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SAHPRA - Relevance of the New South African Health Products Regulatory Authority and Opportunities Ahead

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Abstract

Regulatory environments are constantly evolving, and South Africa has witnessed some significant developments in the recent past. Operational launch of the South African Health Products Regulatory Authority (SAHPRA) as new healthcare products regulator marks a key milestone in the establishment of international standards in regulatory practices. Both the Medicines Control Council (MCC) and the Directorate of Radiation Control (DRC) were replaced by SAHPRA to bring control of medicines, medical devices, *in vitro* diagnostic tests and devices, and radiation emitting products under one regulatory body. The new agency was instituted under schedule 3A of Public Finance Management Act as public entity, thereby enabling it to retain the revenue generated. The change has evidently impacted the regulatory practices positively; however, the challenges inherited by regulators and those regulated are enormous. SAHPRA needs to confront the challenges and make the most out of the opportunities ahead. This study aims to focus on understanding the new agency, its evolution over time, objectives set forth, organizational and operational construct, responsibilities, accomplishments so far, outstanding challenges, opportunities ahead, and the collaborative efforts that can support its operation. SAHPRA has had noteworthy achievements as a healthcare products regulator. By making most use of collaboration efforts SAHPRA is all set to work through the challenges and gain from opportunities.

Keywords: SAHPRA, South Africa, MCC, challenges, opportunities, collaboration, coordination

1. Introduction

The regulatory environment in South Africa has seen significant changes in recent times [71, 20]. One of the key advancements towards establishing the global standards in regulatory policies and practices was to legally launch a new health products regulatory agency, the South African Health Products Regulatory Authority (SAHPRA) in February 2018 [54]. SAHPRA is a public entity of the National Department of Health (NDOH) that was formed by the South African government as an independent authority to oversee the regulation of health products. SAHPRA replaced the former Medicines Control Council (MCC), as well as the Directorate of Radiation Control (DRC) that regulated medicines, medical devices, *in vitro* diagnostic tests and devices, and radiation emitting products and devices used in health care and industry. The establishment of SAHPRA was enabled by the Medicines and Related Substances Amendment Act of 2008 and 2015 [25, 28, 45]. Another key step was to approve the institution of SAHPRA as a schedule 3A public entity under the Public Finance Management Act of 1999, so that it can retain the revenue it generates. This has shown positive signs that are evident in the regulatory agency practices [26, 27, 54]; however, the challenges are enormous and SAHPRA needs to overcome them and make the most out of the available opportunities [71, 26].

The scope of this paper is to examine the reorganization of the regulatory agency as SAHPRA, its goals, organization, functions and responsibilities, accomplishments, outstanding challenges, and opportunities. Furthermore, this paper reflects upon how collaborative measures by SAHPRA can help deal with inherited and forthcoming challenges.

The MCC and DRC were national authorities in South Africa that regulated medicines and medical devices before the establishment of SAHPRA. These agencies were responsible for the regulation, assessment, registration, inspection, and control of medicines, medical devices, clinical trials, scheduled substances, and associated matters in the interest of public health. The legislative responsibilities of these authorities were to make certain the required standards of quality, safety, and efficacy of medicines and devices available in South Africa were met [21, 31].

In the last five decades, South Africa had established a medicinal products regulatory authority with some international reputation. The MCC was the South African regulatory agency

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in matters related to medicines and related substances, whereby it was involved in providing the supervision, assessment, regulation, examination, inspection, licensing, and control of medicinal and related substances. Further, the MCC was also responsible for controlling clinical trials, medical devices, and related matters in the public interest, along with the DRC. The MCC has been heavily dependent on external experts as members of its committees [22].

On the other hand, DRC had been struggling to operate optimally for several years. There were also troubles associated with the potential overlaps in functions with the National Nuclear Regulator (NNR). To ensure international compliance on conduct and safety, it was necessary to work on approaches to define work areas and the development of national source and dose registers. In the past, the DRC had been performing dual roles in regulating both health-related and other products. It was essential to ascertain appropriate organization for the DRC to manage health related products, while NNR could handle other products [31]. These regulatory agencies have been working to ensure public health. However, they were struggling with numerous structural or functional challenges on the following issues [9, 21, 31]:

- The pharmaceutical industry had been facing enormous challenges with the regulatory evaluation process; timelines for approval of submissions were as extensive as three to five years for innovative drugs or post-approval changes.
- It was becoming extremely difficult for the MCC to deal with the volume of applications being received for clinical trials and new drugs.
- The DRC had been struggling with lost sources in the absence of proper recording, theft from premises or loss in transit in the absence of regulatory prescripts for inspections, regulatory inefficiencies, and incorrect information.
- Both the DRC and the MCC had been struggling with insufficient regulatory policies and backlog of work.
- The resource constraint was a common challenge, and both regulatory agencies were dependent on external part-time expertise with hardly any performance oversight in place. This model of utilizing external expertise for the majority of review work was in line with the international leading practices of the 1960s, but outdated now.
- The agencies had been lagging behind other internationally recognized drug and device regulators like those of the United States and Europe in authorizing clinical trials and new drugs or devices. This had progressively led to setbacks in approval of medicinal products or devices and inaccessibility of novel or cost-effective therapeutic innovations by the public.
- Lack of process transparency and accountability, infrastructure capabilities (lack of formal quality and document management systems) and financial independence.
- The agencies, due to limited support structures, had problems to achieve harmonization.

