Keyter (2019) regarding inefficient operational and increased volume of registration applications. Processes that contribute to the delay in drug registration. The losing of applications found in this study confirms the finding by Chorniy et al., (2021). These delays are part of the disadvantages of slow and heavy bureaucracy. The slowness of administrative action is, without a doubt, one of the main characteristics of modern bureaucracy. Several justifications are given for delays, most of which revolve around obstacles in the way of procedures or the incompetence of bureaucrats (Potter, 2017). Bureaucratic decision-making can be used as a way to avoid political oversight and make it more likely that an agency's decision will stand. Bureaucrats may postpone decisions in more divisive political climates until those conditions change.

4.3.2 Theme 2: Insufficient Capacity

The participants believe that the regulatory authority does not have adequate human resource capacity to manage the applications received from drug manufacturers. Some of the capacity challenges have to do with technical skill, lack of accountability due to inadequate monitoring and supervision. This is evidenced by the dossiers that get lost by the personnel dealing with the applications. The following quotes express some of the participants' views:

> "*There's insufficient human resources for evaluation of applications."* - ***Participant F.***
>
> *"There's insufficient technical/human resources."* ***- Participant L***
>
> *"There is no accountability."* - ***Participant O***

The above finding are in line with Keyter (2019), Leng et al. (2016) and Ncube et al. (2022). That resource constraint is one of the contributing factors to drug registration delays. It is further in line with the Resources based theory. RBT, or resource-based theory, which is a well-known method for strategic management. Maintaining a competitive advantage requires the organization to frequently use an organizational framework to identify essential resources. The theory offers a crucial framework for deriving explanations for and projections of the primary drivers of a firm's performance and competitive advantage (Utami & Alamanos, 2022). That view is explained by the backlog that was point out by the respondents, hence the registration process taking more than five years. Which is a concern, and more so for a lifesaving activity.

4.3.3 Theme 3: Misalignment with other regulatory authorities

The participants have expressed in their responses that one of the delays is the misalignment of the Health Authority with the reliance model to align with other regulators that South Africa is affiliated to such as the EU and ZaZiBoNA. From the perspective of the participants, it seems there is a sense that there is no collaboration or lack in changing the

mindset to better the ways of working for the benefit of the patient. These are some of the participants' sentiments.

> "There's *misalignment with other Regulatory Authorities eg EU."* - ***Participant G***
>
> ***"****No alignment with other RRA's."* - ***Participant J***
>
> *"Not using reliance model for other RRAs like ZAZIBONA."* - ***Participant L***

4.3.4 Theme 4: Poor Communication

Some participants pointed out miscommunication as one of the delay factors for the registration. These communication challenges include feedback not being received from personnel dealing with the applications; no explanation or information regarding the causes of backlogs, and lack of transparency regarding the expected timelines to process applications. Their sentiments on this poor communication are expressed below:

> *"There is no specific answer provided to the Applicant regarding the cause for the backlog."* ***Participant M***
>
> *"Poor communication including miscommunication from the HA and lack of feedback from responsible persons."* ***- Participant O***

The above findings confirm the findings by Allison (2020), that the benchmarking milestone do not reflect the total approval time for cancer drug registration and no target timeline for important review milestones. Establishing effective interpersonal connections that are non-confrontational and centered on achieving shared objectives is the goal of communication. Factors that form the cornerstone of effective management must be considered in managerial communication. According to writers, interpersonal leadership includes communication management (Bodie & Crick, 2014).

Ineffective communication can increase the likelihood of miscommunication, harm relationships, destroy trust, and exacerbate resentment and fury and mostly delay the registration aspect. Poorly matched strategies, a failure to carry them out, and the use of the incorrect communication tool, poor timing, and even subtleties like word choice or tone of voice can all lead to ineffective communication (Beattie & Ellis, 2014).

From the developed conceptual framework, the researcher assessed whether the independent variable of improving cancer drug applications from the pharmaceutical companies would indeed reduce the delays in cancer drug registration. When analyzing the impact that the drug applicants benefit that it will minimize the time the back and forth communication between the two parties if a good quality application has been submitted. It is also evident that should the regulator improve on their review processes, this will have a positive impact in that the drug registration will be available in the market for patient use timeously. .

