Transparency in medicines registration decision making: A closer look at National Medicines Regulatory Authorities (NMRAs) within the Southern African Development Community (SADC) region.

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Title

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Declaration

I, Mphako Brighton Ratlabyana, declare that this thesis that I now submit for assessment on the programme of study leading to the degree Master of Science in Pharmacy Administration and Policy Regulation has not been submitted for the purpose of a degree at this or any other higher education institution. It is entirely my own work and has not been taken from the work of others save to the extent that such work has been cited and acknowledged within the text of this work.

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Abstract

Background

Medicines registration decision-making and regulatory best practice involve transparent and consistent rule making and processes with publicly available published assessment decisions and reports (Kaine, 2020). Publication of information relating to evaluation of medicines in the form of Public Assessment Reports (PARs) is one way of ensuring transparency in medicines registration decision making. It is however not clear whether National Medicines Regulatory Authorities (NMRAs) in the Southern African Development Community (SADC) region are in a position to generate or even publish such PARs / summary basis for registration of medicines.

Objectives

The study investigated transparency in medicines registration decision-making processes for NMRAs within the SADC region. Specifically, the availability or non-availability of PARs / Summary basis for registration of medicinal products. To establish if all SADC NMRAs have legislative frameworks for regulating medicines and to investigate the sources of funding for SADC NMRAs

Methods

A cross-sectional exploratory descriptive study design with qualitative techniques by questionnaire as a data collection tool was used. Questionnaires were sent *via* email to senior members / key informants of 11 regulatory authorities belonging to SADC. Trend analysis was conducted based on the emerging themes from questionnaire response.

Results

The study revealed that currently five (5) NMRAs are operating as semi-autonomous agencies namely: BOMRA, MCAZ, PMRA, SAHPRA and TMDA .While NMRC, DNME of Angola, ACOREP of DRC and DNF of Mozambique are functioning within their respective Ministries of Health Departments. Furthermore, all NMRAs have a legislation framework governing the regulation of medicines in their respective jurisdictions. However, DNME of Angola's legal framework is not yet officially formalised and as such, they follow a Presidential decree enacted in 2010. Four (4) of nine (9) NMRAs (44 %) reported to have more than 20 internal assessors / evaluators. This indicates a significant milestone for SADC NMRAs in terms of

capacity building within the region. The study findings indicated that the SADC NMRAs are receiving funding from multiple sources ranging from a minimum of one to maximum of four funding sources. There were only two NMRAs, MCAZ and PMRA, that were not receiving funding from their governments. The study results further indicates that only TMDA is able to generate and publish PARs amongst SADC NMRAs.

Conclusions

The findings in this study suggest that the majority of NMRAs within SADC are not yet matured as compared to countries in the developed world such as the US, Europe, Canada and Australia. It can also be concluded that for SADC NMRAs to be efficient and responsive, they will require massive financial resources. For example, the budget for a matured NMRA such as the US Food and Drug Administration (US FDA) for the 2019 financial year was estimated at US$ 5.7 billion. Literature further indicates that publication of the summary basis of approval or PARs is a norm for mature NMRAs and acts as a tool for regulatory authorities to build and establish confidence in their review processes and provides assurance regarding safety of medicines. The study results indicate that TMDA is publishing PARs or summary of grounds on which approvals are granted. This demonstrates a significant level of transparency in the TMDA medicines registration processes and therefore other SADC NMRAs can benchmark with TMDA to implement this key parameter.

Keywords

Transparency

SADC

Medicines Registration

Regulatory Decision Making

Public Assessments Reports

National Medicines Regulatory Authorities (NMRAs)

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List of Abbreviations

AU	African Union
AUDA NEPAD	African Union Development Agency New Partnership for Africa's Development
AMA	African Medicines Agency
AMRH	African Medicines Regulatory Harmonization
BOMRA	Botswana Medicines Regulatory Authority
EMA	European Medicines Agency
ACOREP	Congolese National Medicines Regulatory Authority
HoAs	Head of Agencies
ICH	International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use
DNF	National Directorate Of Pharmacy of Mozambique
MCAZ	Medicine Control Authority of Zimbabwe
NMRAs	National Medicines Regulatory Authorities
NMRC	Namibia Medicines Regulatory Council
NRA	National Regulatory Authority
NEPAD	New Partnership for Africa's Development
PMPB now PMRA	Pharmacy, Medicines & Poison Board now Pharmacy and Medicines Regulatory Authority, Malawi
SADC	Southern African Development Community
SADC MRH	Southern African Development Community Medicines Registration Harmonization
SAHPRA	South African Health Products Regulatory Authority
DNME	National Directorate of Medicine and Equipment of Angola
TMDA	Tanzanian Medicines and Medical device Authority
TGA	Therapeutic Goods Administration of Australia
US FDA	Food and Drug Administration (of the United States)
WHO	World Health Organization
WHO PQT	World Health Organization Prequalification Team
ZAMRA	Zambia Medicines Regulatory Authority
ZaZiBoNa	Collaborative registration procedures involving Zambia, Zimbabwe, Botswana and Namibia

Chapter One

1.1. Introduction

1.1.1. Background

The World Health Organization (WHO) defines medicines regulation as “a processes encompassing various activities aimed at ensuring the safety, efficacy and quality of drugs, as well as the appropriateness and accuracy of product information. Its ultimate goal is to promote and protect the public” (WHO, 1999). Effective medicines registration depends on appropriate legal framework supported by adequate administrative structures, to ensure that the scientific evaluation of new medicines (generic or innovator) can be undertaken in a rigorous, effective, transparent and efficient manner. Political support, financial and other resources are critical (Hill, 2004). It is therefore imperative that these assessments processes are conducted in a fair and transparent manner to ensure credibility and accountability in the process and to minimize the risk of corruption. Mukanga (2020) states that due to the increasingly complex global regulatory environment and supply chains, it is critically important that the global regulatory landscape adopt agile, transparent and predictable approaches.

The pharmaceutical sector is the most regulated sector due to the complex nature of the business that revolve around the health and well-being of the society. Mukanga (2020) defines a regulatory system as a system which “consists of all organizations, people and actions whose primary intent is to ensure access to essential medicines and other health products of assured quality, safety and efficacy or performance”. This indicates that across the pharmaceutical value chain, there are many stakeholders involved, such as the manufacturers, regulatory agencies, government departments, research institutions, wholesalers, distributors, Non-Governmental Organizations (NGOs), hospitals, pharmacies and general public. As such, based on the vast nature of the pharmaceutical environment, the sector becomes particularly vulnerable to various forms of corruption, fraud, favouritism and collusion. The World Health Organization (WHO) indicated that the impact of corruption on “people’s health should not be underestimated, as children and adults may end up taking unsafe or low quality medicines” (World Health Organization, 2006). For these reasons, it is therefore imperative that pro-active systems are put in place to mitigate and minimise such risks.

Across the globe, National Medicines Regulatory Authorities (NMRAs) play a critical role of safeguarding the public and ensuring sustained access to quality-assured medicines with scientifically proven safety and efficacy. The assurance of quality, safety and efficacy of health products by the regulatory agencies are conducted through various mechanisms, such as Good Manufacturing Practice (GMP) inspections of the manufacturing sites and evaluations of safety and efficacy data in health product dossiers submitted by the manufacturers / applicants to the regulatory agencies. Regulatory agencies are responsible for a variety of activities such as inspections of manufacturing facilities, Clinical Research Organizations (CROs) and wholesalers, law enforcement at border controls and port of entries and assessment of a variety of health products (medicines, vaccines, blood products, traditional or herbal medicines and medical devices).

This study focuses only on publication of Public Assessment Reports (PARs) for orthodox medicines as their regulation are well established in most countries, and does not include discussions on assessment reports for traditional or herbal medicines and medical devices due to varying approaches across jurisdictions. Moreover, this study is limited to NMRAs within the Southern African Development Community (SADC) region, particularly those with capacity to issue Marketing Authorization (MA).

In most cases, due to intellectual property protection issues, these inspection and assessment reports remain confidential between the regulatory agencies and the applicants. It is in this context that the medicines registration decision-making processes should be robust, fair, transparent and open. Regulatory best practice involves: transparent and consistent rule making and processes; risk-based review pathways framed in public health need / priority, which are efficient and thereby saving time for both regulatory agencies and manufacturer; regulatory reliance that allow timely access to medicines and market; and publicly available published guidelines, procedures, NMRA decisions and reports (Kaine, 2020). Matured regulatory agencies such as the European Medicines Agency (EMA), United States, Food and Drug Administration (US FDA), Health Canada and Therapeutic Goods Administration (TGA) in Australia publish information relating to their evaluation of medicines *via* PARs, as part of their commitment to transparency (Papathanasiou *et al*., 2016).

SADC is the Regional Economic Community (REC) consisting of 16 member states, namely; Angola, Botswana, Comoros Islands, Democratic Republic of Congo (DRC), Lesotho, Madagascar, Malawi, Mauritius, Mozambique, Namibia, Seychelles, South Africa, Swaziland (Now Eswatini), United Republic of Tanzania, Zambia, and Zimbabwe as shown in Figure 1 (SADC, 2020). Increase in counterfeit and substandard medicines as well as long medicines registration timelines still prevail amongst SADC countries and other Low to Middle Income Countries (LMIC's) (Ndomondo-Sigonda *et al*., 2017). NMRAs within the SADC region face similar challenges of weak regulatory systems and are therefore unable to fully execute their public health mandate of ensuring that medicinal products marketed in their jurisdiction meet international standards of quality, safety and efficacy. Furthermore, Kamwanja *et al.* (2010) and Mahlatji (2017) indicates that in the SADC region, due to varying regulatory capacity, currently only 11 member states are actively issuing market authorization for pharmaceuticals marketed in their countries and registration may be waived under various conditions in some countries. For this reason, 11 regulatory agencies within SADC region were evaluated for the purpose of this study.

Figure 1: Map of SADC showing all sixteen member states (SADC, 2020)

1.1.2. Problem Statement

Sharing information with stakeholders is crucial in building trust and enhancing stakeholders' relationships towards success of any initiative. Applicants / Marketing Authorization Holders (MAH), as well as patients and healthcare professionals in developing countries also have rights to information about the scientific basis for the approval and use of their medicines. Matured regulatory authorities in the developed world fulfil this by publication of PARs on their websites as stated earlier (Papathanasiou *et al.*, 2016).

Lack of transparency in the medicines registration decision-making processes have potential to damage reputation and public confidence in these NMRAs. In addition, lack of transparency in decision-making can lead to high levels of corruption, especially for NMRAs in LMICs countries faced with multiple challenges of financial and human resources constraints.

Publication of information relating to evaluation of medicines in a form of PARs or any summary basis for registration is one way of ensuring transparency in medicines registration decision making. It is however not clear, whether NMRAs in the SADC region are in a position to generate and publish such PARs / summary basis for registration as a commitment to transparency in medicines registration decision making or not. The aim of this study is therefore to investigate whether NMRAs within the SADC region have PARs as scientific basis of accepting or rejecting registration of medicinal products; and to establish if such PARs are publicly made available by regulatory agencies within the SADC region.

A recent study by Keyter, Salek, Banoo, and Walker, (2019) focusing on comparing the review processes of the South African Health Product Regulatory Authority (SAHPRA) with those of Australia, Canada, Singapore and Switzerland, recommended that in order to build quality into the review process and enhance transparency and communication, publicly available summaries for the basis of approval can be developed using an Universal Methodology for Benefit-Risk Assessment (UMBRA) as template.

In addition, another study on whether standardisation of the PARs improve benefit-risk communication concluded that if the SAHPRA can use a structured template that supports transparent and quality decision making, the template could have a major impact in ensuring consistency in their benefits / risk assessment of new medicines. These will ensure that the agency is trusted, responsive, and accountable to its stakeholders (Keyter *et al.*, 2020a). The study demonstrated that if a standardized template on benefits / risk assessment is adopted by the agency and subsequently published, there is a greater potential to improve stakeholder relations and ensure consistency in the regulatory decision-making processes. For this reason, there was a clear need that this study be conducted to contribute to the knowledge gap and provide recommendations to these SADC NMRAs in order to improve their overall performance.

Most of the studies conducted in this area focussed on European countries and how the publication of their PARs improved public confidence and pharmaceutical industry perception towards the regulatory decision-making processes. A study focussing on the EMA and TGA by Papathanasiou *et al.*, (2016), indicated that the degree of openness represented by the publication of public assessment reports was a major pioneering step for the two regulatory bodies and ongoing communication between regulators will allow for the sharing of ideas and continued evolution of PARs.

While this research builds our understanding from the perspectives of transparency in medicines registration decision-making process, this work focuses predominantly on the publication of information relating to evaluation of medicines *via* PARs or a summary basis for registration for NMRAs in the SADC region as a commitment to transparency in medicines registration decision making.

1.1.3. Research Objectives

This study aims to ascertain whether NMRAs within the SADC region have PARs for their scientific basis of accepting or rejecting registration of medicinal products; To investigate, if those public assessments reports / summary basis for registration are publicly available for the purpose of transparency; To investigate if all SADC NMRAs have fully implemented key transparency and communication parameters to enhance stakeholder relations; To establish if all SADC NMRAs have legislative frameworks for regulating medicines; To investigate the sources of funding for SADC NMRAs. Lastly, the study will propose strategies to address identified discrepancies.

1.1.3.1. Primary research question

- Does your NMRA have a public assessment report for the scientific basis of accepting or rejecting registration of medicinal products?

1.1.3.2. Supplementary research questions

- If the answer to the primary question is yes, is this public assessment report / summary basis for registration made public for the purpose of transparency?
- If the answer to the primary question is No, what steps do your NMRA have in place to ensure transparency in medicines registration decision making?

Chapter Two

2.1. Literature review

2.1.1. Global Regulatory Environment

The Constitution of the World Health Organization (WHO) affirms, "The enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being" (WHA, 2014). Goal 3 of the United Nations Sustainable Development Goals (SDGs) aims to ensure healthy lives and promote well-being for all at all ages. Target 3.8 for goal 3 is to "achieve universal health coverage, including financial risk protection, access to quality essential health-care services and access to safe, effective, quality and affordable essential medicines and vaccines for all" (UN, 2020). Governments across the globe thus have the huge responsibility of ensuring universal access to basic healthcare services to everyone. In order to achieve this important objective, countries across the globe should ensure that the basic human right of access to quality healthcare services is entrenched in their constitutions. The COVID-19 pandemic indicated that the majority of health systems across the world are under resourced and this threatens already achieved health outcomes (UN, 2020). Therefore, health system strengthening should be at the forefront of every government policy. The pandemic has also exposed high levels of poverty and inequality especially in developing countries.

Medicines are global commodities and the high burden of disease (both communicable and non-communicable), outbreaks of pandemics such as the current COVID-19 pandemic and emergence of antibiotic resistance has presented regulatory authorities with multiple challenges. To tackle such challenges UN SDG 3 target 3B is derived to ensure support and development of vaccines and medicines that primarily affect developing countries, resulting in increased access to all (UN, 2020). Moreover, rapid movement of people and illnesses across borders in today's world present regulatory agencies in developed and developing countries with similar challenges necessitating a need for regulatory agility and harmonization (National Academy of Sciences, 2020). Furthermore, WHA Resolution 67.20 recognized the critical role regulators play in public health and local production as it indicates that regulators are an essential part of the health workforce and effective regulatory system can support expansion of local or regional production of quality medicines (WHO, 2017).