2. South African Health Products Regulatory Authority (SAHPRA)

The South African Health Products Regulatory Authority has been instituted with a mandate to act as regulator, manage the regulatory policies, registration, and control of all types of medicines and relevant health products. These products may include medical devices, *in vitro* diagnostic products, cosmetics, disinfectants, and traditional African medicines. SAHPRA is expected to overcome the challenges being faced in patient access to safe, quality, and cost-effective medications by accelerating the registration process for medicinal and healthcare products and cutting down on the backlogs.

The original idea to establish SAHPRA started in 2010 as a workstream of a broader, 5-year healthcare initiative named 'South Africa Revitalized Response to AIDS/HIV and Health Program' (SARRAH). In 2012, SARRAH submitted an all-inclusive business plan for SAHPRA describing operational strategies and procedures to the National Department of Health (NDOH). The idea was to fill gaps for MCC to handle the backlogs in registration and regulations of medicines and health-related products more efficiently. It was estimated that upon successful establishment, SAHPRA would work towards achieving the prompt availability of essential drugs and ensuring price control measures through encouragement of generic medicines. This healthcare initiative was instrumental in facilitating the interactions of NDOH and MCC to allow the establishment of SAHPRA. It also provided technical support in the development of legislations and regulations [12].

SARRAH aided in devising an electronic document management system and facilitated appointment of added transient resources to fast-track the assessment of submissions for new medicinal products and devices. SAHPRA was designed with an expanded scope to cover not just medicines but to regulate medical devices, including *in vitro* diagnostics, and elements of radiation control. The new agency shall continue to make use of the external expertise model in the interim; however, over time, it will dynamically develop the in-house capabilities to manage the main part of the workload, including clinical trial evaluations and license registration of medicinal products. Furthermore, SAHPRA is expected to work with global regulators to accomplish fast-track evaluation timelines [54].

SAHPRA was established with strategic objectives to ensure independence, consolidation, efficiency, transparency, trust, and adoption of global standards and scientific working approaches [12, 54, 61].

3. Operation of SAHPRA

SAHPRA, as a healthcare regulator, is accountable for regulating all medicinal products, medical devices, and *in vitro* diag-

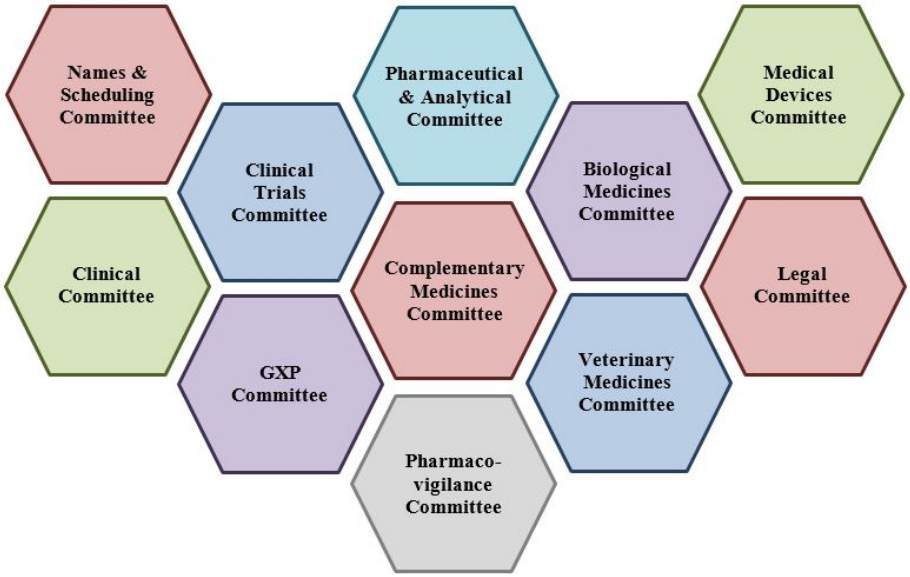

Figure 1: Various Committees of SAHPRA

nostics, complementary medicines, radiation emitting devices and radionuclides. Further, its responsibilities comprise regulatory compliance and supervision of clinical investigations and pharmacovigilance. SAHPRA has more responsibilities than those previously assigned to MCC in view of the range of services and potential size.

SAHPRA reports to the Ministry of Health via a governing board. The SAHPRA board is designated by the Health Minister in line with the conventions of the Medicines and Related Substances Act of 1965 and amendments. The various functional committees of the board are channeled through the board members. These committees aid in the supervision of functioning in the operational spheres of risk management, governance and audit, finance, information technology and communication, human resources, scientific administration, and regulatory policy. The operations of the MCC were taken over by SAHPRA through reorganization [25, 26, 54].

The structure of the SAHPRA board includes a chairperson and vice-chairperson and thirteen other members who are experts from numerous segments of local or global public health, medicinal products regulations, along with other areas of medical research, ethics, governance, finance, and law. A Chief Executive Officer (CEO) is appointed by the board in consultation with the Department of Health to provide an oversight of the operations of SAHPRA. The executive management of SAHPRA comprises also a Chief Regulatory Officer, a Chief Financial Officer, a Chief Manager of Support Services, and the Company Secretary. The CEO and the management committee are accountable for the overall management of the agency [61]. To assist with the performance of its functions, the board and CEO appoint various committees. These committees furnish the required support in executing the duties of the agency [61]. These committees are presented in Figure 1.