According to the literature, pharmaceutical companies' drug application submissions lack a strategic plan to build the correct plan ahead of time and meet with regulators for assistance and clarification on required data during pre-submission conversations, according to researcher Parascandola (2021).

However, according to the literature, the high cost of developing a new drug should be considered one of the major drivers of drug registration delays and the reason why few drugs make it to market. Keyter (2019) argue that the high cost of developing a new drug should be considered as one of the major drivers of drug registration delays and the reason why few drugs make it to market.

The findings of this study show that there are delays in cancer drug registration. It has been revealed by literature and by the participants that the stakeholders being the manufacturers, drug applicants and regulators are all contributing to these delays. From the developed conceptual framework, it is evident that should there be better strategies and planning as well as submitting good quality dossiers from the drug applicant this can minimize the amount of time the regulator might have to ask for any additional data. It is also evident that should the regulator implement and enhances better systems and processes for a smooth and less time reviewing process, the results will have a great impact on patients receiving their drugs timeously. Lastly, the drug development, if WHO (2018) could intervene in the

present pricing policies (or the lack thereof), it would be beneficial for manufacturers and the patients who need to receive the drug on time.

4.4 Objective 2: Proposed solutions to address the drug registration delays

This study also elicited participants to propose solutions that would address delays. The study yield five themes, namely, improving internal systems and processes, increasing capacity with qualified human resources, aligning processes with other regulatory bodies globally, submission of quality application by pharmaceutical companies, and improving communication. These themes are discussed and interpreted in detail in the following sections.

4.4.1 Theme 1: Improving internal systems and processes

Participants believe that one of the solutions to addressing delays in the registration of drug is for SAHPRA to improve its internal systems and processes such as the introduction of online registration platforms to mitigate applications being lost; improve the use of reliance model to shorten the drugs review process for products that have already been approved and introduced in other markets that South Africa aligns with. The participants' expressed these solutions as follows:

> *"Implement better systems."* - ***Participant H***
> *"Electronic systems to avoid losing hard copies"* - ***Participant U***
> *"Abbreviated Medicines review process for products already marketed in other markets that South Africa aligns with."* - ***Participant N***

Organization (2021) believes that regulators can reduce the time it takes for drugs to reach patients by improving registration effectiveness and refining the importance in registration methods, processes, and systems used. Investing in the development of local processes and systems by mature National Regulatory Agencies (NRAs) according to Roth et al., (2018) could have a substantial impact on continuing quality product availability. The adoption of some of the Classical Management Theories would provide would resolve these

inefficiencies. For example, the Administrative Management theory is planning, organizing staffing, direction, coordinating, reporting and budgeting (POSDCORB) can provide a comprehensive solution for the whole organization.

4.4.2 Theme 2: Increase qualified human resources

The participants believe that increasing the capacity with qualified staff such as dedicated and technically knowledgeable people; supervision of staff for accountability, and getting assistance from other Health Authorities would be beneficial. Their sentiments are highlighted below.

> *"Increase qualified human resources for evaluations of applications. Required"* - ***Participant G***
> *"SAHPRA can better respond to this if with manpower."* ***Participant B***
> *"Assign dedicated persons, their back-up and the responsible person for accountability."* ***- Participant O***

The adoption of the Scientific Management Theory in the recruitment of qualified staff, as well at the training and development will address the challenges of delayed drug registration.

4.4.3 Theme 3: Align with other regulatory bodies

Participants believe that for the SAHPRA to expedite the registration of drugs, they should align with other regulatory bodies by placing reliance on other regulatory bodies where applications that have been approved by ZAZIBONA are automatically approved. These are the participants quoted views:

> *"Improve ZAZIBONAs mandate - meaning approval received with ZAZIBONAs should automatically receive automatic approval to all affiliated countries."* - ***Participant L***
> *"To fully align with other countries requirements and accept recommendations made by their authorities."* ***- Participant A***

"Reliance from other RRA countries." - ***Participant I***

These findings confirm Sit whole et al., (2021) about the importance of initiatives such as several application pathways used in the African continent for example Zambia, Zimbabwe, Botswana and Namibia (ZaZiBoNa) and the Southern African Development Community (SADC) collaborative medicines registration to improve the drug registration processing times.