According to the WHO global benchmarking tool (GBT) for evaluation of national regulatory systems for medical products, the National Regulatory Authority (NRA) is the institution

responsible for assuring quality, safety and efficacy of medical products (such as medicines, vaccines, blood products, traditional or herbal medicines and medical devices) as well as ensuring the relevance and accuracy of product labelling (WHO, 2018).The key objective of any NRA is to promote and protect public health and to provide guarantees on the quality, safety and efficacy of health products circulating in their markets. Consequently, well-functioning NRAs will ensure an independent and competent oversight of medical products in order to protect their citizens against substandard and falsified (SF) products (WHO, 2018). The GBT facilitates coordination and improves the effectiveness of regulatory strengthening efforts (Guzman, O'Connell, Kikule and Hafner, 2020).

A study on the public health and socioeconomic impact of substandard and falsified medical products by WHO indicate that approximately 10 % of products are substandard or falsified in low and middle-income countries (WHO, 2017). The report further indicates that this leads to serious socioeconomic and health impact such as increased poverty, lack of productivity, high disease prevalence and progression of antimicrobial resistance. According to a systematic review of 265 studies comprising 400 647 drug samples and meta-analysis of 96 studies comprising 67 839 drug samples, the prevalence of substandard and falsified medicines in low- and middle-income countries was 13.6 % overall (19.1 % for antimalarials and 12.4 % for antibiotics). Data on the estimated economic impact were limited primarily to market size and ranged widely from US$ 10 billion to US$ 200 billion (Ozawa *et al*., 2018).

Increased globalization of production presented regulatory authorities with multiple challenges in regulating these medicinal products. More and more global regulatory cooperation and harmonization initiatives have been established to allow greater information sharing platforms among regulators such as the International Council on Harmonization (ICH) and the International Pharmaceutical Regulators Programme (IPRP) (National Academy of Sciences, 2020). This is particularly important because globally, regulatory authority capacity for health products varies widely (Mak *et al.,* 2020). Therefore, the level of trust to rely on each other's work and reduce duplication of efforts would largely depend on the transparency in terms of decision-making processes within these regulatory agencies. Effective regulatory systems are an essential component of any health system and contribute to desired public health outcomes and innovation (WHO, 2020). A robust regulatory system should thus be fair, transparent, effective, efficient and predictable (Mukanga, 2020).

Tafuri (2013) states that the basis of regulatory decisions is benefit / risk assessment, in the form of dossier assessment of quality, non-clinical and clinical data submitted by applicants. The core mandate of any regulatory agency is to make sure that the benefits of a new medicinal product outweigh the risks and ensuring that only products with a positive benefit / risk balance are accessible to the public in their jurisdiction. With the emergence of biosimilar and other advance therapy medicinal products, the majority of regulatory agencies in various regions across the globe, and particularly in developing countries such the SADC region, are faced with similar challenges of ensuring rapid market access to this much-needed therapeutics. On the other hand, they need to ensure a comprehensive review of data on the benefits and risks of the new drugs with limited capacity and resources. In essence, Tafuri's argument is that scientific evidence supporting the use of a new product is mostly incomplete. Decisions have to be made under conditions of uncertainty and therefore the basis and process of the regulatory decisions should be both implicit and explicit. This in turn creates a problem of communicating the reasons and the rationale for regulatory decisions. For the purpose of transparency, regulatory processes, guidelines and decisions should be publicly available and easily accessible.

Coplan *et al.* (2011) indicated that the current process of benefit–risk assessment of medicines relies primarily on intuitive expert judgment. Therefore, there is a clear need for standardization of frameworks and guidelines to ensure transparent and defensible decision making that benefits patients, drug developers, and decision makers. Furthermore, Tafuri (2013) states that a properly conducted benefit / risk assessment should be able to combine objective elements (data and uncertainties) with subjective elements, leading to consistent decisions and should be communicated to various stakeholders in a transparent manner. A delicate balance of benefits and risks thus underpins the Marketing Authorization (MA) decision-making by regulatory agencies. According to a review of selected European agencies, licensing decisions are made intuitively following extensive data analysis and discussions amongst various experts (Pignatti *et al*., 2015). For this reason, inconsistency may exist within similar product ranges and it is therefore imperative to publish information on regulatory decision-making processes.

Various regulatory agencies have embarked on policy reforms in the quest to make their processes more transparent. For example, over the past 4 years the EMA developed two critical policy frameworks to publish clinical trial data and policy on access to documents. Bonini,

Eichler, Wathion, and Rasi (2014) confirm a 2010 policy on access to documents as well as a 2014 policy on publication of clinical data to demonstrate the EMA's commitment toward transparency in executing their public health mandate. In addition, Papathanasiou *et al. (*2016) indicated that the EMA and TGA publish information following evaluation through PARs as part of their commitment to transparency.

Furthermore, in Canada, recent legislative amendments and the introduction of Health Canada's Regulatory Transparency and Openness Framework aim to enhance the transparency of the regulatory review processes, and to provide public information about Health Canada's review decisions (Health Canada, 2015). A study by Leong, Walker and Salek (2014) comparing public assessments reports of the US FDA, EMA, TGA and Health Canada with the Benefit-Risk (BR) documentation template developed by the Centre for Innovation in Regulatory Science (CIRS), indicated that the formats of the publicly available assessment reports from the four reference agencies are similar and offer much needed information about risk based decision making during medicine evaluation.

Leong, Walker, and Salek (2015) further indicated that it is necessary that regulatory decisions and processes be openly communicated to various stakeholders for transparency. As such, there is a need to use standardized templates in order to enhance communication between regulators and other stakeholders, in a manner that would uphold transparency, consistency and standards. Leufkens and Eichler (2011) concurs that new standards and tools should be developed to evaluate and assess the benefit-risk balance of medicines to facilitate a sound and transparent decision-making process. Another study by Klein, Hardy, Lim, and Marshall (2016) concluded that there is growing recognition of the value, with respect to regulatory benefit-risk assessment, of information that could be gathered from patients. Liberti *et al*. (2013) indicated that decision frameworks can facilitate a more complete understanding of the factors that lead agencies to their complex decisions, particularly where different conclusions are reached by individual agencies when presented with essentially the same application data.

The growing pressure to increase transparency and accountability and to provide explanations as to how decisions are reached, favours the use of structured decision frameworks. The study by Bonini *et al.* (2014) concluded that patients have a right to know about the scientific basis for the approval and use of their medicines and that transparency of clinical trial data is

therefore essential. According to WHO (2003) the key components for effective regulation are transparency in regulatory processes as well as consistency in decision making by using structured frameworks that aid in the communication of the differences in opinion between regulators and the applicants. Communicating the rationale of how a particular regulatory decision was made will promote trust in the regulatory system. Therefore, it is critical that regulatory authorities provide full disclosure of information on internal discussions and assessment reports related to regulatory decision making (Tafuri, 2013). Furthermore, Pignatti *et al*., (2015) states that the reasons and rationale for regulatory decisions should be easily accessible to patients in order to assist them in making informed treatment decisions. Mature regulatory agencies publish their assessment reports, which include a summary of the data and the conclusions reached. Therefore, SADC NMRAs should adopt similar approaches to demonstrate transparency, fairness and openness in their decision–making processes.

Openness and transparency are critical parameters for medicines regulators. Sound regulatory systems globally are underpinned by the principle of transparency where patients and healthcare professional have access to regulatory decisions to guide them when making therapeutic decisions. Lack of transparency in medicines registration decision making processes have potential to damage the reputation and public confidence in those NMRAs tasked with executing a mandate of ensuring that only medical products which meet international standards of quality, safety and efficacy are allowed to be marketed in a particular jurisdiction. In addition, lack of transparency in decision-making can lead to high levels of corruption, especially for NMRAs in low and middle-income countries. Despite calls for a more consistent and robust process as indicated by the studies above, improved transparency and communication of regulatory decision making processes is still a problem in the SADC region, which necessitated the need for this study.

2.1.2. Regulatory Environment in Africa

Reports estimated that the value of Africa's pharmaceutical industry rose from US$ 4.7 billion in 2003 to US$ 20.8 billion in 2013 (Holt, Lahrichi, and Santos da Silva, 2015). Currently, reports indicate that Africa's pharmaceutical industry is one of the world's fastest growing industries. In the past ten years the market has exploded to US$ 21 billion, with a projected estimate of US$ 60 billion by the end of 2020 (PMPA, 2012). In essence, global pharmaceutical companies are starting to expand their market share with Africa as a potential investment destination. This places massive pressure on already struggling NMRAs tasked with ensuring safety and efficacy of these pharmaceutical products to protect their citizens.

According to the World Population Review (2020), Africa is the second-largest and second most populous continent and had an estimated population of 1.2 billion people in 2016. Due to high burden of disease (both communicable and non-communicable), the life expectancy is also low – less than 50 in most African states. Berger, *et al*., (2010) also states that though Africa has 11 % of the world's population, it utilises less than 1 % of the global health expenditure and carries 25 % of the world's burden of disease. These points indicate that Africa still have a long way to go in improving the quality of life of its citizens.

The WHO report on assessment of medicines regulatory systems in sub-Saharan African countries, conducted between 2002 and 2009 and including NMRAs in 26 African countries, indicated that African countries generally rely heavily on imports of pharmaceuticals and has limited local pharmaceutical production capacity. Many NMRAs were unable to execute a full range of their regulatory functions / mandate as their operational models provide them little power and autonomy. Unsustainable funding models were also identified in the report as a major setback for majority of these NMRAs, which ultimately restrict their operations. Furthermore, the report state that virtually all NMRAs lacked skilled human resource capacity such as assessors and inspectors to fully execute their regulatory tasks and most of their regulatory processes were not in line with international best practice. Because of these drawbacks, medicines regulation was not being carried out fully (WHO Drug Information, 2010). A 2004 questionnaire survey conducted by WHO in 38 African Member States, found that 90 % of countries were unable to adequately carry out full regulatory functions (WHO, 2006). In addition, reports from WHO Drug Information (2010) revealed that 7 % of the 46 sub-Saharan African countries have NMRAs, which are under-developed in terms of capacity. To

improve the situation, African countries thus need to invest heavily in financial and human resources.

The lack of good quality medicines, poor health infrastructure, inadequate financial and human resources are some of the main factors towards low life expectancy. Ultimately, these add significant burden on the healthcare systems of many African countries leading to high mortality rate from preventable diseases. This has led to increased demand for medicines of good quality and processes to ensure safety and efficacy. The role of African NMRAs should be to provide a conducive environment for manufacturing companies to thrive while protecting their citizens from substandard and falsified medicines. This will in turn accelerate access to much-needed therapeutics to curb the spread of both communicable and non-communicable diseases and improve the quality of life for citizens.

According to Ndomondo-Sigonda *et al.,* (2017) all countries in Africa, with the exception of Sahrawi Republic, have NMRAs, but with varying operational structures and capacities. Some authorities function as autonomous entities, some are semi–autonomous and others operate within health ministries. Regional regulatory harmonization and convergence efforts in Africa such as the African Medicines Regulatory Harmonization (AMRH) Initiative, establishment of an African Medicines Agency (AMA) through domestication of the African Union (AU) model law as well as regional collaboration initiatives such as the East African Community (EAC) and the Southern African Development Community (SADC; called ZaZiBoNa), have become imperative.

2.1.3. Regional Regulatory Harmonization Efforts in Africa

Across the 54 NMRAs in Africa, the full picture of regulatory maturity is not completely known (Kaine, 2020). Many of these NMRAs are faced with similar challenges of limited financial and human resources, long registration timelines due to lack of well-trained assessors or evaluators as well as lack of political will from the policy makers. These challenges may lead to an increase in counterfeit and substandard medicines due to poorly developed regulatory systems and procedures to ensure the safety and efficacy of medicines. Inefficient regulatory systems themselves can be a barrier to access to safe, effective and quality medical products (Kaine, 2020). As such, harmonization and convergence of technical requirement for medicines registration across various regions in Africa becomes particularly important.

Mashaki *et al.*, (2018) indicate that while each country has autonomy in their regulatory decision-making, regulatory best practice is also to recognize the value of benchmarking regulatory models and sharing best practices with other agencies. Furthermore, a report by National Academy of Sciences (2020) states that formal and informal recognition or reliance arrangements will follow once trust and confidence between authorities is established. These will significantly reduce medicines registration timelines and duplication of efforts and regulatory authorities in low- and middle-income countries should build on previous collaboration to share both confidential and public information expeditiously, to enable timely local decision-making (National Academy of Sciences, 2020)

African Medicines Regulatory Harmonization (AMRH) since its inception in 2009 has made strides to strengthen regulatory harmonization and convergence initiatives across Africa. These include the establishment of AU Model law, establishment of Regional Centres of Excellence (RCOREs) in 2014 and joint dossier assessments activities across various Regional Economic Communities (RECs) for example, East African Community (EAC) and Southern African Development Community (SADC).

2.1.3.1. African Medicines Regulatory Harmonization (AMRH) Initiative

In order to strengthen regulatory systems in Africa, the African Union established the African Medicines Registration Harmonisation Initiative (AMRH) in 2009, led by the African Union Development Agency – New Partnership for African Development (AUDA-NEPAD), to encourage harmonization of the fragmented regulatory systems in the continent (Sithole *et al*., 2020). The vision of the AMRH initiative is to have transparent regulatory processes with clear timelines, stronger, institutionalized regulatory capacity, systems strengthening programmes and faster registration with a regional approach. The AMRH initiative divided the African continent into 5-7 Regional Economic Communities (RECs) and medicines harmonization initiatives were implemented through these RECs. Currently, the EAC and SADC are some of the RECs in African continent that had demonstrated success in their medicines harmonization projects (Ndomondo-Sigonda *et al*., 2020a). Ultimately, these initiatives will increase access to the much-needed good quality, safe and effective medicines in the African continent.

The overall objective of the initiative is to have a single set of requirements, clear guidelines, and fewer dossiers to prepare (for example one per REC) across the continent, reducing duplication of efforts by pooling resources and information sharing, leading to more harmonized requirements. According to Ndomondo-Sigonda *et al*., (2018) more than 85 % of Sub-Saharan Africa is covered with medicines registration harmonization (MRH) projects at different levels of implementation (see Table 1). The AMRH initiative plays a critical role and has gone a long way towards augmenting the findings of a 2012 survey, wherein the majority of representatives from African pharmaceutical companies indicated that technical requirements related to registration of medicines were problematic (Narsai, Williams, Mantel-Teeuwisse, 2012). However, sometimes manufacturers still view Africa as a small market resulting in delays in availability of many new products (Kamwanja *et al*., 2010).

Table 1: Implementation status of RECs medicines harmonization initiatives (adapted from AMRH Publications and presented by Ndomondo-Sigonda -AUDA-NEPAD, 2020a).

REC progress		
REC's	**Status**	**Comments**
East African Community (EAC)	Implementation	Launched March 2012
Organization of Coordination for the Fight Against Endemic Diseases in Central Africa (OCEAC / ECCAS)	In progress	Launch Nov 2016
Economic Community of West African States (ECOWAS)	Implementation	Launched Feb 2015
Southern African Development Community (SADC)	Implementation	Launched July 2015
Intergovernmental Authority on Development (IGAD)	Preparatory Phase	2016

Currently the AMRH initiative is expanding its scope to cover other regulatory functions & products e.g. EAC Pharmacovigilance Project, African Vaccines Regulatory Forum (AVAREF), and clinical trials ethics and regulatory oversight.