The heads of the principal operational areas lead each program. There are five programs at SAHPRA. These programs were instituted as part of the strategic plan, which the agency follows over a period of five years. These programs are [55, 61, 57, 69]:

- *Program 1 - Administration*
- *Program 2 - Authorization Management*
- *Program 3 - Inspectorate and Regulatory Compliance*
- *Program 4 - Medicines Evaluation and Registration*
- *Program 5 - Medical Devices, Diagnostics and Radiation Control*

SAHPRA is instituted as a 3A public unit and therefore can retain the revenues generated by its endeavors. This supports SAHPRA financially with a different revenue model, instead of having all its revenue allotted by the central government. The agency also receives a portion of its funds from the national health budget and the rest is raised through fees for services rendered by the authority. SAHPRA is also entitled to receive donations but is expected to generate most of its funds from the services being delivered, which may have higher tariffs justified by the improvement in the quality and speed of the services. Furthermore, SAHPRA is authorized to pay its staff at par with the market standards to increase its capacity to retain and attract talent. This is a useful human resource tool important to compete [4, 21, 25, 27, 57].

4. Performance of SAHPRA

SAHPRA is likely to bring a noteworthy outcome in the longer term, as some of the effects of the reforms taken are yet to emerge. How well the new organization continues to engage with the national and regional level stakeholders will be revealed with time [12].

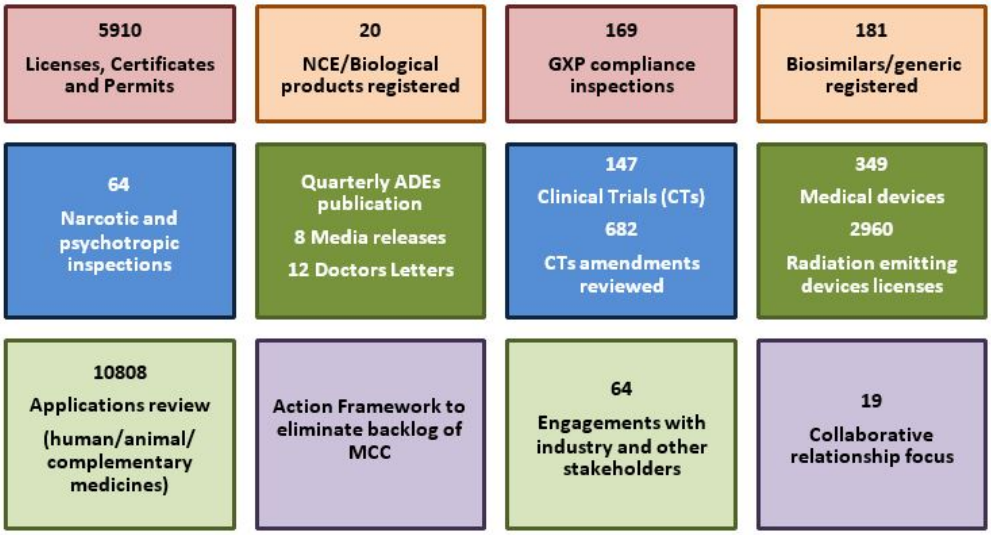

Figure 2: Performance of SAHPRA in 2018-19

The new agency has evidently shown signs of progress towards the goals it was established for. Initial signs of improvements were visible from the implementation of an Electronic Documents Management System (EDMS), training of staff, update to certain key policies, devices regulations discussed with the pharmaceutical industry, remuneration survey completed, a proposal completed for new grading system, etc. There have been various independent studies performed as well, such as the official audit conducted by the Auditor-General of South Africa. In addition, there were several initiatives implemented to bring reforms in the health sector. These initiatives include creation and implementation of a framework to eliminate the backlog of registrations; a strategy to increase the collaboration with and reliance on other health regulatory agencies; operational and technical system upgrades at par with global leading practices; cope up with novel health care regulation areas of breakthrough therapies, biologicals/biosimilars and complex medical devices; and improvements on vigilance and reporting.

Overall, in the year 2018-19, SAHPRA achieved 58 percent of the defined Key Performance Indicators (KPIs) [61]. A view of the performance output of SAHPRA in this period is presented in Figure 2.

Considering the environment in the organization during the inception phase, these can be considered as significant accomplishments. SAHPRA continued to achieve the set targets in the key performance areas (KPIs) of registration of health products, inspections, clinical trials, and licensing.

Administration and productivity were impacted by an inefficient memorandum of understanding (MoU) between SAHPRA and NDOH, and further, by a year-long labor discontent. Steps were taken by the organization to apply in-house procurement procedures to ensure vital administration personnel. This improved human resource, finance, and management of the supply chain. Due to the loss of productivity, decisions were made to emphasize aspects of highest significance to public health, access, and safety. This benefitted the essential function of managing applications to market unregistered medicinal products [12, 55, 61].

4.1. Performance in Administration

1. The aim to establish a full functioning regulatory agency by appropriately staffing it and training was a mixed success. While the target to recruit was achieved by utilizing the former MCC structure, the goal to train the staff was not achieved because of labor unrest and absence of critical human resources.

2. SAHPRA created awareness about the organization by successfully running an employment opportunities campaign in leading publications.

3. The target to improve efficiency was not met; performance agreements were not signed on time due to labor unrest and SAHPRA relocation activities.