1. Theme 4: Quality applications from pharmaceuticals

Participants acknowledged the fact that dossiers submitted by pharmaceutical companies do not meet the required thereby causing delays when they are returned, as expressed by the following sentiments.

"Support the HA as much as we can with providing quality dossiers." - ***Participant S***

This finding is in line with Carino and Hadid (2018) that pharmaceutical companies have control on the quality of submissions by ensuring that project managers experienced with regulatory submissions anticipate, avoid, mitigate, and overcome the challenges faced during the application process; and also keep a close eye on global rules since they frequently change, and these changes may have an impact on product submission requirements.

2. Theme 5: Improve Communication

The last theme for addressing delays in the registration of drugs is for SAHPRA to improve its communication, especially being transparent with the processing time for registrations.

"Transparency wrt time-lines." - ***Participant T***

Transparency is a common remedy for troubled relationships between a company and its stakeholders. Researchers have so far only asserted the advantages of transparency in this situation. Transparency is not a one-dimensional concept, contrary to what most scholars believe. There is little agreement on what transparency means.

4.9 Chapter Summary

This Chapter presented and explained data obtained during the study based on research questions. Generative themes in this chapter indicated that participants responded to the online interviews distributed in Gauteng, South Africa. The themes generated in this chapter indicated that participants responded to the online interviews by expressing how they feel and the impact, which delays in drug registration, has affected on them. Several themes were identified that were in line with what the literature has mentioned. The researcher found herself interpreting the thematic data while compiling the different themes. In this way, a simultaneous process of analysis and interpretation was completed. In Chapter five, the findings are discussed and interpreted in the context of the literature review. The order of the results and the discussion mirrors that of Chapter three.

CHAPTER FIVE: SUMMARY, CONCLUSION, AND RECOMMENDATIONS

5.1 Introduction

The summary of the study is discussed. The discussion is based on the results received in line with research objectives as outlined in chapter one. Limitations of the study, Conclusion, and recommendations are made based on the discussion.

5.2 Summary of Findings

The findings are divided into two sections, the findings from the literature review and the finding from the primary data.

5.3 Findings from the literature

The literature reviewed highlighted the three Classical Management School of Thought, namely, Scientific Management Theory, Administrative Management Theory and Bureaucratic Management Theory. It was shown how these theories are still relevant in today's organizational management.

Statistics on the cancer globally was also provided, According to the World Health Organization (2021), 8.8 million people die from cancer each year because of late diagnosis, with the majority of these deaths occurring in low- and middle-income countries. Regulatory reliance, harmonization, and task sharing have increased in recent years. This has led to more sharing of information between regulators, which has helped them make better use of their limited resources. There is still a lot of confusion about how to sign up, what countries are taking part, and how long it takes to sign up for evaluation. The process of registration involves numerous steps and potential opportunities for missteps. The goal of a good submission is to help patients by making their lives better or maybe even saving their lives. Carino and Hadid (2018) talk about some problems that drug company's face when they send regulators applications for new drugs. Cancer drugs are unquestionably one of healthcare's most significant expense drivers.

The cost of developing a new drug has been the subject of debate, with recent estimates ranging from $314 million to $2.8 billion. In addition, regulatory delays may affect pharmaceutical companies' future R&D initiatives. The longer it takes treatment to begin, the greater the dangers and fatalities due to delays. According to BMJ (2020), cancer treatment delays are an issue in health systems worldwide. A surgical delay of 12 weeks for all patients with breast cancer for a year would lead to 1,400 excess deaths in the U.K. and 6,100 in the U.S. Regulators are the gatekeepers of the supply chain of drug products. They are in charge of making sure those medicines, vaccines, blood and blood products, medical devices, and traditional or herbal remedies are good, safe, and effective.