As indicated earlier, sub-Saharan African countries import most of their pharmaceuticals. The African Union Heads of State and government took it upon themselves to develop a plan, which will promote local manufacture of medicines in Africa. In 2005, the African Union (AU) decision 55 established a framework for development of a Pharmaceutical Manufacturing Plan for Africa (PMPA) in order to build African states' healthcare capacity and to promote access to quality and affordable medicines as well as ensuring the security of supply through the integration of local production. In 2012, a PMPA business plan was published and the primary vision for this strategic framework was to ensure availability of safe, effective and good quality medicines for the African continent as well as developing a pharmaceutical market that is competitive to ensure self-reliance. AU PMPA, 2012). The promotion of local production will ensure a sustainable supply of quality-assured medicines for the long term as well provision of job opportunities.

2.1.3.2. African Medicines Agency (AMA)

African Heads of states and governments at the African Union Summit in Addis Ababa, Ethiopia, in January 2016 officially endorsed the Africa Union's AU Model law on medical products regulation (Ndomondo-Sigonda *et al*., 2020b). The aim is to develop legislative frameworks to guide RECs and AU member states to regulate medicinal products. In addition, the model law is expected to contribute towards implementation of the PMPA as well as the establishment of an African Medicines Agency (AMA). This will be in line with World Health Organization best practice in medicines regulation on safety, efficacy and quality. Furthermore, the model law is expected to strengthen national law on medicine regulations and promote autonomous NMRAs. This is a clear demonstration that African leaders are committed to building robust regulatory systems that are agile and responsive to the healthcare needs of all Africans.

It is therefore imperative that the continent streamline and harmonize local and regional medicine regulations to encourage investment in Africa. To achieve this vision of African Heads of States and government, a commitment and support from policy makers is essential and currently, only 17 countries have adopted the model law. Furthermore, the potential establishment of the AMA is an opportunity to improve NMRAs' capacity in Africa (Ndomondo-Sigonda *at el*., 2017). The Pharmaceutical sector in Africa may also benefit from the newly proposed African Continental Free Trade Area (AfCFTA),

which will allow for integration of African markets through intra-African trade by making Africa a single market (Ndomondo-Sigonda *et al*., 2020b).

2.1.3.3. East African Community (EAC)

East African Community (EAC), a regional economic community, comprises six member states namely: Burundi, Kenya, Rwanda, South Sudan, Tanzania, and Uganda. The EAC MRH initiative was officially launched in March 2012 in Arusha, Tanzania, as a region-wide Medicines Regulatory Harmonization (MRH) initiative, intended as a 5-year pilot for the broader African Union's African Medicines Regulatory Harmonization (AMRH) initiative (Sillo *et al.*, 2020).

According to Mashingia *et al.,* (2020) the initiative has significantly reduced registration timelines in the region. From 2012 to 2017, the timeline for registration of medicines decreased from roughly 24 months to 8–14 months when evaluated through the joint assessment session. This demonstrates that harmonization efforts are beneficial when they are well coordinated and monitored. The above is supported by a study from Giaquinto *et al*., (2020), which concluded that the initiative may be able to further improve access to essential medicines by increasing transparency, inviting and responding to feedback from industry partners and consistently meeting its advertised assessment and registration timelines as well as benchmarking on other similar initiatives. Furthermore, the study recommended that strengthening the EAC MRH's legal framework, such that member states are legally required to respect joint regulatory decisions instead of being bound only by goodwill, will be important for securing the initiative's future (Giaquinto *et al*., 2020).

Harmonization initiatives such as this one are expensive and require massive financial support. A study by Ndomondo-Sigonda *et al*., (2020c) indicate that an average total annual budget for all the EAC countries during the study period 2011–2015 ranged from US$ 824 328.67 to US$ 10 724 536.50.

The initiative is also planning to have a cadre of regional technical officers (RTOs), through a Cooperation Framework Agreement between the NMRAs of EAC Partner States, and a sustainable funding mechanism for regional assessment (Arik *et al.,* 2020). However, Sillo *et al.,* (2020) indicate that the registration process often lacks transparency, with no clear timeline or accountability. Therefore, improvements are required in the EAC medicines registration processes. Interestingly, Dansie, Odoch and Ardal (2019) conducted a study on industrial perceptions of medicines regulatory harmonization in the East African Community which concluded that improvements are required to the current EAC processes to meet the vision of harmonization and highlighted challenges such as length of time to receive the actual marketing authorization and challenges in getting all EAC countries to recognize EAC approvals and smaller, less attractive markets.

Lastly, Ndomondo-Sigonda *et al*., (2020a) indicated that the lessons from the East African Community, during their piloting of the Medicines Regulatory Harmonization initiative, could be used to benchmark other RECs across the African continent. Tanzania's NMRA recently became the first in Africa to attain World Health Organisation maturity level 3 in December 2018 (Sillo, 2019). Maturity level 3 indicates a stable, well functioning, and integrated regulatory system (Arik *et al, 2020*). Other African NMRAs should emulate this significant milestone.

2.1.3.4. Southern African Development Community (SADC)

The Southern African Development Community (SADC) is a regional economic group with 16 member states (SADC, 2020). However, due to varying regulatory capacity, currently only 11 member states are actively issuing market authorization for pharmaceuticals marketed in their countries. As such, only 11 SADC NMRAs were investigated for the purpose of this study. The eleven (11) SADC regulatory authorities included in this study are: South African Health Products Regulatory Authority (SAHPRA), Medicines Control Authority of Zimbabwe (MCAZ), Namibian Medicines Regulatory Council (NMRC), Tanzania Medicines and Medical Devices Authority (TMDA), Botswana Medicines Regulatory Authority (BOMRA), Zambian Medicines Regulatory Authority(ZAMRA), National Directorate of Medicine and Equipment (DNME) of Angola, National Directorate Of Pharmacy (DNF) of Mozambique, Congolese National Medicines Regulatory Authority (ACOREP), Madagascar and lastly,

Pharmacy, Medicines & Poison Board (PMPB) now Pharmacy and Medicines Regulatory Authority (PMRA) of Malawi.

In October 2013, a regional collaboration and harmonization initiative for registration and GMP inspections of pharmaceuticals called ZaZiBoNa was established by four countries, namely Zambia, Zimbabwe, Botswana and Namibia. The ZaZiBoNa initiative was established with the aims of reducing workload amongst the participating countries through joint assessment and to facilitate harmonization of regulatory requirements in the SADC region as well as providing a platform for training and capacity building of NMRAs in the SADC region. As at March 2019, there were 13 participating member states, which are at different level of regulatory capacities. South Africa joined the initiative in 2016 and Tanzania in 2018.

Efforts towards regulatory harmonization and convergence have been evident over the last 20 years (WHO, 2000). These efforts led to standardization of technical regulatory requirements for the quality, efficacy, and safety of medicines and improving quick access to much needed therapeutics. In addition, Ward (2014) indicated that NRAs have also been encouraged by the WHO to consider regulatory convergence and to collaborate with and recognize work done by other regulators to ease the regulatory burden. SADC NMRAs are also facing similar challenges as NMRAs in low and middle-income countries as mentioned earlier. Therefore, comparisons between NMRAs in low and middle-income countries play a critical role in identifying gaps and challenges encountered by these resource-limited agencies. These comparative studies will enable the identification of positive aspects, which can be recommended for implementation in other NMRAs within the SADC region in order to improve their processes and operations.

Several studies have been conducted in this regard. For example, a study conducted by (Keyter *et al*., 2019) focused primarily on the comparison of SAHPRA with countries such as Australia, Switzerland, Canada and Singapore. The study recommended that SAHPRA should consider implementing facilitated regulatory pathways and developing publicly available summaries for the basis of approval to enhance transparency and improve communication through the implementation of electronic document management (Keyter *et al.*, 2019). Ndomondo-Sigonda *et al*., (2017) conducted a broader study from the African perspective to evaluate Medicines Regulation in Africa. The study concluded that apart from the Sahrawi Republic, every country in Africa currently has a NMRA, although the functionalities are variable across countries and

they are at different levels of growth, maturity and expertise. It went further to say that, there is a need to benchmark African NMRAs in a more transparent and objective manner, and based on agreed criteria, to identify the different levels of capacities and performance. The outcome of the benchmarking process will be useful to support the ongoing harmonization efforts within the SADC region and built required capacity among all 16 SADC member states and beyond.

A study by Keyter, Gouws, Salek and Walker (2018a) assessed the regulatory review process in South Africa from 2015 to 2017, as well as the effectiveness of measures to ensure consistency, transparency, timeliness, and predictability in their review processes by means of a questionnaire. The study indicated that the agency had no target for overall approval timelines and recommended that as the agency is transitioning to a newly established agency called SAHPRA, it should enhance its regulatory review processes and should consider models such as abridged assessment and reliance. These models are currently being implemented by SAHPRA and are proving to be very effective (Keyter *et al.,* 2020b), however further studies should be conducted in this regard. Furthermore, Keyter, Banoo, Salek and Walker (2018b) in another study recommended establishing a quality management system to safeguard accountability, consistency and transparency including quality decision-making practices.

A more recent study by Sithole *et al*., (2020), evaluating the success of the ZaZiBoNa initiative using publicly available literature and statistics, meeting records, terms of reference and unpublished documents belonging to the initiative, concluded that the success of this initiative is attributed to leadership commitment and a clear, documented operating model, processes and objectives. The study recommended that other similar regional harmonization initiatives on the African continent and beyond could benchmark from the ZaZiBoNa initiative to improve their efficiency and effectiveness. Therefore, this kind of collaborative joint assessment can be used as benchmarks to encourage other regions to do the same.

Publication of information relating to evaluation of medicines in the form of public assessment reports or any summary basis for registration is one way of ensuring transparency in medicines registration decision making. As stated earlier, the purpose of this study was to investigate whether NMRAs in the SADC region are in a position to publish such PARs / Summary basis for registration as a commitment to transparency in medicines registration decision-making or not. Currently there are no data and information on this issue.

Chapter Three

3.1. Methodology

Qualitative research seeks to understand the ways people experience events, places, and processes. Rather than trying to measure and quantify aspects of a singular social reality, qualitative research draws on methods aimed at recognizing the complexity of everyday life and of influences that shape human lived experiences (McGuirk and O'Neill, 2016). Based on the primary research question, a qualitative approach was found to be the most suitable study methodology that could be employed to assist in achieving the study objectives. A similar study by Keyter *et al.* (2020a), focusing on regulatory authorities in Australia, Europe, Canada, South Africa and the United States, used focus groups to discuss the use of PARs as potential knowledge management tools for stakeholder understanding of regulatory decision-making.

A cross-sectional exploratory descriptive study design with qualitative techniques was employed. This was in the form of a standardised questionnaire (As indicated in Appendix A), containing four sections, namely, demographic details and parts A to C addressing the research objectives. Firstly, Part A covered the organizational structure of the selected NMRAs including aspects such as the organizational set-up (Autonomous or semi-Autonomous), availability or non- availability of legislative framework, regulatory functions carried out by the selected NMRAs, technical staff complement, availability or non- availability of advisory committees and conflict of interest policies as well as the funding models used by the NMRAs. The second part of the questionnaire (Part B) covered ten pre-established transparency and communication parameters to enhance stakeholder relationships in regulatory decision-making practices of NMRAs in the form of yes or no selection. Lastly, Part C of the questionnaire included the main research question and supplementary questions in the form of open and closed ended questions.

The advantages for using a questionnaire data collection method is that it saves time and money and allow for a smooth and coordinated data capturing. Questionnaires are cost effective as they can be easily standardized and provide structured questions to a group of individuals. Furthermore, McGuirk and O'Neill (2016) states that "questionnaires are useful for gathering original data about people, their behaviour, experiences and social interactions, attitudes and opinions, and awareness of events". Moreover, questionnaires are extremely flexible as they

are able to collect qualitative and quantitative data. Therefore, a questionnaire was the primary data gathering strategy used in this study to provide in-depth perspectives of the transparency in medicines registration decision-making processes amongst NMRAs within the SADC region. Particularly, the generation and publication of PARs / Summary basis from which decisions on accepting or rejecting medicines applications are based were assessed. Emergent themes from this three-part questionnaire were used to analyse research findings and to provide in-depth discussions on the study results for the purpose of answering the primary research question. Secondary data was obtained from an extensive search of books, journals, research projects and various other publications such as presentations to add substance to the literature review. Database searches included mostly google scholar, using keywords as stated above. Various books, publications, Acts, government reports, annual reports and previous dissertations were consulted throughout the study in order to extract useful information and assist in achieving the objectives of the research.

A study sample consisting of 11 NMRAs in the SADC region was used in the study. The 11 regulatory authorities were selected based on their ability to issue marketing authorization. Currently, out of the 16 SADC member states, only 11 are actively issuing Marketing Authorization (MA) and comply with the inclusion criteria. A purposive sampling method was used, targeting key informants / senior members of the selected NMRAs. Contact details (email addresses) for each participant were obtained from a SADC ZaZiBoNa coordinator. The standardised questionnaires together with the information sheet and consent to participate in research (As indicated in Appendix B) were sent *via* email to these key informants / senior members in the eleven (11) regulatory authorities selected for this study. The regulatory authorities included in this study are: South African Health Products Regulatory Authority (SAHPRA), Medicines Control Authority of Zimbabwe (MCAZ), Namibian Medicines Regulatory Council (NMRC), Tanzania Medicines and Medical Devices Authority (TMDA), Botswana Medicines Regulatory Authority (BOMRA), Zambian Medicines Regulatory Authority(ZAMRA), National Directorate of Medicine and Equipment (DNME) of Angola, National Directorate Of Pharmacy (DNF) of Mozambique, Congolese National Medicines Regulatory Authority (ACOREP), Madagascar and lastly, Pharmacy, Medicines & Poison Board (PMPB) now Pharmacy and Medicines Regulatory Authority (PMRA) of Malawi.

Although, the sampling methods might appear biased towards senior members / key informants within the NMRAs, their first hand institutional knowledge, and involvement within NMRAs'

decision making processes was beneficial to the study. The data from the 11 NMRAs were collected between July 2020 and August 2020 by using the standardised questionnaire format as described above, to allow for appropriate capturing and analyses of information collected from multiple NMRAs within the SADC region. Only nine (9) NMRAs responded to the study questionnaire, and as such, the data analysed in Chapter Four (4) represents the nine (9) NMRAs that participated in the study. It excluded ZAMRA and Madagascar, who did not respond.

3.1.2. Piloting of the Questionnaire

The questionnaire was formulated using data obtained during the preliminary literature review in the research proposal based on the primary research question. In addition, data from the WHO global benchmarking tool rev. VI ver. 1, for evaluation of National Regulatory System (RS), was adapted to design a questionnaire with an aim of achieving the research objectives (WHO, 2018). The WHO global Benchmarking tool is a yardstick used by the World Health Organization in determining the maturity level of the National Regulatory Authorities (NRAs). Most of the questionnaire questions were derived from indicators and sub indicators obtained from this WHO global benchmarking tool (WHO, 2018). More especially those indicators and sub-indicators that deal with promotion of transparency, accountability and communication as well as information on decisions related to regulatory activities were utilised. Based on the above, the questionnaire was designed in a standardized format with a checklist and open and closed ended questions. The questionnaire was formulated in English, and data collected therefore had a bias towards English-speaking countries within the SADC region as no translation was used for non-English speaking countries.