4. A communication strategy to improve stakeholder relations and interactions was drafted but not approved and published due to lack of timely support from the Government Communication and Information System (GCIS).

5. The target to create awareness about the new agency and its roles was achieved through communications events, media releases, and interaction with stakeholders.

6. The goals to apply accountability, appropriate administration, and good governance were not met primarily due to constrained inherent controls because of resource limitation.

7. Having a plan in place for the utilization of information and communication technology (ICT) and its monitoring was achieved by developing the appropriate policy and striving to approve it.

8. Strengthening collaborative relationships was achieved by working through increased number of agreements to enhance the reliance models with other global regulatory authorities. Furthermore, service-level agreements were signed with contract laboratories.

9. The target to achieve a quarterly update of the register for medicines and medical devices was not met due to labor unrest and lack of progress in the development of the electronic register.

4.2. Performance in Authorization Management

1. The goal of facilitating regulatory decisions on all backlog applications by defining a framework, conducting a pilot run, and starting to apply the framework was achieved. However, there were no targets set about percentage completion of the backlog for the first year (2018-19).

2. Although the authorization management activities like license, permit, certificates, etc., were significant considering the circumstances, they were still under the set targets. This can be attributed to labor unrest and relocation resulting in unavailability of staff. Efforts to address this situation are now underway.

4.3. Performance in Inspectorate and Regulatory Compliance

1. The annual target achievement to conduct Good Practices (GxP) inspections for establishments saw a shortfall of eight percent. This was majorly due to limited availability of staff due to labor discontent and relocation activities.

2. The accomplishment of the target to carry out compliance inspections for the establishments of narcotic and psychotropic substances was exceeded. This is explained by the mobilization of inspectors to the field, by focusing on the cannabis sites, and applications and minimizing the routine work of inspection team while addressing the risks of such work.

4.4. Performance in Medicines Evaluation and Registration

1. SAHPRA exceeded the goals for evaluation of clinical trial protocols and their amendments as per requisite benchmarks. This was made possible by the services of the community pharmacists appointed temporarily to the departments.

2. Similarly, support from the community pharmacists and digitalization were instrumental in exceeding expectations in processing the applications to market medicinal products.

3. On the other hand, there was no progress on the target on evaluation of new chemical entities (NCE)/biological and generic/biosimilar applications and their amendments for regulatory decisions. The range of times spent for most of the applications was much higher than the target. This is attributable to labor discontent.

4. Additionally, the performance parameters in relation to quarterly publication of new reviewed adverse events exceeded the expectations. This resulted from more active reporting by professionals and encouragement by SAHPRA. The development and approval of an all-inclusive vigilance program was not applied to first year performance.

4.5. Performance in Medical Devices, Diagnostics and Radiation Control

1. The finalization of applications for licenses of medical devices was above the annual target. The output was achieved through services by community pharmacists appointed temporarily to the departments to tackle the backlog of 2017-18.

2. SAHPRA's achievement in the regulatory evaluation of radiation emitting devices was outstanding.

3. Development and implementation of a system to register medical devices was put in place for group 3 and 4 devices. A restructuring of the system will be done to improve on the capacity and range.

From an economic standpoint, a grant of rand (R) 125.1 million was received by SAHPRA from the South African government budget for fiscal year 2018-19. In addition, there was a revenue of (R) 76.9 million generated through service fees and interest. A surplus of (R) 31.2 million was accrued in this fiscal year. A request was made by the agency to retain this fund for next fiscal year keeping in mind the impending operational needs. As part of its capacity to receive donations, SAHPRA has been able to secure significant financial aid from the Bill and Melinda Gates Foundation to fund the backlog clearance project [55, 23, 61, 57, 69].

There have been other tasks formerly of MCC that SAHPRA has taken and improved. One of them is the implementation of the electronic common technical document format submission. The necessary guidelines were put in place by the MCC, but it was far behind on the implementation in comparison to some of the major global regulatory agencies. However, SAHPRA, despite the reorganization of the health authority, has kept progress on track by issuing updates to the guidance, thereby providing an efficient process route to applicants [51, 56].

In November 2016, the MCC joined the International Council for Harmonization (ICH) as an observer. SAHPRA has continued to be ICH observer and thereby ensures that there are opportunities to collaborate with other global regulatory agencies and adopt some of the leading practices in the healthcare regulatory domain [13, 52].

Furthermore, to ensure safe use of medicinal products, SAHPRA is working towards public awareness about the safe use of the drugs and prevention of drug abuse, and alerting healthcare professionals and patients through pack inserts and prescribing information updates about safe use of medicines that may not be suitable for an age group, such as pediatric patients.

As a signatory to international treaties and conventions, South Africa is committed to preventing any illicit drug activities related to cannabis/marijuana, due to its potential harmful effect. This is classified as controlled substance under Schedule 7 of NDOH, South Africa. The cultivation, possession, sale, and use of cannabis is illegal due to its classification. However, to promote the necessary medical use of this controlled substance, provisions have been made to allow measures to access its use and cultivation for medical, scientific, and clinical research purposes. This regulatory framework was identified by the MCC and is being managed effectively by SAHPRA to create the necessary provisions and awareness [7, 24, 70, 34, 50, 53, 65, 48].