The literature further provided some of the contributing factors for delays in drug registration. These included lacks of clears are still unclear registration processes, information about the participating nations and the lengthy registration periods for evaluation (Sithole et al., 2021). Poor application submissions to regulators due to lack of experience and ownership were also found to contribute to the delays (Carino & Hadid, 2018).

SAHPRA's strategic plan for 2020–2021–2024–2025 is to connect with other health product regulators worldwide. Cancer drugs are costly to develop and take time to develop. The time it takes to review a drug application is lengthy. However, it can be minimized if specific processes are adopted and adapted by the regulator. If the above-described challenges can be ironed out, this will improve timeous access to drugs for their treatments. Cancer kills one out of every six people worldwide, making it the second leading cause of death. According to the research, the death rate increases the longer a patient takes their drug. South Africa has made it clear for the past 20 years that they want to improve their regulatory frameworks and structures.

5.4 **Findings from primary research**

Poor communication can be attributed to the failure or absence of the communication process' success and efficacy (Abdullatif et al., 2017). Lack of clarity is classified as a communication barrier hence the party might struggle to agree on the process. Failure of a

shareholder to recognize what and for whom they are accountable results in unclear duties. Poorly matched strategies, a failure to carry them out and the use of the incorrect communication tool are factors that lead to ineffective communication. Bureaucratic decision-making can be used as a way to avoid political oversight and make it more likely that an agency's decision will stand.

Bureaucrats may postpone decisions in more divisive political climates until those conditions change. Strategic scheduling affects the publication of legally binding final rule judgments and the federal rule-making process. The internal process was also outline as one of the registration delaying factors. The internal process resulted in two main constructs or sub-themes namely the scale of the employee frustration and the change in mindset. The participants have expressed in their responses the misalignment that the Health Authority has about the reliance model to align with other regulators. The World Health Organization (2021) believes that regulators can reduce the time it takes for drugs to reach patients by improving registration effectiveness and refining the importance in registration methods, processes, and systems used. Investing in the development of local processes and systems by mature NRAs could have a substantial impact on product availability.

From the data, the majority of the participants that completed the online interviews did highlight that they did experience delays from the regulator about delays in cancer drug registration. However, it was also evident from the literature that not only the regulator plays a role in contributing to these delays. Evidence from literature has shown that the pharmaceutical companies responsible for submitting drug applications also show to be one of the factors that contribute to delays in cancer drug registration. Lack of strategic planning, resource constraints amongst others were found to be some of the factors highlighted.

5.5 The Researcher

The researcher's comments on her motives for this study and the journey have been an important component of the research process. Many novel cancer drugs have been created to improve patient outcomes, according to Uyl-de-Groot, Heine, Krol, & Verweij (2020). However, throughout Europe, including other nations such as South Africa, access to these drugs is delayed compared to other countries such as the United States of America (USA).

The researcher records her reflections on her study path in this section. It is written in the first-person perspective.

"I chose this specific topic as it has affected me personally in my life. I have lost many loved ones to cancer, and this was a result of the cancer drug not being approved or registered in the country. In addition to that, I work in the pharmaceutical sector whereby my outcome at the end of the day is to ensure that patients have the necessary drugs approved by the regulator for them to get the help they need. I wanted to understand what challenges and better solutions other pharmaceutical companies working in the Drug Regulatory Departments who are dependent on the regulators to receive a drug approval could give for a better framework to be created to receive faster drug approvals. I also wanted to understand if other pharmaceutical companies experienced the same delays in drug registrations. The findings emanating from this study have provided me with great insight and have provided me great confidence to step forward and be the change I want to see for our patients".