The questionnaire was validated and received ethics approval (approval number: BM20/5/10) in May 2020 from UWC Biomedical Research Ethics Committee. All 11 selected NMRAs were involved in the questionnaire piloting phase, the same NMRAs were also included in the final questionnaire. The questionnaire was therefore accepted as a suitable data collection tool for the purpose of this study. After the study title and ethics approval, the standardised questionnaires together with information sheet and consent to participate in research were sent *via* email to study participants in the eleven (11) regulatory authorities selected for this study. The detailed data collection process is described below in the next section. With this collective input from senior members / key informants as well as the recognition of public health mandate

of all NMRAs, the study managed to achieve its objectives based on the results as discussed in Chapter four (4) from which the study conclusion and recommendations in Chapter 5 are derived from.

3.1.3. Distribution of Questionnaire

Initially the study questionnaires were planned to be distributed to study participants at one of the ZaZiBoNa meetings. ZaZiBoNa is a collaborative registration procedure involving Zambia, Zimbabwe, Botswana, Namibia (ZaZiBoNa) and all other SADC countries at various level of participating status (e.g. Active, Non-active and observers) as already described in Chapter 2. Ideally under normal circumstances ZaZiBoNa meetings takes place quarterly (Four times in a year, i.e., February, June, August and December). This particular platform was chosen to improve the response output for the study as it provides opportunity to find all SADC member states under one roof. However, due to the spread of, and global Covid- 19 pandemic, all planned face-to-face ZaZiBoNa meetings were cancelled. This resulted in a change of plan for questionnaire distribution. Contact details for the Head of Agencies (HoAs) as well as those of medicine assessors / key informants were obtained from the ZaZiBoNa Coordinator. Emails were sent to all contacts in the 11 selected NMRAs in SADC region, requesting their participation in the study. The email request included two attachments, which were the standardised questionnaire and an information sheet with consent to participate in the study.

Some Agencies acknowledged receipt of the email and indicated that the request will have to receive internal Agency approval once all relevant units are informed, while other agencies did not respond. Where no response was received from the questionnaires within two weeks, reminder emails were sent, with a further email follow-up after two months. If no response was received after two months (between July and August 2020) from distribution of the questionnaire, it was assumed that the Agency was unwilling to participate.

Interestingly participants from non-English speaking countries such as DRC, Mozambique and Angola were quick to respond (within five days of acknowledging receipt of the study materials). Some English speaking countries such as Malawi, South Africa and Namibia also provided a quick response (within 10 days of acknowledging receipt of the study materials). The delay in response from Botswana, Zimbabwe and Tanzania can be attributed to the internal study approval process from the HoAs. Apart from the slight delay, eventually Botswana,

Zimbabwe and Tanzania responded to the questionnaire. Zambia and Madagascar did not participate in the study as was initially expected, even after two follow up emails and therefore they were excluded in the final data analysis.

A qualitative method was used to investigate whether NMRAs in the SADC region are in a position to generate and publish PARs / summary basis for registration as a commitment to transparency in medicines registration decision making. The standardized questionnaire with both open and closed ended questions provided for freedom of expression from the participants. Themes derived from the literature research conducted, and those emerging from the questionnaire responses were used to draw up conclusions and recommendations.

3.1.4. Data Analysis

3.1.4.1. Contents Analysis

Texts from open-ended and structured questions were inferred into thematic unit categories for interpretation. Trend analysis was conducted, involving an in-depth analysis of patterns.

3.1.4.2. Data Collection and Analysis Process

Data generated from the questionnaire was coded and analysed into themes based on the response received from the study participants. Where necessary tables, charts, figures and graphs were employed to simplify the data and for easy interpretation.

In summary, the data collection and analysis processes were as follows:

- Questionnaires were formulated and send for validation and ethics approval.
- Upon receiving ethical approval from UWC Biomedical Research Ethics Committee, questionnaires were then sent out *via* email to participants.
- Completed questionnaires were collected.
- Data were coded into themes and exported into Visio software and Microsoft excel for further analysis and presentation.
- Content analysis and identification of relevant themes and trends concerning availability or publication of PARs / Summary basis for decision to register or reject medicinal products within SADC NMRAs was performed.

3.1.5. Ethics

Approval to conduct the study was obtained from the University of the Western Cape Biomedical Research Ethics Committee (approval number: BM20 / 5 / 10) in May 2020. In addition, each NMRAs provided their own approval through their HoAs and expressed their willingness to participate in the study *via* an email reply.

The study questionnaire was accompanied by an information sheet and informed consent form to be completed by the study participants. The Information sheet and consent form included in Appendix B, clearly state that participation in this research is voluntary and that participants may withdraw participation at any point, and in the event of refusal / withdrawal of participation, the participants will not incur any penalty or loss of benefit to which they are normally entitled. Participants incurred no costs to participation in the study. Consent forms and questionnaire transcripts were kept confidential and only anonymized and combined responses are available on request. The study provided no direct benefits to participants, but based on the findings, the study provides recommendations to SADC NMRAs in order to improve their overall performance and to assist them to reach WHO maturity level 3 & 4 as described in the WHO global Benchmarking Tool for Regulatory Systems. Since the study participants were NMRAs staff, approval from each NMRA local Ethics Committee was not necessary.

3.1.6. Limitations

The first challenge observed was the cancellation of face-to–face ZaZiBoNa meetings due to the Covid-19 pandemic, where the questionnaires were initially planned to be distributed in order to improve participation and study output. The output was indeed affected by this unforeseen circumstance as only 9 out of 11 NMRAs (82 %) responded to study questionnaire. Secondly, another anticipated challenge was the language issue as some SADC member state are not English speaking and the questionnaire was formulated in English only. Interestingly enough, participants from non-English speaking countries such as DRC, Mozambique and Angola were quick to respond. A participant from Mozambique responded in both English and Portuguese. Therefore, the English language used in the questionnaire might have been a challenge on their side in the absence of an interpreter.

Thirdly, although the targeted population in the study were senior members / key informants, almost all the participants in the study were technical staff at various level of experience within NMRAs and mostly involved in dossier assessments (See Table 2 and Figure 2). However, based on their years of experience in the NMRAs, the study population was well justified to provide their first hand institutional knowledge, especially on their involvement within NMRAs decision-making processes.

Lastly, the study only focused on the NMRAs, without involving external stakeholders such as industry representatives and patient groups to find out their views and what they would like to see from the regulators in their quest to be transparent, fair and open. This might be a missed opportunity, but due to the limited time frame and scope of this study, could not be included. However, further studies can be conducted in this regard to understand the perspective of those who are regulated and those the regulators seek to protect.

Chapter Four

4.1. Analysis of results and Discussion

4.1.1. Introduction

The previous chapter described the methodology that was applied for this study and data collection tools used to answer the research questions. This chapter focuses on the analysis and interpretation of data collected from the respondents in the study to draw conclusions and make generalisations of findings to a problem statement (Creswell, 2014). The survey contained four (4) sections, namely, demographics, part A, part B and part C to address the research objectives. The questions asked were a combination of open-ended and a selection of yes or no.

The responses were captured on a spreadsheet where a cleaning process was conducted. Data was coded into themes, exported into Visio software for further analysis, and presented according to the objectives of the study. The results were presented in the form of charts, tables and graphics to assess whether the research questions were adequately addressed.

4.1.2. Response rate and respondents' profile

The response rate for the study was nine (9) out of eleven (11), giving an 82 % response rate. Therefore, data collected for the study were deemed sufficient to be analysed. The demographic profile of respondents from different NMRAs comprised designation and years in agency, which are provided in Table 2.

Table 2: Demographics

Factor	Item	Total
Designation	Pharmacist	4
	Registration officer	4
	Regulatory officer	1
Years in agency	Less than 2	1
	2-5	1
	6-10	5
	11 – 15	2

4.1.2.1. Designation

Table 2 and Figure 2 shows that there were pharmacists, registration and regulatory officers from the purposefully stratified respondents. However, it is possible that Regulatory and Registration officers are also pharmacist as these titles are general terms/ job titles commonly used within the medicines regulatory environment and do not represent a specific profession.

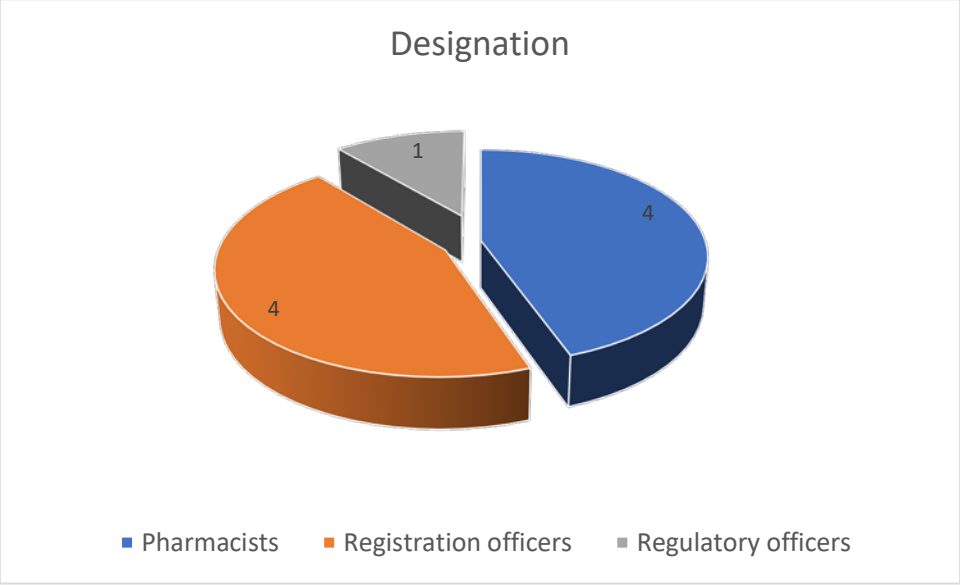

Figure 2: Designation

4.1.2.2. Years in the agency

Of the nine respondents indicated in Figure 3, one (1) respondent was employed in the agency for less than two (2) years, one (1) for a period of between 2 – 5 years, five (5) were employed in their respective agencies for a period of between 6 – 10 years and two (2) respondents had been in their agencies for a period of 11 – 15 years. The results indicate that most of the respondents were in their respectively agencies for 6 years or more. It can be concluded that the respondents are well experienced and possess the requisite first hand institutional knowledge to understand the regulatory decision-making processes within their respective agencies.

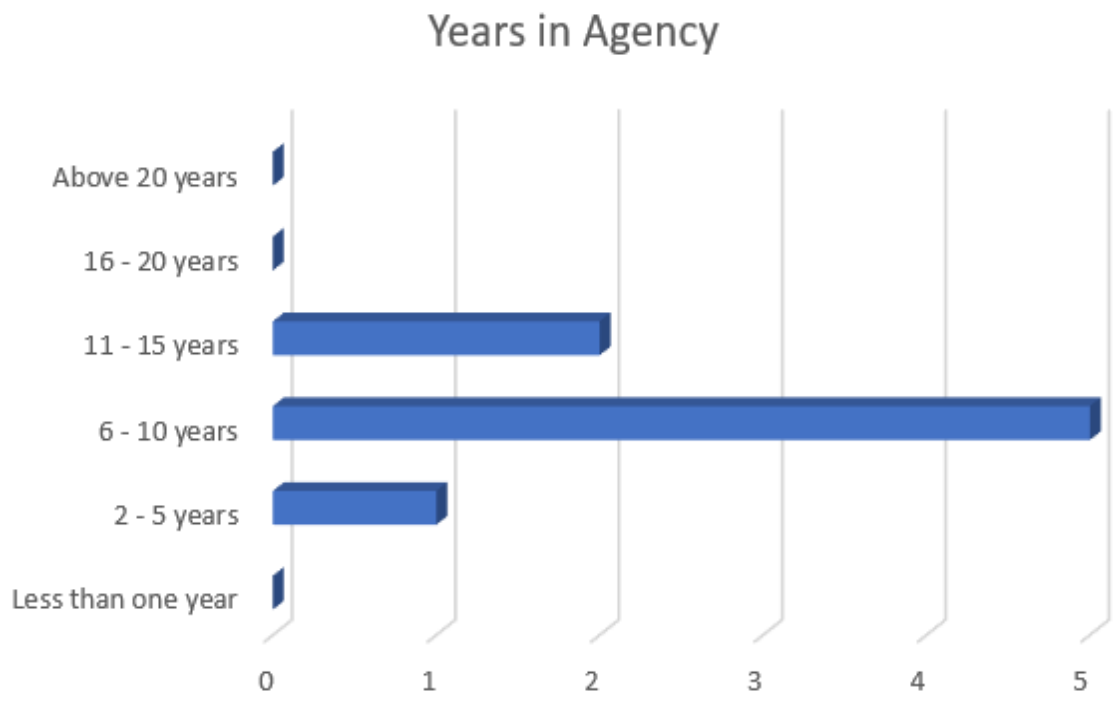

Figure 3: Years in agency

4.1.3. Descriptive analysis

Since the study population is specific to the industry being studied, purposive sampling was conducted targeting key informants within the NMRAs as already described in Chapter three (3) to ensure that the final sample of respondents was manageable. An introduction email containing an information sheet, informed consent and study questionnaire was sent to selected respondents in a phased approach between July and August 2020. Eleven (11) questionnaires were sent to potential respondents. Completed response datasets were considered when the respondent had returned a completed questionnaire.

Only nine (9) questionnaires were completed, which represented an 82 % response rate. The completed datasets obtained from the study were deemed sufficient to produce reliable results. The completed dataset was copied and graphs were produced using a Microsoft Excel®. Thematic analysis was done for the open-ended responses by creating themes based on responses that were similar. Thematic diagrams were produced on Microsoft Visio®.

The respondents from nine (9) NMRAs that participated in the study were coded as highlighted in Table 3.

Table 3: Respondents coding

Code	Country (Agency name)
1	Botswana (BOMRA)
2	DRC(Congolese National Medicines Regulatory Authority, ACOREP)
3	Angola (National Directorate of Medicine and Equipment ,DNME)
4	Tanzania (TMDA)
5	Zimbabwe (MCAZ)
6	Namibia (NMRC)
7	South Africa (SAHPRA)
8	Mozambique (National Directorate Of Pharmacy, DNF)
9	Malawi (PMRA)

4.1.4. Data Presentation

The results are presented in themes, figures and written descriptions. The results of the study are presented as per the objectives in Chapter one (1).

- Investigate whether NMRAs within the SADC region have PARs for their scientific basis of accepting or rejecting registration of medicinal products.
- Assess whether these PARs / summary basis for registration are publicly available for the purpose of transparency to enhance stakeholder relations.
- Identify discrepancies and offer possible recommendations to assist SADC NMRAs in achieving WHO maturity level 3 and 4 status as defined in the WHO Global Benchmarking tool for National regulatory systems (WHO, 2018).

To achieve the above objectives as per study title “Transparency in medicines registration decision making: A closer look at National Medicines Regulatory Authorities (NMRAs) within the Southern African Development Community (SADC) region.” The findings are categorised into three (3) main categories as depicted in Figure 4, namely:

- Organizational Structure (Part A)
- Transparency and communication parameters (Part B)
- Core of the study (Part C) – ability to generate and publish PARs.