5. Challenges for SAHPRA

Reorganization of a regulatory agency is not a minor undertaking and has needed quick turnarounds and multifaceted contributions. As indicated by the SAHPRA chairperson, despite the faults of the system in the starting years, the focus in coming years will be to reenvision and rebuild to meet the challenges. SAHPRA is on the right track and has begun to achieve progress.

5.1. Operational Environment

A challenging operational backdrop continues to be the inadequacies in some SAHPRA operations. The agency needs to reinforce the management team and the departments under their charge. Continuation of efforts to stabilize SAHPRA and its supervision would be key. A careful review of the fees for service and adjustments should be part of the evaluation of efforts to ensure financial sustainability. Resource management has been a consistent challenge for SAHPRA, which is continuing to make progress by processing the recruitment of over 100 new and urgently required posts at various levels [3].

5.2. Effective Working via CEO-CRO Model

Effective implementation of the CEO model to ensure there are strategic plans and leadership for the organization would be another focus. The need to oversee and back up different divisions called for appointing a chief regulatory officer who should be a knowledgeable regulator. The top three priorities for this model would be defining the operational environment, engaging with stakeholders to change the narrative of regulations being barriers, and enabling innovations [3].

5.3. Setting Up Standards

Challenges to establish global-level standards of operation in areas such as radiation control and medical devices need renewed attention from SAHPRA to resolve identified inadequacies. These areas will require careful development and improved implementation of policies and legislation [61].

5.4. Drug Safety

For about four decades, South Africa has been involved in ensuring drug safety and pharmacovigilance activities by assessing adverse drug reactions and their impact. Such activities have come a long way from the state of reflexive regulatory reporting to incorporate active surveillance mechanisms. The mass treatment programs for the Human Immunodeficiency Virus (HIV) and Tuberculosis (TB) epidemics brought about improved comprehension of the burden of adverse drug reactions (ADRs) on the healthcare system and consumers. Such complicated regimens targeted for mass usage bring new pharmacovigilance challenges. Nearly eight percent of hospitalizations have been reported as due to ADRs, and 16 percent of deaths in adult's hospitalization were caused by ADRs. Approximately 50 percent of such fatalities can be prevented, indicating the need of careful monitoring and research to make information available and transform clinical practice, and of shared responsibility in optimization of the safe use of medicines by collaborative efforts of crucial stakeholders. The Pharmacovigilance (PV) surveillance capability can be increased using high-tech clinical, laboratory, and dispensing records. The sustainability and value addition of PV models would need to be evaluated while these challenges endure. Issues like poor quality and no value reports, for example, reports covering instances of Antiretroviral (ARV) medicines not being effective but not about the toxicity of these medicines or information on another medicines not part of ARV treatment.

Keeping the surveillance system at par with the global standard is a challenge. This may be countered by moving away from passive to active PV activities, establishment of patient registries, simultaneous focus on medicines for noncommunicable diseases (i.e., hypertension, diabetes, inflammation, and stroke), and development of an electronic health information system [29, 61].

5.5. Tuberculosis as Disease of Concern

One of the other major challenges for SAHPRA is tuberculosis (TB), reported to be one of the top cause of fatalities in South Africa. Although over the last decade South Africa has seen a substantial decline in TB infections, mortality remains extremely high. By World Health Organization (WHO) estimates, South Africa had over 0.3 million TB cases in 2017. Many of the patients diagnosed have multi-drug resistant and extremely drug resistant TB. Such patients have limited options for treatments with stretched duration but low success rates. Although the TB programs in South Africa provide free diagnosis and treatment, the access barriers to health facilities obstruct the timely diagnosis and start of treatment. By WHO estimates, South Africa is able to diagnose and treat only about 68 percent of individuals with TB. An adequate investment in the development of new diagnostics and treatments for TB should be helpful to confront this challenge [8].

5.6. Maintaining Transparency

Communication is key to transparency. SAHPRA realized the need to continue to do a lot of work in this area to ensure

Table 1: Non-exhaustive List of Legislations Impacting the Functioning of SAHPRA

Medicines and Related Substances Act	Electronic Communication and Transactions Act
Medical Schemes Act	Employment Equity Act
Consumer Protection Act	Skills Development Act
Competitions Act	Labor Relations Act
The Copyright Act	State IT Act
Public Finance Management Act	Protection of Personal Information Act
Customs and Excise Act	Child Care Act
Occupational Health and Safety Act	Pharmacy Act
Nursing Act	Health Professions Act
Environmental and Waste Management Act	Foodstuff
Cosmetics and Disinfectants Act	Drugs and Drugs Trafficking Act
Animal Disease Control Act	Fertilizers, Farm Feeds, and Agricultural Remedies and Stock Remedies Act

the receipt and send out of information to applicants and the wider public. Efforts to develop and maintain an appropriate webpage and overhauling of the information technology system need constant focus. Appropriate and timely communication engagements with stakeholders are important to explain positions on certain matters and work with greatest transparency. All this includes transparency in the context of timelines, processes, and change management. Some of this shall be addressed through the improved IT systems under development [3].

5.7. Legalities Around Cannabis

It is a challenge to not just control or regulate the cultivation, possession, sale, and use of cannabis but also to promote the legitimate use of it for medicinal use, largely because of the abuse associated with it. Responding to clarifications sought for such substances and keeping well informed on developments in the field enabling decisions like rescheduling of cannabidiol, are challenges for SAHPRA [3, 5].