"My research experience has been challenging but an amazing journey of discovery of making new connections, trusting myself to persevere when the going got tough, working hard, and committed to getting this far through long days and late nights. I am grateful for all the people I have met who allowed me to be myself and so willingly allowed me in their space. I see my personal development and growth as a lifelong journey one in which I am looking forward to further exploring"

5.6 Limitations of the Study

Some of the limitations that can be encountered are participants that wish not to participate in answering the online interviews; this would limit the study in that the data required may not be fulfilled in completing the study. Another limitation is the uncertainty over the validity of the data collected from participants. There might be some concerns around the design, implementation as well as evaluation of the online interview schedule.

The limitations that were experienced in the study were the time constraints in collecting the data from the participant, as it took a long to receive the data. A total number of 20 online interview schedules were not completed from 24. The researcher has identified from the

research questions; the participants did not put sufficient data forth to answer some of the questions highlighted in chapter one.

5.7 Conclusion

The main research question from chapter one was to find the key factors contributing to the delays in cancer drug registration. It is evident from the literature that several key factors are contributing to the delays experienced by pharmaceutical. Mainly from the literature, it was evident that relevant stakeholders both the regulator and the pharmaceutical companies both contribute to the delays in drug registration. The key points highlighted by both stakeholders were mainly from the internal resources, systems, processes, and frameworks that hinder faster drug registrations. The identified gaps, measurement and monitoring of the application review to registration approval must be established, formalized, measured and monitored.

5.8 Recommendation

5.8.1 Recommendations for Action

Knowing and having a clear picture of the problem may benefit understanding the key factors, impact, and relationship between the key factors and stakeholders contributing to delays in cancer drug registration. It is hereby recommended that the regulator be enhanced by adding the recommended suggestions to better benefit the patients.

1. Timelines for regulatory review establish and enforce realistic regulatory review timelines and analyze and evaluate regulatory performance metrics regularly.
2. Improvements in regulatory performance, approval timelines, and most importantly evaluation milestones are all on the horizon. As a result, proper mechanisms and a culture of precise metrics collection and monitoring of key performance indicators, as well as their ongoing improvement, will be implemented.
3. Drug evaluation and registration can be expedited according to the priority of the drug where necessary. This will form alignment with the national legislative frameworks like the AU Model Law on Medical Products Regulation.

4. Regulators are recommended to outsource competent and knowledgeable resources to clear the backlog as soon as possible.
5. The regulator should consider aligning itself with other regulators example the EU and other developed markets with facilitating regulatory paths, creating a reliance strategy, and implementing a quality management system, among other suggestions for improvement.
6. Regulatory pathways that are available for use should be adopted by the regulator for faster drug approvals for the benefit of the patients.
7. Improve on the already existing model for regulatory review for SAHPRA.
8. The Health Authority could improve on the already existing internal processes by mapping out the current challenges faced and streamlining better and faster ways of evaluating each drug application immediately. This will require a thorough evaluation of the internal processes, a relook at what is working, and what is not.
9. A survey can be distributed to relevant stakeholders (regulators, pharmaceutical companies, and perhaps the end-users (patients) to get a general view or feedback that could help all parties improve on lacking processes and systems.
10. Enforce better and quicker ways of aligning with other stringent regulatory authorities in other countries, for faster drug registration

5.8.2 Recommendations for Future Research

The following suggestions are made for future research related to this study:

The interview schedules were positively focused by design. The researcher was deliberately looking for responses from the pharmaceutical companies and the outcomes of their experiences. However, it was only normal to assume that only negative responses would emerge from the participants about the regulator. Future studies could investigate interviewing the regulators themselves and get a sense of where they are in this process and how they can better improve on delivering faster drug registrations. They may provide valuable additional insight and further depth to the study.

The study was also limited only to pharmaceutical companies in South Africa that are in the Regulatory departments. Further studies could include other departments in or outside the pharmaceutical sector that are impacted or affected by drug registration and not only in cancer drugs. The study was based on a small sample of fourteen participants. Future studies could be expanded to include a larger sample for better outcomes. The data was collected by using online interviews due to COVID-19 and face-to-face interviews were not ideal at that time. Future studies could look at collecting data face to face to get better outcomes from the participants. Factors, impact, and the relationship between the key factors and stakeholders could be researched further, incorporating, and building on the existing data that emerged from this study.

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