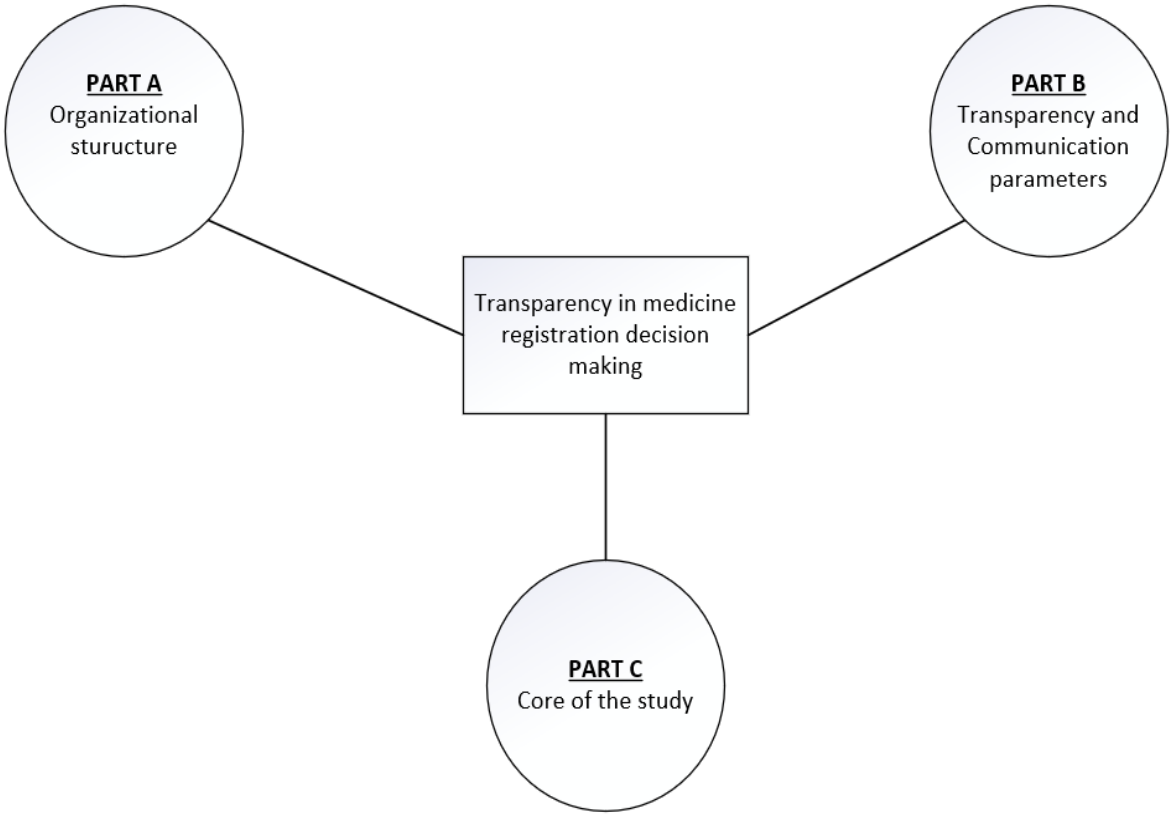

Figure 4: Broader thematic structure

4.1.4.1. Organizational structure (Part A)

The responses were organised thematically as reflected in Figure 5. The organizational construct has been further thematically organised into eight sub-themes. Furthermore, other unique themes were identified on the sub-themes.

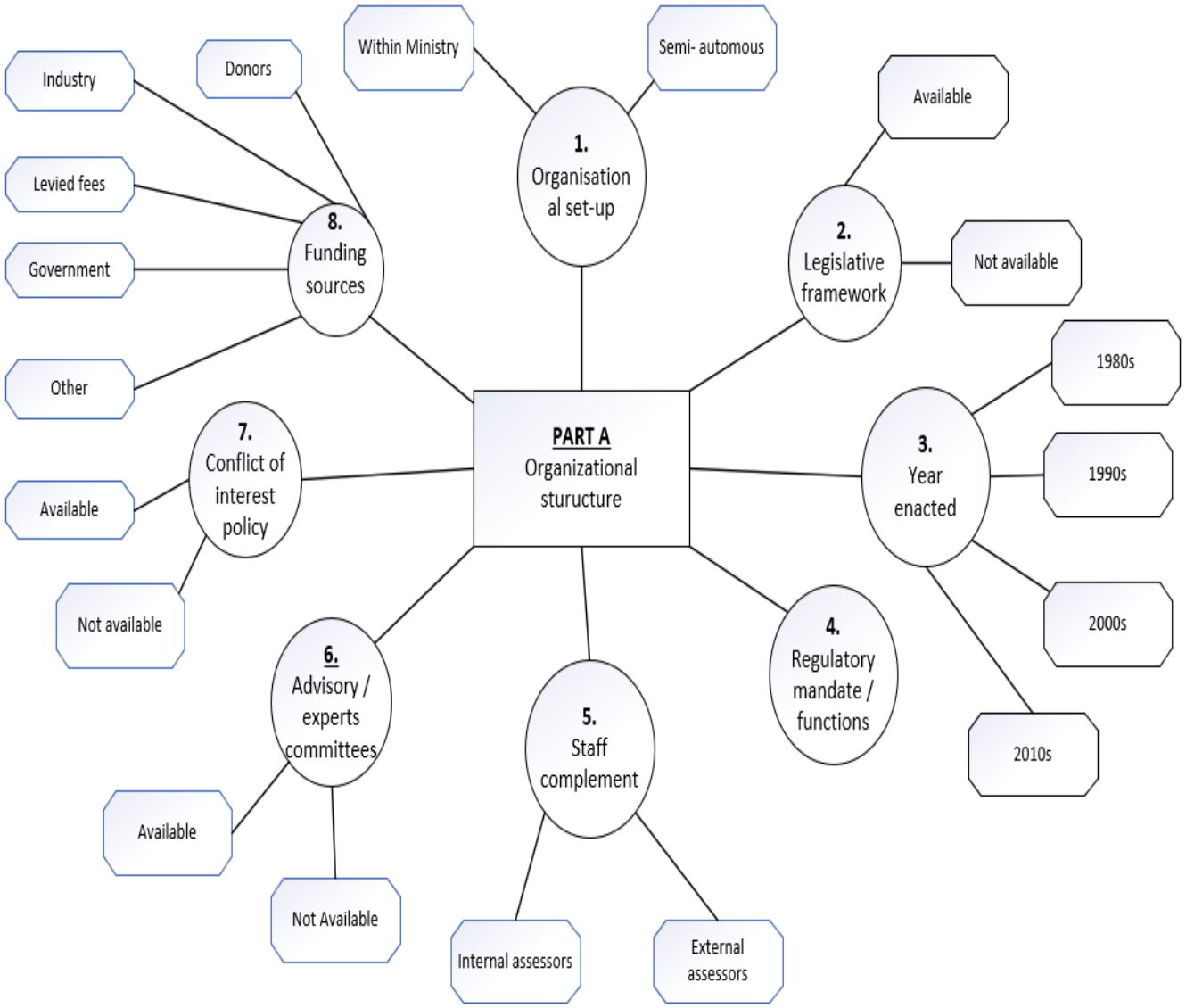

Figure 5: Part A themes

4.1.4.1.1. Organizational set-up

The specific organizational set-up will have an impact on the autonomy, flexibility, responsiveness and accountability of an NMRA and would affect efficiency in medicines control (WHO, 2010). This study revealed that currently five (5) NMRAs are operating as semi-autonomous agencies namely: BOMRA, MCAZ, PMRA, SAHPRA and TMDA. For BOMRA, SAHPRA and PMRA, the legislative frameworks that allowed these agencies to function as semi-autonomous were enacted in the last three (3) years – (2018, 2017 and 2019 respectively. This indicates a significant improvement in the level of autonomy of these NMRAs to allow them to function efficiently and effectively. Moreover, as the global medicines supply chain becomes more and more complex, the regulatory frameworks for these agencies had evolved over time to keep abreast of the current trends in the medicines regulatory landscape. Mukanga (2020) states that due to the increasingly complex global regulatory environment and supply chains, it is critically important that the global regulatory landscape adopt agile, transparent and predictable approaches. These NMRAs had therefore demonstrated their ability to be agile and responsive to complex global regulatory environment.

The NMRC, DNME of Angola, ACOREP of DRC and DNF of Mozambique were functioning within their respective Ministries of Health Departments (Figure 6).

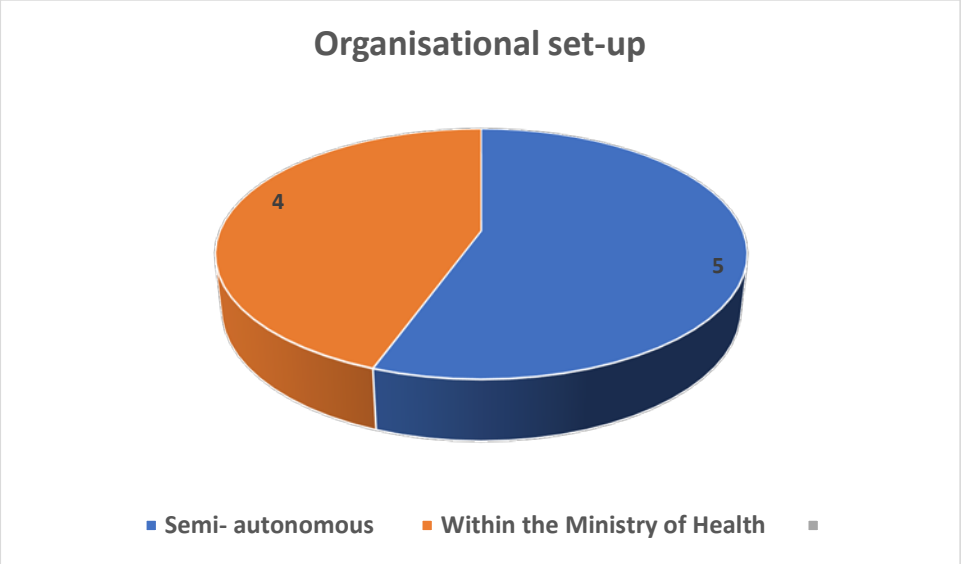

Figure 6: Analysis of organisational set-up

4.1.4.1.2. Legislative Framework

All NMRAs that responded had a legislation framework governing the regulation of medicines in their respective jurisdictions. The legal framework allows for effective implementation of policies and provide adequate powers to the NMRAs to execute their mandate of ensuring that medicinal products are safe, effective and of good quality. However, the Angola NMRA's legal framework is not yet officially formalised and as such, they follow a Presidential decree enacted in 2010, which include some aspects of regulation of medicines.

4.1.4.1.3. Year Enacted

The legislative frameworks to regulate medicines evolves over time due to the complex global supply chain of medicinal products across the globe. The findings from the consolidated responses from SADC NMRAs indicate that their legal frameworks are not static. The legislative frameworks were enacted in the years from 1965 (amended 2017; SAHPRA), 1981 (ACOREP), 1988 (amended 2019; PMRA), 1997 (MCAZ), 1998 (amended 2017; DNF), 2003 (amended 2019; TMDA), 2003 (NMRC), 2013 (amended 2018; BOMRA) and 2010 presidential decree (DMNE) for all NMRAs. The amendments of these laws indicate that SADC NMRAs are generally striving towards expanding their regulatory mandates and adapting to the complex regulatory landscape.

4.1.4.1.4. Regulatory Mandate / Functions

Regulatory scope and functions vary across the globe for NMRAs depending on their size and other resources such as human and financial resources. Ideally, NMRA should be able to cover all medicines regulatory functions. For example, matured agencies such as the US FDA have extended mandate to regulate Foods and tobacco products, whilst small agencies have limited scope and regulate only medicinal products. Six (6) of nine (9) NMRAs (67 %) in the SADC region reported to be performing all the regulatory functions listed in Figure 7. Interestingly, the three (3) NMRAs (33 %) that did not perform all regulatory functions as listed, were noted to be those NMRAs which are still operating under their Ministry of Health. Therefore, there is a need to study if policy reforms that will allow these NMRAs some level of flexibility and autonomy can be considered in order to expand their regulatory functions.

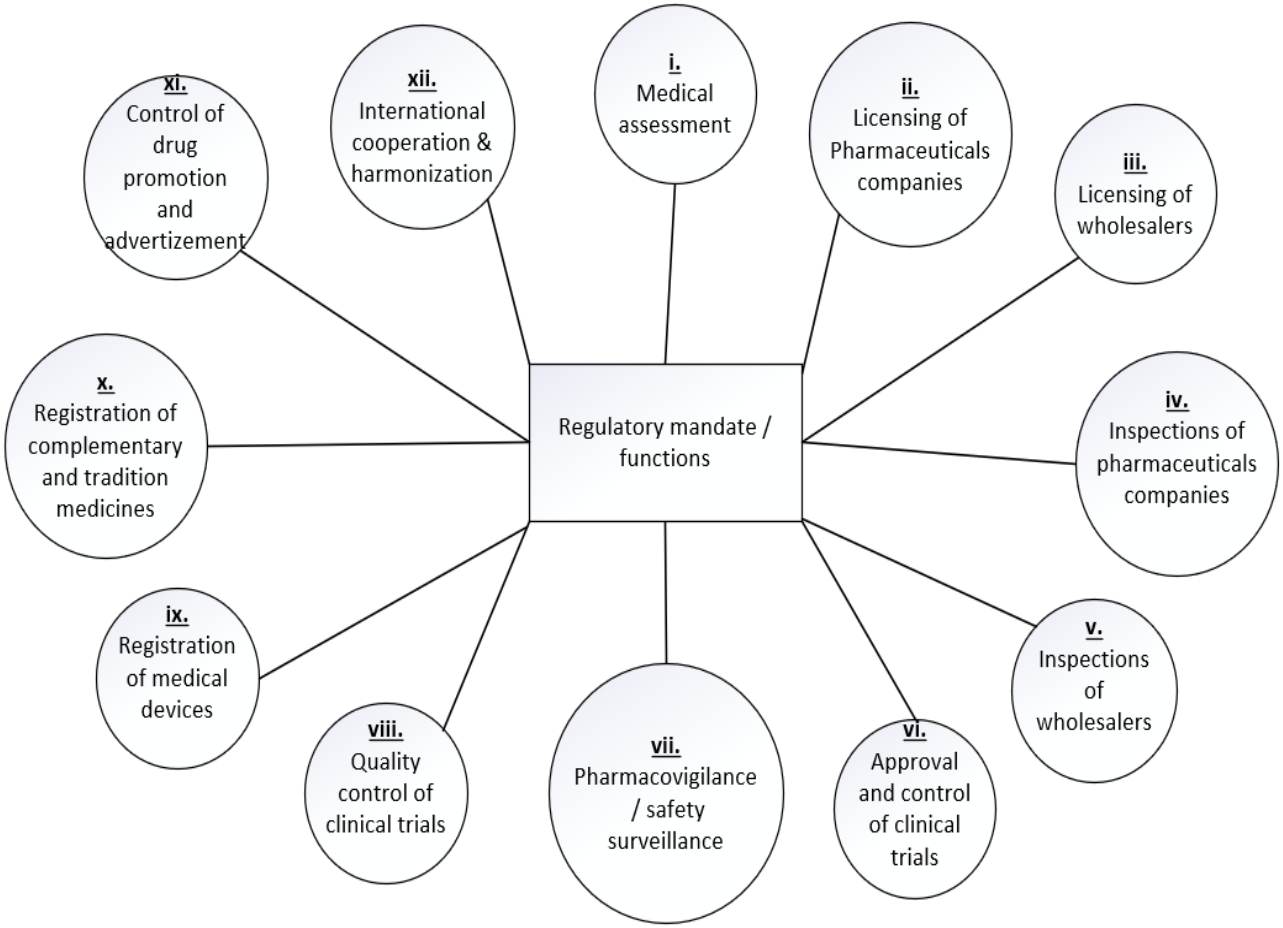

Figure 7: Regulatory mandate / functions comprising twelve (12) sub-themes as highlighted from this study.