5.8. Policy Mandates and Related Legislation Impacting SAHPRA Functioning

As SAHPRA is an entity of the state, it must have mandates aligned with the national policies and vision for medium and longer terms. These may be as per the policies associated to the national development plan vision 2030 and the policy of the National Department of Health (NDOH). The alignment of implementation of different legislations to meet the collective priorities under these legislations will be challenging. The different legislations that have influence or affect functioning of SAHPRA are covered in Table 1.

The national priorities that impact the policy mandate of SAHPRA are focused around areas of life expectancy, HIV/AIDS and TB prevention, infant and child mortality reduction, healthcare cost reduction, improved quality of healthcare, universal health coverage, and primary healthcare expansion [55, 35, 36, 37, 38, 69].

5.9. Health Priorities vs. Plasma-Derived Medicinal Products (PDMP)

Focusing on the provision of PDMP is difficult for a nation like South Africa. Regardless of being on the list of essential medicines (EML), the adequate facilities to allow patient access to effective and safe PDMPs continues to be a challenge. This is due to many competing health priorities in the region, with constrained resources and limited investment in healthcare. Blood plasma fractionators are challenged by the evolving regulatory and operating environment. Currently, the success of fractionators relies on adopting international leading practices, tactical cooperation with industry associations, and close collaboration with SAHPRA [30].

5.10. Backlog Clearance

The major challenge for SAHPRA since its inception in 2018 has been the backlog clearance for medicinal product submissions. SAHPRA inherited a backlog of work from the MCC that amounts to about 16,000 preapproval or maintenance submission applications, with almost 90 percent of this bulk being generic medicines, duplicate applications, and multi-strength products. Such backlogs in medicinal products registration go against the interest of patients' access to affordable medicines [21, 22, 61].

This is being addressed by adopting various ways of working and collaborating with the pharmaceutical industry. A roadmap was developed to clear the backlog in a period of two years by using inventive approaches like digitalization, prioritization based on public health needs, limiting the submissions requiring evaluation, and collaboration with other global and regional authorities. A careful utilization of internal capacity to pace up evaluations and make use of external expertise for peculiar activities may be the kind of things to look at. Working through a dedicated task group to address the backlog and minimize the impact on the routine workload is being tried. Furthermore, a standardization of assessment procedures to allow

comprehension of the requirements by applicants and timescale estimates are also being done [3, 58, 59, 60, 62, 57, 46, 66, 67].

5.11. Challenge to Keep Up the Expectations as Regulator for Medical Devices

As the responsibilities of SAHPRA include the regulation of medical devices along with medicinal products, the authority is expected to face challenges to keep up to the expectations of industry. Industry associations like the South African Medical Device Industry Association (SAMED) have been critical about the slowness in the past. Although the industry association has a positive opinion about SAHPRA, it points out the need of keeping pace around developments in medical devices regulations [33].

6. Where are the Opportunities and What Needs to be Accomplished

SAHPRA has evolved from part of NDOH to a self-governing, schedule 3A public body reporting to the Minister of Health, analogous to international patterns. Maintaining transparency, efficiency, and sensitivity to its operational environment are going to be the key plans, along with continuing to operate free from public, political, or commercial pressure. The regulatory space for SAHPRA has been widened to incorporate all kinds of medicinal products, radiation emitting and medical devices, and radioactive nuclides. Hence, SAHPRA is expected to be a key player in attaining fair, effective, safe, and quality healthcare coverage for everyone and in the development of a National Health Insurance.

6.1. Antimicrobial Resistance (AMR) National Strategy Framework

Development of resistance against antimicrobials is a worldwide challenge and becoming a threat to public health. The national AMR tactical plan can be reinforced by SAHPRA through the application of its mandate. This can be achieved by ensuring availability of good quality, safe, and effective antimicrobial medicinal products. Furthermore, the promotion of rational usage and application of suitable post-marketing supervision, including testing facilities to screen quality and vigilant reporting mechanisms would form the basis to tackle the AMR threat.

SAHPRA needs to collaborate with important stakeholders like the Department of Agriculture, Forestry and Fisheries (DAFF), since antimicrobials are not just used in humans but also in animals and livestock for treatment or growth promotion. This will safeguard better mechanisms and suitable utilization of antimicrobials. SAHPRA is already interacting with these stakeholders to formulate stringent regulations to alleviate development of resistance for important antimicrobials like colistin [55].

6.2. Universal Healthcare Coverage (UHC) and National Drug Policy

Expenditure in healthcare is a burden and gets worrisome by the growing costs of medicinal/healthcare products and medical technologies. A bill named National Health Insurance (NHI) Bill has been announced to alleviate some of the voids in extending quality healthcare benefits to the public. The bill shall be in effect in the forthcoming years as a healthcare funding mechanism intended to pool funds to deliver affordable and quality healthcare services to the South African public as needed, regardless of their socioeconomic level. SAHPRA, as a healthcare products regulator, has a key role to play in support of the efficient execution of the approach to universal health coverage. SAHPRA needs to rationalize businesses and optimize productivity to address such health priorities. The authority will need to maintain an active engagement with the NDOH and other stakeholders to ensure synergies [55, 39, 69].

6.3. Management of the Registration Process

The old framework and policy challenges of the MCC have led to ineffective management of timeline targets for the assessment of medicinal products, despite setting forth the internal timelines. Information sharing and management, rationalization of processes and procedures, and program management techniques can help support changes to deal with medicinal product registrations. SAHPRA is looking forward to employing solutions like case or portfolio managers that will facilitate the process and management of resources [55, 61, 69].

6.4. Revisiting the Revenue Generation for Ambitious Objectives

SAHPRA needs to strengthen its financial sustainability utilization and generate more revenue by moving to an appropriate fee structure necessary for financial independence. This will provide the basis for quality services [55, 69].

6.5. Skill Development

There is a need to speed up the recruitment and training of in-house human resources to bring efficiency to the assessment process and turn-around time of applications. SAHPRA will be utilizing the performance management system for external evaluators to facilitate the skill development of in-house staff. This will help build the critical assessment skills and facilitate undertaking a peer review of applications, as recommended by WHO. Moreover, an appropriate setup for quality assurance must be established in line with other regulatory agencies to safeguard uniform standards of technical assessment and technical writing. External evaluators can be incorporated for defined periods to assume responsibilities on a prearranged program. There are many technical activities other than the assessment work, which may include the pre-processing and validation of applications, preparing meeting minutes, engagement with sponsor and assessors, etc., that require different skill levels, and development of them is paramount to the success of regulatory agencies [55, 61, 69].

6.6. Regulating Active Pharmaceutical Ingredients (APIs) and Clinical Trials (CTs)

With the adoption of a harmonized framework to regulate APIs worldwide it is important for SAHPRA to strengthen the capabilities and capacity of its inspection staff, which is currently limited in experience due to limited production of APIs in South Africa. In addition, the agency has an opportunity to increase its participation in the global fora working on harmonization of API requirements. Similarly, SAHPRA has an opportunity to make use of the global networks to harmonize the requirements for clinical trials. This will help SAHPRA to be responsive to changing approaches to bring products to market urgently after phase 3 studies [55, 69].

6.7. Vigilance for Drug Safety

SAHPRA has done a lot of work already in recognizing gaps in the existing framework of pharmacovigilance. There are more opportunities in the form of applying novel strategies to use Good Vigilance Practice (GVP) standards, risk management plans as part of assessment verdicts, enhancing supervision for therapeutic efficacy, quality problems, drug abuse, overdose toxicities and off-label applications, etc., and come up with a framework for communication and feedback on drug safety matters to stakeholders and the public. Furthermore, building the surveillance capacity of the vigilance system and refining the quality and frequency of reporting should be emphasized to fortify the pharmacovigilance of veterinary medicines, medical devices, and complementary and traditional African medicines during the framework development. The attention towards pharmacovigilance, including preemptive stakeholder engagement, will be vital in safeguarding public health by ensuring the safety of healthcare products [55, 29, 61, 69].

6.8. Regulating Biologicals, Medical Devices, Veterinary Medicines, Complementary and African Traditional Medicines

With the noteworthy advancements in biotechnology research, the quantum of biological medicinal products necessitating regulatory limits has increased. Such regulatory provisions require decision-making approaches encompassing all stages of a product's life cycle, particularly with developing technologies like biosimilars. The need for being effective in this area to tackle the regulatory and compliance aspects demands strategic deliberations and collaborative partnerships with other regulators. In the context of Complementary Medicines (CMs), development of the regulations was started by South Africa regulators in 2011. However, an information management system integrated with information technology is still needed.

Further, the regulatory skills in this area are presently inadequate in SAHPRA. This can be remedied through the organization of training programs and mentoring by experts. As the business of CMs is underregulated, it requires a better comprehension and regulatory makeover to safeguard compliance. SAHPRA has established an Industry Task Group (ITG) forum to partner with industry on dossier content assembling and regulations through several workshops. The agency is also engaging other global regulators like the Therapeutic Goods Administration (TGA), Australia, and Health Canada to learn leading practices in the domain of CMs. Efforts are under way since 2016 to finalize a regulatory outline involving the African National Healers Association to develop regulations and controls for traditional African medicines (TAMs).

The discussions with the NDOH and some other departments are progressing to look at streamlining the veterinary medicines regulations. With the background of emerging antimicrobial resistance, the need to minimize the use of antibiotics in animals is paramount from the veterinary perspective.

SAHPRA should bolster novel approaches in the registration of medical devices to be at par with worldwide leading practices. The mechanism of regulating medical devices would be based on the endorsements of the International Medical Device Regulatory Forum (IMDRF). There are further opportunities in this area, like accelerating collaboration with leading regulators such as the United Kingdom and Japan, aligning the vigilance system to regulatory outline and benchmark systems, enhancing skills through training programs, understanding, and acknowledging accreditation by IMDRF and WHO, developing an information management system, etc. [55, 21, 22, 32, 69].

6.9. Benchmarking General Leading Practices

Aligned to its mandate to work with various stakeholders to benchmark practices in marked operational and technical areas, capacity building, information management/sharing, and mutual acknowledgement of regulatory requirements and product approvals, SAHPRA is engaging with various global regulators including the U.S. Food and Drug Administration (FDA), Medicines and Healthcare Products Regulatory Agency (MHRA), European Medicines Agency (EMA), Regulatory Authority of Switzerland (SwissMedic), and WHO. SwissMedic is a similarly sized regulator that underwent a similar change in management and should be a valuable partner to work with. To be included on the list of WHO's Stringent Regulatory Authorities, SAHPRA would need to implement a Quality Management System (QMS) assessed by WHO [55].