DMNE of Angola reported the functions of medicines assessment and registration as well as approval and control of clinical trials as not applicable to them as it was indicated earlier that their legal framework is not yet officially formalised. NMRC reported not performing approval and control of clinical trials, as well as not participating in international cooperation & harmonization. DNF of Mozambique reported not performing registration of complementary and tradition medicines as well as control of drug promotion & advertisement. An overview of all the responses is presented in Table 5 of Appendix C.

4.1.4.1.5. Staff Complement

Human resource capacity is a critical factor to enable NMRAs in executing their public health mandate / functions. This study was limited to gauging the number of medicine assessors / evaluators both within the NMRAs and outside NMRAs (External / part time assessors). Four (4) of nine (9) NMRAs (44 %) reported to have more than 20 internal assessors / evaluators. This indicates a significant milestone for SADC NMRAs in terms of capacity building and the pool of evaluator / assessors could play a significant role towards realization of an African Medicines Agency (AMA). Literature also indicates that the EAC MRH initiative is planning to have a cadre of regional technical officers (RTOs) which could assist in the establishment of the AMA (Arik *et al.*, 2020).

DMNE of Angola, NMRC, DNF of Mozambique and PMRA of Malawi recorded to have less than 10 evaluators / assessors (both internal and external combined). This could be attributed to a general shortage of skilled labour force in these countries. For example, according to WHO Global Atlas of Health Workforce, in Angola (28.8 million people) the ratio of physicians per 1,000 population is 2.146 and the ratio of pharmacists is 0.49 per 10 000 population (WHO, 2018). Furthermore, a study by WHO (2010) on African NMRAs indicated that those NMRAs operating within their ministry of health are generally lacking flexibility and autonomy and are unable to employ and attract more personnel that are skilled. The size of the pharmaceutical market in these countries could also be a contributing factor towards these observed lower numbers of evaluators / assessors.

Five (5) of nine (9) NMRAs (56 %) reported to make use of external evaluator / assessors. From the five (5) NMRAs making use of external evaluators / assessors, SAHPRA (respondent no. 7) has the highest number of external evaluators / assessors. SAHPRA is also the only NMRA with the number of external evaluators / assessors exceeding that of the internal evaluators / assessors and it could be suggested that SAHPRA work on building much needed internal capacity to avoid too much reliance on external evaluators / assessors. However, due to the size of pharmaceutical market in South Africa, this may be seen as a positive aspect, indicating a pool of skilled personnel outside of SAHPRA available to assist the authority whenever they are required to do so. Respondents 2 (ACOREP), 5 (MCAZ), 6 (NMRC) and 9 (PMRA) stated that there were no external assessors in their respective agencies. As such these NMRAs are encouraged to consider making use of external assessors to bolster their human resource capacity, the same approach is being used globally by other NMRAs such as TGA, FDA, Singapore's Health Science Authority (HSA), and Turkish Medicines and Medical Devices Agency (TITCK).

A study by Mashaki *et al*., (2018) indicates that the TGA and HSA use external experts on an *ad hoc* basis. Moreover, the study stated that TITCK use 120 external experts as evaluators in addition to the internal experts. Farrell *et al*., (2006) indicates that the US FDA utilizes external expert consultants during dossier assessments to offer their scientific expertise and assist the agency in making science based decisions. All external consultants are required to declare any conflict of interests. The study further indicate that in Europe, although external consultants are used, the level of their involvement varies depending on the complexity of the evaluation. From the above, the use of a mixture of internal and external assessors is a well-established practice across the global regulatory landscape and therefore, ACOREP, MCAZ, NMRC and PMRA should consider formalising this in their agencies to complement the internal evaluators.

DMNE of Angola (respondent 3) reported to have the least number of evaluators / assessors with four (4) internal evaluators / assessors and two (2) external evaluators / assessors. This might be attributed to the absence of proper legislative framework as already indicated above and DMNE of Angola could work on establishing a legal framework to allow effective implementation and provide adequate powers to the NMRA. This will assist DMNE of Angola to be on par with its SADC counterparts in the near future. An overview of staff complement in terms of assessors / evaluators is presented in Figure 8.

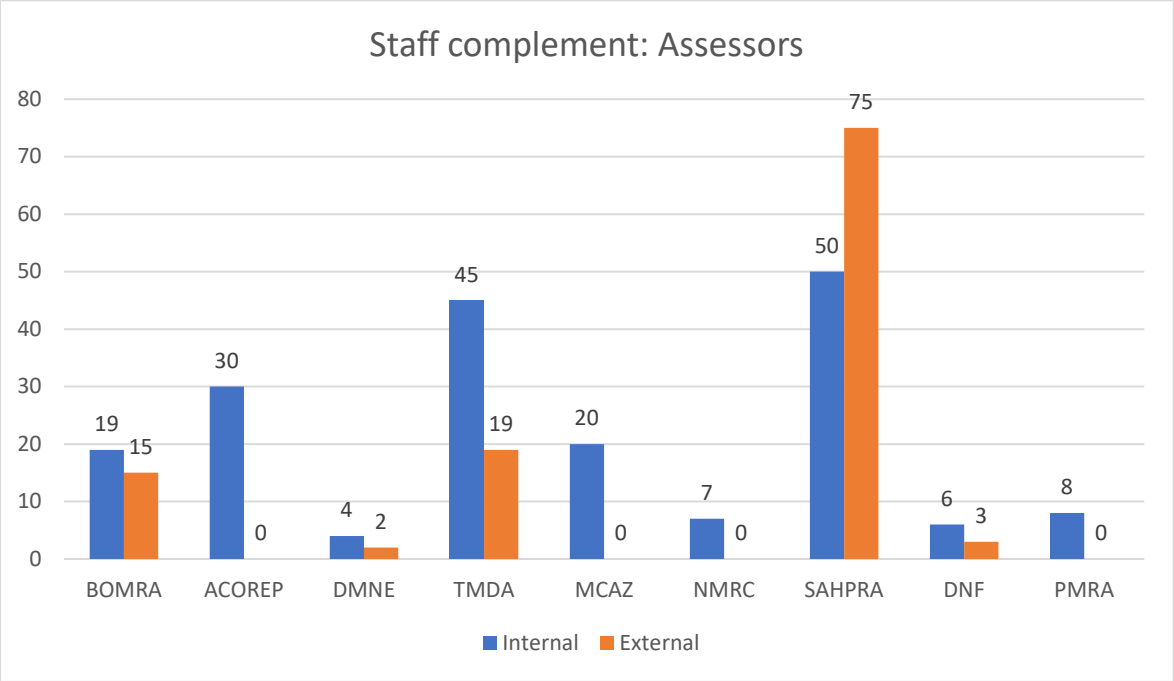

Figure 8: Overview of staff complement

4.1.4.1.6. Advisory / expert committees

A well functional regulatory system should have advisory / expert committees to advice on complex technical issues. Majority of NMRAs in this study indicated to have functional advisory / expert committees with the exception of DMNE of Angola and DNF of Mozambique, which stated that advisory / expert committees were not available in their respective agencies.

4.1.4.1.7. Clear conflict of interest policy

All nine (9) NMRAs indicated that they have a conflict of interest policies for both internal and external evaluators / assessors. Medicines regulation is a public duty by NMRAs to regulate pharmaceutical industry activities in order to ensure safety, efficacy and quality of pharmaceutical products. The availability of conflict of interest policies in all nine NMRAs is therefore an important step towards fairness, impartiality and transparency to all stakeholders, particularly by ensuring that all known and perceived conflicts of interest are recognized and appropriately managed.

4.1.4.1.8. Funding Sources

Various funding models are used across the globe to fund the activities and day-to-day operations of NMRAs. The study findings indicated that the SADC NMRAs are receiving funding from multiple sources ranging from a minimum of one to maximum of four funding sources. There were only two NMRAs, MCAZ and PMRA, that were not receiving funding from their governments. Seven agencies indicated that they receive funding from their governments. Only two agencies receive funding from industry and two agencies indicated receiving funding from donors. One interesting fact was that one agency (NMRC) only rely on government funding (Table 4). Furthermore, the findings indicate that SAHPRA is utilizing multiple sources of funding, which might be the reason why SAHPRA is able to employ a large pool of evaluators (both internal and external) compared to other SADC counterparts as demonstrated in Figure 8 above.

Medicines regulation is a public policy and therefore NMRAs should receive a major part of their funding from their governments as well as fees levied for service. Therefore, SADC NMRAs should guard against competing, or conflict of, interests that may exist if the majority of funding comes from donations and manufacturing companies. Industry funding could clearly create a conflict of interest and bias while donor funding, though well appreciated to establish a regulatory system, should never be used to sustain regulatory systems.

Table 4: Analysis of SADC NMRAs funding sources

Code (Name of NMRA)	Government	Fees levied	Industry	Donors
1 (BOMRA)	**X**	**X**		
2 (ACOREP)	**X**			**X**
3 (DMNE)	**X**			
4 (TMDA)	**X**	**X**		**X**
5 (MCAZ)		**X**		
6 (NMRC)	**X**			
7 (SAHPRA)	**X**	**X**	**X**	**X***
8 (DNF)	**X**	**X**	**X**	
9 (PMRA)		**X**		

*Did not indicate receiving donor funding for day to day operational functions, but received donor funding for Backlog project.

The budget for a matured NMRA such as the US Food and Drug Administration (US FDA) for the 2019 financial year was estimated at US$ 5.7 billion, 55 % of which (US$ 3.1 billion) was provided by the federal government and the remaining 45 % (US$ 2.6 billion) paid for by industry user fees. The FDA budget includes 17,599 full time equivalents (FTEs) (FDA, 2019). The Medicines and Healthcare products Regulatory Authority (MHRA; United Kingdom), on the other hand, derives its total income from licensing fees paid by the pharmaceutical industry (Lexchin, 2012). This model might however not be sustainable for SADC NMRAs due to the size of the pharmaceutical industry in the continent.

To attain effective, fair and transparent regulatory systems, SADC NMRAs will thus have to find a balance between Government funding as National resource and self-sustainability through fees for work / functions.

4.1.4.2. Transparency and communication parameters (Part B)

All regulatory authorities across the globe should strive towards improving their engagement with stakeholders. The engagements between regulators and their stakeholders is an on-going process throughout the product lifecycle management. To execute their mandates, regulators should be open, transparent, fair and responsive. The purpose of this section of the questionnaire was to establish whether SADC NMRAs have implemented all pre-established key transparency and communication parameters to enhance stakeholder relationships as stipulated in a study conducted by Keyter *et al*. (2019).

Table 6 in Appendix C represents the study findings of key transparency and communication parameters from all nine SADC NMRAs. The study results indicates that TMDA is publishing PARs or summary of grounds on which approvals are granted. This demonstrates a significant level of transparency in the TMDA processes and therefore other SADC NMRAs can benchmark with TMDA to implement this key parameter. Literature indicate that publication of the summary basis of approval (PARs) is a norm for mature NMRAs, acts as a tool for regulatory authorities to build and establish confidence in the review process and provide assurance regarding safety of medicines (McAuslane *et al*., 2009). From the ten (10) transparency and communication parameters, TMDA implemented nine (9) of ten (10), with the only exception being that the meeting dates of their advisory committees are not made

publicly available. MCAZ, NMRC and SAHPRA all implemented eight (8) out of ten (10) transparency and communication parameters. The remaining NMRAs have three (3) to five (5) transparency and communication parameters not implemented by their agencies.

Based on the results presented in Table 6 of Appendix C, it can be concluded that the majority of SADC NMRAs should enhance their stakeholder engagement frameworks in order for them to be more transparent and responsive. Recently SAHPRA published a document called SAHPRA Stakeholder Engagement Framework, which provide detailed information on how the agency is planning to improve its communication with stakeholders going forward (SAHPRA, 2020). Other SADC NMRAs are encouraged to have similar strategies publicly available to improve stakeholder relations.

4.1.4.3. Core of the Study (Part C) - ability to generate and publish PARs.

This section formed the core of the study and contain the main research question as well as follow-up questions to allow for a valuable assessment of SADC NMRAs, particularly with regard to their ability to generate and publish PARs. The purpose of this section of the questionnaire was thus to establish whether SADC NMRAs have a PARs / Summary basis for registration that is publicly available for the purpose of transparency in medicines registration decision making within their agencies. A thematic analysis method was used to assess the transparency in medicines registration as highlighted in Figure 9.

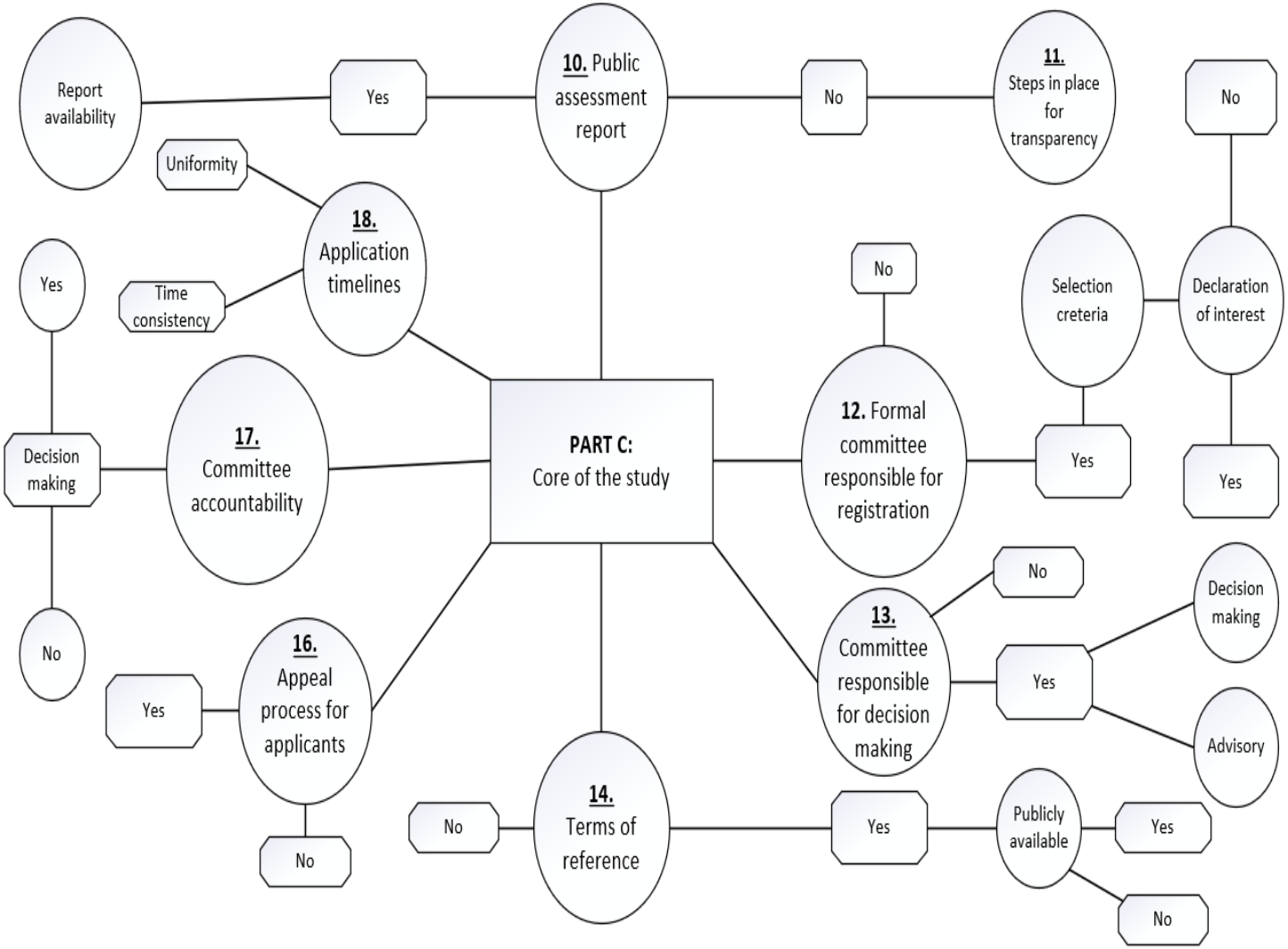

Figure 9: Core of the study – ability to generate and publish PARs and themes developed from that

4.1.4.3.1. Availability of Public Assessment Reports (PARs) within SADC NMRAs

A primary research question was asked to assess the availability of PARs within SADC NMRAs and if these reports are publicly available. Only one (1) respondent, TMDA (respondent no. 4), confirmed that such reports exist in their agency and was made publicly available on their agency's website. The respondent (TMDA) further stated that:

> "*…these reports (internally referred to as TPAR's) are published in the website. Initially we have started with publication of SmPC's.*"

All remaining eight (8) respondents indicated that their agencies are currently not in a position to generate and publish PARs / Summary basis for registration.

Respondent no. 7, SAHPRA, outlined that their agency has a process as indicated below:

> "*Currently SAHPRA does not have public assessment reports. But there is a process of making our assessments reports public, by indicating our basis of registration of the process.*"

A response from respondent no. 8, DNF, on the other hand indicated the future plan of their agency:

> "*NO. But we have in our agenda and we planned to publish in 2021*."

From the literature in chapter two (2), matured regulatory authorities such as EMA), US FDA, Health Canada and TGA all publish information relating to their evaluation of medicines *via* PARs, as part of their commitment to transparency (Papathanasiou *et al*., 2016). Therefore, based on the study findings it can be concluded that NMRAs within the SADC region are not matured as compared to those in the developed world. The majority of SADC NMRAs are currently not generating and publishing PARs with the exception of TMDA of Tanzania. Consequently, literature states that Tanzania's NMRA recently became the first in Africa to attain World Health Organisation (WHO) maturity level 3 in December 2018 (Sillo, 2019). Maturity level 3 indicates a stable, well functioning, and integrated regulatory system (Arik *et al., 2020*). For these reasons, it's not surprising that TMDA is the only SADC agency that is able to generate and publicly publish TPARs on their website.

The study therefore, recommends that all other SADC NMRAs should benchmark with TMDA of Tanzania in order for them to implement this key transparency parameter and to enable them to achieve WHO maturity level 3 and 4 status.

4.1.4.3.2. Steps in place to ensure transparency in medicines registration decision-making

A follow up question from the main research question was asked to provide for a broader overview of steps in place to ensure transparency in medicines registration decision-making, particularly for those NMRAs that indicated that they do not have PARs / Summary basis for registration in their agencies. TMDA did not respond to this question as they indicated that they do have TPARs in their agency. From the questionnaire responses, there were diverse responses from respondents as is outlined below:

Respondent's no. 1 (BOMRA) and 6 (NMRC):

> "*The NRA has a process in place where the application is assessed by two different people before being tabled to the department for peer review. The final report from the review is tabled at the Registration committee and the registered products are published*"

> "*Assessment reports are peer reviewed before finalization and all products to be registered go through advisory committees then to the Council for the final decision."*

Respondent no. 2 (ACOREP):

> "*We do not have a public assessment report so far, but we manage to inform the applicant regarding all issues raised after assessment through a letter and copies send to the permanent secretary and to the health ministry*"

Respondent no. 3 (DMNE):

> "*Just from the question number 10, the NMRA does not register the medicine yet for those who are imported to Angola because of lack of a legal authorization. It seems that, to make a scientific decision the NMRA goes throughout to the ICH guidelines, WHO, SADC, EMA etc.*"

Respondent no. 5 (MCAZ):

> "*The Authority first issues an intent to approve or intent to refuse registration before products are approved or rejected. The applicant has a chance to respond to the intent before the final decision is issued. The refusal letter clearly states the reasons for refusal Registers of approved products are published on the MCAZ website and in the Government Gazette.*"

Respondent no. 7 (SAHPRA):

> "*SAHPRA does not have public assessment reports. However, there is a process of making our assessments process transparent, by using a peer-review mechanism. Moreover, currently a registrar of all registered products and their Professional Information (PI) are publicly available on the SAHPRA website.*"

Respondent no. 8 (DNF):

> "*…we have in our agenda and we planned to publish in 2021. We have our website and every month we publish the status of the products; We have internal guidelines with the timelines of registrations process; The applicants can approach DNF to request the status of products.*"

Respondent no. 9 (PMRA):

> "*Following registration of the medicines, the list of registered medicines is updated. There is currently no formal procedure for making that information publicly accessible to the general public except the updated list of registered medicines. (It should be noted that the Authority is currently in a transition period from what used to be the Pharmacy, Medicines and Poisons Board (PMPB). The transition includes the process of developing regulations and guidelines to be in line with the expanded scope of the newly enacted Pharmacy and Medicines Regulatory Authority Act. The old Act which the PMPB derived its powers from was enacted in 1988 and it did not cover a lot of regulatory areas).*"

From the above responses, it can be concluded that BOMRA, MCAZ, SAHPRA DNF and PMRA publish a list of registered medicines on their websites as an effort to enhance transparency in medicines registration decision-making processes within their agencies. In addition, SAHPRA publishes Professional Information (PI) of their registered products. Furthermore, it was noted that BOMRA, NMRC and SAHPRA are utilizing their internal peer review mechanism to ensure transparency in medicines registration decision making. Interestingly, DMNE indicated that they currently do not register medicines due to lack of legal framework as they rely on a 2010 presidential decree. Lastly, PMRA indicated that there are reforms in their legal framework to expand their mandate in order to cover many regulatory areas. Therefore, all these eight (8) NMRAs should benchmark with TMDA, as already recommended above, to improve their efforts towards transparency in their medicines registration decision-making processes.

4.1.4.3.3. Availability of formal committees responsible for medicines registration

Expert committees play critical roles within the medicine regulatory landscape. These committees can either operate as advisory committees or be involved in the decision-making processes of the regulators, depending on the individual operating models of the agencies. The committees should comprise experts from diverse educational background. Eight (8) respondents out of nine (9) clearly indicated that there are formal committees responsible for

medicine registration (89%) in their agencies with the exception on DNF. Interestingly, Respondent no. 8 (DNF) stated that:

> "*At the beginning of the registration process, there was a committe called CTRM that was responsible for issuing opinions for the approval of the registration, however in 2016, with the update of our guidelines, there was a need to extinguish that commission because majority of member no longer work at DNF. But and a an internal organization process to create the new commission that is expected to take effect next year*."

The results demonstrate that SADC NMRAs do recognize the importance of having these formal committees to instil credibility and confidence in the regulatory decision-making. From the eight (8) respondents; five (5) pointed out that their formal committees are involved in regulatory decision making, while three (3) respondents indicated that their formal committees are only available to offer advisory service but are not involved in the operations or decision making processes of the agencies. All eight agencies indicated that Terms of Reference (TOR), which describe the purpose of the committees, its processes and duration are available within their respective NMRAs.

Since the majority of these expert committees' members are external people, not permanently employed by the agencies, and some employed in the private sector, various competing interest may exist. The data indicate that all eight (8) agencies with committees have conflict of interest policies in place for their formal committees. Therefore, the availability of conflict of interest policies in all nine NMRAs is an important step towards fairness, impartiality and transparency to all stakeholders. It was also noted that these committees report to the boards, councils, director generals in the ministry of health or unit managers depending on the operational model of the agency.

4.1.4.3.4. Availability of an appeal process for rejected applications.

To enhance stakeholder relations, appeal processes should be in place for regulatory authorities to promote fairness and afford applicants the opportunity to present their case. Registration of medicines is based on a risk-based approach, supported by science, and literature states that the current process of benefit–risk assessment of medicines relies primarily on intuitive expert judgment. Therefore, there is a clear need for

standardization of frameworks and guidelines to ensure transparent and defensible decision-making that benefits patients, drug developers, and decision makers (Coplan *et al.*, 2011). Table 6 in Appendix C indicates that six (6) out of nine (9) SADC NMRAs (67 %) have appeal process in place, the exceptions being ACOREP, DMNE and DNF. The following comments were noted from some of the respondents as outlined below:

Respondent no. 1 (BOMRA) said:

> "*Applicants may appeal decision made by the Committee to the Board; Board decision may be appealed to the Appeals Committee under the Ministry of Health, although the Appeals Committee is still to be formed.*"

Respondent no. 4 (TMDA):

> "*Yes, there is an appeal process prescribed in the law and regulations of medicines registration*"

Respondent no. 6 (NMRC):

> "*Yes, in terms of section 34 of the Medicines and Related Substances Control Act, 2003 (Act 13 of 2003).*"

Respondent no. 7 (SAHPRA):

> "*Yes, the appeal process is there. Where SAHPRA is obliged to indicate the reasons for rejection and the applicant is also allowed to indicate why they the rejection must be reversed. The rejection must be based on science, SAHPRA and global regulatory guideline (ICH). Supported by section 24A (3) of the medicines and related substances control Act (Act 101 of 1965, as amended) and regulation 48 to the Act.*"

Both MCAZ and PMRA indicated that they have appeal process in their respective agencies.

In contrast, Respondent no. 2 (ACOREP) indicated that:

> "*The write down appeal procedure does not exist however the applicants are free to appeal.*"

Respondent no. 8 (DNF):

> "*Currently, we do not have rejected drugs but cancelled for the following reasons: Lack of responses for LOQ's feature. Non-import of products for 2 years after authorization*"

Respondent no. 3 (DMNE) stated that the appeal process for applicants who have their medicine applications rejected was not applicable to their agency.

4.1.4.3.5. Consistency in registration timelines from application to application.

Consistency in registration timelines from application to application is crucial within the regulatory landscape, as it provides predictability in the regulatory processes and thereby improves stakeholder relations. Furthermore, this ensure fairness in the regulatory processes. The responses below reflect answers that were received from questionnaires returned. All the respondents responded uniquely to the question about the consistency in registration timelines from application to application.

Respondent no. 1 (BOMRA):

> "*The timelines are published to applicants and are consistent. They are in line with the assessment pathways adopted by the authority. And all the pathway is made public to the applicants. These are not always the same based the quality of submissions.*"

Respondent no. 2 (ACOREP):

> "*It depends case by case: for the normal submission at level country the timelines are uniform (first in first out) but we have also other submissions under Zazibona process, WHO-CRP, emergency (Ebola, Covid-19 and other orphan diseases medicines) for these kinds of submission it is different*"

Respondent no. 3 (DMNE):

> "*Once the registration process starts it will work as SADC member states.*"

Respondent no. 4 (TMDA):

"*Yes, and the same are outlined in the Clients Service Charter which is a public document.*"

Respondent no. 5 (MCAZ):

"*We have different review pathways which include expedited review and WHO PQ collaborative procedure. Timelines are uniform for each review pathway.*"

Respondent no. 6 (NMRC):

"*To a certain extent, yes but because we use various pathways of registration, it may not be uniform from application to application.*"

Respondent no. 7 (SAHPRA):

"When dossier is allocated for evaluation, the person allocating this, tells the internal or external evaluator of the due date of the reports. The timeline depends on the nature of the application. For example, generics with (e.g. tablets) or without bioequivalence data (e.g. injectable) and also the new chemical entity with clinical data."

Respondent no. 8 (DNF):

"*complete registration – 1 year, abbreviated registration – 9 months, mutual recognise/collaborative process(who/sra) – 3 months, zazibona process-"*

Respondent no. 9 (PMRA) simply stated that their timelines are not consistent from application to application without elaborating further.

From the above findings, it can be concluded that SADC NMRAs registration timelines are dictated by variety of factors such as; the review pathway employed e.g. full review, abridged or verified review ; the complexity of the molecule under review e.g. generic or new chemical entity and emergency reviews or fast tracked reviews e.g. emergency vaccines during pandemics. Therefore, it becomes very difficult to have fixed timelines from application to application, but some form of commitment as seen in the TMDA Clients Service Charter could go a long way towards improving stakeholder relations.

4.1.4.4. Conclusion

This chapter presented the results of the demographics of the respondents, followed by the analysis of all three constructs. The questionnaires were analysed and presented according to the research objectives as indicated in Chapter One. Key issues found from the questionnaire were grouped as follows:

- Organizational Structure
- Transparency and communication parameters
- Core of the study - ability to generate and publish PARs.

The data collected for the purpose of this study has allowed for a valuable comparison between SADC NMRAs. A number of conclusions was reached and recommendations can be provided and is included in the next Chapter. These inform areas of improvement that may be considered by SADC NMRAs to enhance the transparency in their decision-making processes towards their stakeholders.

Chapter Five

5.1. Summary and Conclusion

The objectives of the study was to investigate whether NMRAs within the SADC region have public assessments reports for their scientific basis of accepting or rejecting registration of medicinal products; To investigate, if those public assessments reports / summary basis for registration are publicly available for the purpose of transparency; To investigate if all SADC NMRAs have fully implemented key transparency and communication parameters to enhance stakeholder relations; To establish if all SADC NMRAs have legislative frameworks for regulating medicines; To investigate the sources of funding for SADC NMRAs. Lastly, to identify discrepancies and offer possible recommendations to assist SADC NMRAs in achieving World Health Organisation (WHO) maturity level 3 and 4 status as defined in the WHO Global Benchmarking tool for National regulatory systems (WHO, 2018). The summary and conclusion on three key themes are presented below.

5.1.1. Organizational Structure

All SADC NMRAs have legislative framework governing the regulation of medicines. The legal framework allows for effective implementation of policies and provide adequate powers to the NMRAs to execute their mandate. The assessment of staff complement in these NMRAs demonstrated that DMNE of Angola, NMRC, DNF of Mozambique and PMRA of Malawi have less than 10 evaluators / assessors (both internal and external combined); this could be linked to their organizational set up as they are all still operating within their ministry of health with the exception of PMRA which is currently undergoing reforms to expand its scope. Furthermore, study by WHO (2010) on African NMRAs indicated that those NMRAs operating within their ministry of health are lacking flexibility and autonomy and therefore are unable to employ and attract more personnel that are skilled. It could thus be recommended that these NMRAs should consider reforms that will allow them to operate outside their ministry of health. BOMRA, MCAZ, PMRA, SAHPRA and TMDA are currently operating as semi-autonomous agencies.

The use of external evaluators is a globally accepted phenomenon employed by the matured NMRAs and a mixture of internal and external assessors is a well-established practice across

global regulatory landscape. ACOREP, MCAZ, NMRC and PMRA, who reported that their agencies are not using external assessors, could thus consider formalising this in their agencies to supplement their human resource capacity. Only five (5) of nine (9) NMRAs (56 %) reported to make use of external evaluator / assessors and of these five NMRAs, SAHPRA is the only NMRA with the number of external evaluators / assessors exceeding that of the internal evaluators / assessors and it could be suggested that SAHPRA work on building much needed internal capacity to avoid too much reliance on external evaluators.

All nine (9) NMRAs indicated that they have a conflict of interest policy for both internal and external evaluators / assessors. This is an important step towards fairness, impartiality and transparency to all stakeholders.

SADC NMRAs are receiving funding from multiple sources ranging from a minimum of one to maximum of four funding sources. Among the SADC NMRAs, interestingly MCAZ and PMRA indicated that they are not receiving funding from their governments. As medicines regulation is a public policy, NMRAs should receive a major part of their funding from their governments and from fees levied for service for their healthy sustainability. It is also clear that SADC NMRAs should avoid dependence on donations and industry funding, as it is unsustainable and could create a conflict of interest or bias.

Majority of NMRAs in this study have functional advisory / expert committees with the exception of DMNE of Angola and DNF of Mozambique. These committees provide scientific advice on complex technical issues and will in turn add value, build confidence and quality in their regulatory processes.

Six (6) of nine (9) NMRAs (67 %) in the SADC region perform all the regulatory functions listed in Figure 7 while the three (3) NMRAs (33 %) operating under their Ministry of Health did not perform all regulatory functions as listed. Once again, the need of policy reforms that will allow these NMRAs some level of flexibility and autonomy can be considered in order to expand their regulatory functions as recommended above.

5.1.2 Transparency and communication parameters

From the ten (10) transparency and communication parameters; TMDA implemented nine (9) of ten (10) while MCAZ, NMRC and SAHPRA all implemented eight (8) out of ten (10) transparency and communication parameters. Only TMDA is able to publish summary of grounds on which approvals are granted. This demonstrates a significant level of transparency in the TMDA processes and therefore other SADC NMRAs can benchmark with TMDA to implement this key parameter. The majority of SADC NMRAs should thus reform their stakeholder engagement frameworks in order for them to be more transparent and responsive.

5.1.3 Core of the study - ability to generate and publish PARs.

There is a perception that multisource generic medicines are inferior / sub-therapeutic compared to their innovator counterparts even though these generic medicines undergo a rigorous evaluation by regulatory authorities before they are allowed to be marketed. Moreover, New Chemical Entities (NCE) seeking regulatory approval also undergo the same rigorous regulatory evaluation standards to affirm their safety, efficacy and quality. The findings indicate that of the nine (9) SADC NMRAs under study, TMDA generate and publish PARs, called TPARs, on their agency website. TMDA was also the first NMRA in Africa to attain World Health Organisation (WHO) maturity level 3 status (Sillo, 2019).

Most of the remaining SADC NMRAs currently publish only lists of their registered products. This is not enough to inspire confidence in their regulatory decision making processes and it indicates that there is little transparency on how decisions are made within the majority of SADC NMRAs. Therefore, SADC NMRAs should invest resources and work towards attaining this key transparency parameter of generating and publishing their PARs. Ultimately, these in conjunction with implementation of other critical regulatory functions will improve their chances of attaining World Health Organisation (WHO) maturity level 3 and 4 status. One way to do this maybe through benchmarking with TMDA processes using exchange programmes or fellowships, were officials from other SADC NMRAs spend some time at TMDA and learn how PARs are generated. Alternatively, this can be initiated at regional platforms such as ZaZiBoNa first and once enough experience is gained, then implemented at country level.

PARs has the ability to demystify and alleviate misconceptions that exist between innovator products and generic products. Particularly, because PARs contains much more detailed scientific information, including communications between the regulator and the applicants, as well as timelines from initial submission dates to approval dates. Therefore, publicly available PARs will assist not only the applicants but also the patients to have a better insight into regulatory decision-making processes. Consequently, this will empower patients together with their healthcare professionals to make informed decisions regarding their medicines.

For industry stakeholders, availability of such information will ensure that they have confidence and deeper understanding of the regulatory decision-making processes, assisting them in improving their future submissions. Open, fair and transparent processes may also significantly reduce court litigations between industry stakeholders and regulators. Further studies with a greater focus on stakeholder's perspective are however recommended, to have a broader understanding of what they want to see regulators doing for the purpose of transparency.

In conclusion, the study has shown that SADC NMRAs are committed to transparency in their endeavour to regulate and control medicinal products in their jurisdictions, although the majority of them are not yet publishing their summary of grounds on which approvals are granted with the exception of TMDA of Tanzania. However, all NMRAs have implemented more than 50 % of all other key transparency and communication parameters (Table.6 of Appendix C). These include parameters such as availability of guidelines, provision of feedback to industry on submitted dossiers, ability of applicants to track the status of their applications as well as publishing a list of approved products. In this context, the study was able to achieve its objective as stated in chapter one.

5.2. Possible Strategies and Recommendations

The purpose of the research was to investigate transparency in medicines registration decision-making processes for NMRAs within the SADC region, specifically the availability or non-availability of Public Assessments Reports / Summary basis for registration of medicinal products. The study, through the questionnaire responses, has highlighted some gaps that exist amongst SADC NMRAs with regards to transparency and decision-making processes and the following recommendations may be considered by SADC NMRAs in order to enhance transparency in their decision-making processes:

- **Legislative reforms in SADC NMRAs**
  Some SADC NMRAs especially those that are still operating within their ministry of health (Figure 6) should consider undergoing legislative reforms to allow for a greater flexibility and autonomy, change their operating model, expand their mandate and build internal capacity.
- **Publication of summary of grounds on which approvals are granted**
  All SADC NMRAs with the exception of TMDA should consider implementing this key transparency parameter to enhance transparency in their evaluation processes in order to instil confidence and improve their WHO maturity status. Furthermore, all SADC NMRAs should consider implementing all the transparency and communication parameters as shown in Table 6 Appendix C, to enhance their stakeholder relations.
- **Build technical capacity**
  SADC NMRAs should consider building technical staff capacity for assessors. ACOREP, MCAZ, NMRC and PMRA should also consider making use of external assessors (See Figure 8) to expand their capacity. This is seen as a more flexible option, as external assessors can be used on an *ad hoc* basis.
- **Sign African Model Law towards implementation of African Medicine Agency (AMA)**
  All SADC member states should consider becoming signatories of African Model law in order to ensure that the African Union dream of implementing an African Medicines Agency become a reality. The AMA will operate with and almost similar operational model as the current EMA, therefore providing several advantages to Africa. These would result in an increase in local production, provide single market, reduced fragmentation, improved harmonization and regulatory convergence, ensuring quick market access to much needed therapeutics.

- **Ensure consistency in registration timelines from application to application**
  All SADC NMRAs should consider standardizing their review processes across the board depending on the type of review processes employed to ensure fairness, predictability and consistency in registration timelines from one application to the next.
- **Hold regular meetings with manufacturers and other stakeholders**
  Regular meetings with all stakeholder will foster a culture of partnership and co-operation, which will enhance stakeholder relations and encourage transparency.

Though this study focussed on regulatory transparency in decision-making and confidence in SADC regulatory processes, it has highlighted several gaps and needs that will have to be addressed to ensure robust but fair and transparent medicine regulatory systems in the SADC region and Africa. It has also identified multiple areas for further study and development and only with clear information on the interrelated aspects influencing regulatory efficiency and transparency will the required regulatory maturity be possible.

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Appendices

Appendix A Study Questionnaire

Respondent details Name: Designation: Name of the Agency: Years in the Agency: Date:					
PART A: Organizational Structure					
1	*Organisational set-up(please tick applicable one)*	Within the Ministry of Health		Semi-autonomous	
2	*Legislative Framework to regulate medicines(please tick applicable one)*	Available		Not Available	
3	*Year Enacted*				
4	*Regulatory Mandate / functions (please tick applicable one)*				
				Yes	No
i.	Medicines assessment and registration				
ii.	Licencing of pharmaceutical companies				
iii.	Licencing of wholesalers				

iv.	Inspections of pharmaceutical companies				
v.	Inspections of wholesalers				
vi.	Approval and control of clinical trials				
vii.	Pharmacovigilance /safety surveillance				
viii.	Quality control laboratory				
ix.	Registration of medical devices				
x.	Registration of complementary and tradition medicines				
xi.	Control of drug promotion & advertisement				
xii.	International cooperation & harmonization				
5	*Staff complement*				
	How many assessors (Internal) does your NMRA have?				
	How many assessors (External) does your NMRA have?				
6	*Advisory/expects committees(please tick applicable one)*	Available		Not Available	
7	*A clear conflict of interest policy for both internal and external staff members(please tick applicable one)*	Available		Not Available	
8	*What is/are the source/s of funding for your NMRA (please tick all that apply):* ▫ Government ▫ Fees levied by the NRA ▫ Industry ▫ Donors ▫ Other (please specify) _____				

PART B: Transparency and communication parameters			
9	*Key transparency parameters in regulatory decision making*		
		Yes	No
	Feedback to industry on submitted dossiers		
	Details of technical staff to contact readily available		
	Pre-submission scientific advice to industry		
	Official guidelines to assist the industry		
	Industry can track progress of applications		
	Publication of summary of grounds on which approval was granted		
	Appeal process available		
	List of approved products made public		
	Advisory committees meeting dates publicly available		
	Does the drug registration process have an information system?		
PART C: Core of the study			
10	Does your NMRA have a public assessment report for the scientific basis of accepting or rejecting registration of medicinal products? If yes, is this public assessments reports/summary basis for registration made public for the purpose of transparency?		

11	If the answer to question 10 above is No, you can briefly explain what steps does your NMRA have in place to ensure transparency in medicines registration decision making?
12	Is there a formal committee responsible for medicines registration? If yes, what criteria are used for selecting committee members?
13	Is the committee responsible for decision making or does it act in an advisory capacity?

14	Do terms of reference exist which describe the purpose of the committee, its processes, duration, etc.? And, if so, are these available publicly?
15	Are members of the committee or any other officials involved in the medicine registration process formally required to declare any conflict of interest?
16	Is there an appeal process for applicants who have their medicine applications rejected?
17	Who does the committee report to and is this person responsible for making the final decision?
18	Are the timelines from application to decision making uniform from application to application? Consistency in registration time across?

Thanks for taking your precious time to complete this questionnaire.

Appendix B Information sheet and Consent form

FACULTY OF NATURAL SCIENCES
Private Bag X17 Bellville 7535
Telephone +27 21 9592190
Fax +27 21 9593407
09 July 2020

Information Sheet and Consent to Participate in Research

Date: 09 July 2020

Greeting: Dear sir/madam.

My name is Mphako Brighton Ratlabyana from the School of Pharmacy, Faculty of Natural Sciences at the University of the Western Cape.

You are being invited to participate in a study that involves research: Transparency in medicines registration decision making: A closer look at National Medicines Regulatory Authorities (NMRAs) within the Southern African Development Community (SADC) region.

This study aims to find out (1) If NMRAs within the SADC region have public assessment reports for their scientific basis of accepting or rejecting registration of medicinal products; (2) To investigate if those public assessment reports/summary basis for registration are publicly available for the purpose of transparency. The 11 regulatory authorities selected to participate were selected based on their ability to issue Marketing Authorization (MA). To obtain a high number of responses, the questionnaires will be emailed and/or handed out at one of the Zazibona meetings where almost all 16 SADC members state will be meeting.

Consent forms and questionnaire transcripts will be kept confidential and only anonymized and combined responses will be available on request. The study will provide no direct benefits to participants, but based on the findings, the study will provide recommendations to SADC NMRAs in order to improve their overall performance.

Participation in this research is voluntary and participants may withdraw participation at any point, and in the event of refusal/withdrawal of participation the participants will not incur any penalty or loss benefit to which they are normally entitled. No costs will be incurred by participants as a result of participation in the study.

No clinical or confidential information will be collected or disseminated.

This study has been ethically reviewed and approved by the UWC Biomedical Research Ethics Committee (approval number: BM20/5/10).

In the event of any problems or concerns/questions you may contact the researcher at +27 73 015 9543 or brighty@homemail.co.za/ Mphako.ratlabyana@sahpra.org.za/ 3985182@myuwc.ac.za.The Director of the School of Pharmacy at the address or telephone number in the letterhead above, or the UWC Biomedical Research Ethics Committee, contact details as follows:

BIOMEDICAL RESEARCH ETHICS ADMINISTRATION
University of the Western Cape Research
Office
New Arts Building
C-Block, Top Floor, Room 28.
Western Cape, SOUTH AFRICA
Tel: 27 21 959 2948/49/88
Email: info@uwc.ac.za

CONSENT

I (Name and Surname) have been informed about the study entitled 'Transparency in medicines registration decision making: A closer look at National Medicines Regulatory Authorities (NMRAs) within the Southern African Development Community (SADC) region'. by Mphako Brighton Ratlabyana.

I understand the purpose and procedures of the study.

I have been given an opportunity to ask questions about the study and have had answers to my satisfaction.

I declare that my participation in this study is entirely voluntary and that I may withdraw at any time.

If I have any further questions/concerns or queries related to the study, I understand that I may contact the researcher at 073 015 9543 or brighty@homemail.co.za /Mphako.ratlabyana@sahpra.org.za/ 3985182@myuwc.ac.za.

If I have any questions or concerns about my rights as a study participant, or if I am concerned about an aspect of the study or the researchers then I may contact:

BIOMEDICAL RESEARCH ETHICS ADMINISTRATION
University of the Western Cape Research
Office
New Arts Building
C-Block, Top Floor, Room 28.
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_____ _____
Signature of Participant **Date**

_____ _____
Signature of Witness **Date**
(Where applicable)

_____ _____
Signature of Translator **Date**
(Where applicable)

Appendix C Tables from questionnaire responses.

Table 5: Regulatory mandate / functions respondents' responses

Code (Name of NMRA)	Medicines assessment and registration	Licencing of pharma-ceutical companies	Licencing of wholesalers	Inspections of pharmaceutical companies	Inspections of wholesalers	Approval and control of clinical trials	Pharmaco-vigilance / safety surveillance	Quality control laboratory	Registration of medical devices	Registration of complementary and tradition medicines	Control of drug promotion & advertisement	International cooperation & harmonization
1 (BOMRA)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2 (ACOREP)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
3 (DMNE)	N/A	Yes	Yes	Yes	Yes	N/A	Yes	Yes	Yes	Yes	Yes	Yes
4 (TMDA)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
5 (MCAZ)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
6 (NMRC)	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No
7 (SAHPRA)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
8 (DNF)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes
9 (PMRA)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Table 6: Transparency and communication parameters in the nine SADC NMRAs

Code (Name of NMRA)	Feedback to industry on submitted dossiers	Details of technical staff to contact readily available	Pre-submission scientific advice to industry	Official guidelines to assist the industry	Industry can track progress of applications	Publication of summary of grounds on which approval was granted	Appeal process available	List of approved products made public	Advisory committees meeting dates publicly available	Does the drug registration process have an information system?
1 (BOMRA)	Yes	Yes	Yes [a]	Yes	Yes[b]	No	Yes	Yes	No	No [c]
2 (ACOREP)	Yes	Yes	No	Yes	Yes	No	No	Yes	Yes	Yes
3 (DMNE)	Yes	Yes	Yes	Yes	NA	No	No	Yes	No	No
4 (TMDA)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
5 (MCAZ)	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes
6 (NMRC)	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes[d]
7 (SAHPRA)	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes
8 (DNF)	Yes	No	No	Yes	Yes	No	No	Yes	No	Yes
9 (PMRA)	Yes	No	Yes	Yes	No	No	Yes	Yes	No	No[e]

a, Applicants are always assisted whenever they need clarification; b, Though there's no system but via email enquiries; c, If this refers to IT system then no, otherwise we have a manual system; d, but not fully functional; e, There is some form of system in form of excel that tracks products applied for registration from within Secretariat.