6.10. Organizational/Operational Environments

There are opportunities for SAHPRA to focus and refine its operational and administrative procedures. This would help to curb shortcomings and establish the required policies and practices in the areas of supply chain management and procurement. The digital revolution inside SAHPRA and partnering with private research laboratories to accelerate assessment procedures are going to be helpful actions. Incorporation of yearly engagement surveys as part of the operational work culture will ensure that the staff is motivated enough and achieve superior performance [3, 55, 23].

6.11. Stakeholders Engagement

MCC, as the former regulator, was missing the capacity to effectively communicate with its stakeholders, including the

public, patient groups, healthcare professionals, the pharmaceutical industry, fellow regulators, and other collaborators. This led to uncertainty and lack of trust. SAHPRA will need to develop a thoughtful communication strategy channeled through its communication officers. This will ascertain that its stakeholders are reached through multimedia approaches, that they are able to recognize the responsibilities and values of the regulator and are able to work in a transparent fashion, seeking their support for key decisions and developing feedback mechanisms [55, 57, 69].

6.12. Enabling Innovations

SAHPRA could foster a culture of supporting innovation, where ideas are shared and research is focused on the public interest. The agency needs to build and empower the environment for ethical and sound research, supporting novel ideas by facilitating them to reach the marketplace, seeking cost-effective provisions in research and training, and encouraging novel practices and thinking [21, 29].

6.13. Prospective Healthcare Investment Opportunities

With the favorable policies on investment, South Africa is expected to attract USD 100 billion in industrialization over the next five years. The country is the fastest growing and major economy in the African continent, and it is expected to be a low-risk location to attract investors to access the fastest growing consumer market. This has built up hopes for investment in the healthcare manufacturing and practices sector [10, 72].

6.14. Opportunities in Controlling Tuberculosis

More investment in TB research by the South African government is warranted and should include commercialization of health technologies. SAHPRA should support and promote socially responsible licensing, alternative research funding models, development and funding of a national drug development framework, multinational enterprises such as Brazil, Russia, India, China, and South Africa BRICS TB Research Network, and potential WHO R&D Convention, and third-party supervision of access and affordability obligations on publicly-funded International Paper (IP). Establishing a civic searchable databank will help supervise developments by enterprises [8].

7. Collaborative Approaches to Become Contemporary

One of the goal statements for SAHPRA is to establish and strengthen collaboration with other regulators or organizations. The agency has also proclaimed a strategy shift to espouse reliance models through collaboration with other regulators. This will support SAHPRA not only in overcoming challenges like the backlog clearance but also for routine work. For attainment of this goal, SAHPRA has engaged with stakeholders, including the pharmaceutical industry, to ensure effective collaboration and communication.

7.1. International Pharmaceutical Regulators Program (IPRP)

SAHPRA is a member of the International Pharmaceutical Regulators Program (IPRP), a global venture. IPRP is a global forum for regulators and regulatory organizations having about 25 members and observers, including WHO. IPRP detects and focuses on emerging issues of common concern and discusses strategies around them. This is done by instituting a cooperative ecosystem to contribute to regulatory viewpoints on work done by ICH, constraints, and coherent application of ICH guidelines. It also fosters large convergence in regulatory strategies based on global benchmarks and leading practices. Furthermore, it works to establish an inter-regulator collaborative environment to promote effective information exchange, increased communications, and capacity and skills enhancements. IPRP is not directly involved in the development of technical guidelines; however, it hands over the conclusions arrived at on scientific topics to ICH for further action. It has various working groups, including bioequivalence, biosimilars, cell therapy, gene therapy, IDMP (identification of medicinal products), nanomedicines, quality working groups, pharmacovigilance, and information exchange.

In addition to retaining a focus as platform for regulators to exchange leading practices, IPRP is also pledged to involve external stakeholders, which include the following:

- Academic and research institutions, patient organizations, and public health non-governmental organization (NGOs);
- ICH members and observers, industry associations, International Coalition of Medicines Regulatory Authorities (ICMRA), Pharmaceutical Inspection Co-operation Scheme (PIC/S), other regulators;
- General public, student organizations; and
- Standard/harmonization fora, conference organizers, professional societies like the Drug Information Association (DIA), The Organization for Professionals in Regulatory Affairs (TOPRA), and the Regulatory Affairs Professionals Society (RAPS).

The level of engagements includes informing and seeking input. Such activities keep SAHPRA abreast of current affairs. SAHPRA cooperates with all major regulatory members of IPRP. It was disappointing not to witness participation of SAHPRA in the WHO reliance model survey conducted in early 2019 for the members and observers of IPRP. As a developing and aspiring regulator, it is expected that SAHPRA get involved more in such activities and be proactive on the stakeholder engagement plan of IPRP and take part on IPRP's strategic plans and objectives [4, 17, 40, 51, 52, 56, 57, 44].

7.2. Africa Union Development Agency - New Partnership for Africa's Development (AUDA-NEPAD)

AUDA is a regional venture for the Africa continent to coordinate regional priorities and continental development projects to promote regional integration. One of the programs of AUDA

is the African Medicines Regulatory Harmonization (AMRH). This is an enterprise striving to improve the availability of safe, quality, and effective medicines by facilitating an updated and resilient regulatory environment for the pharmaceutical sector in South Africa. AMRH works through by organizing various collaborative events like scientific conferences and publications [1, 2, 69].

7.3. Southern African Development Community (SADC)'s Work Sharing Initiative

SADC was formed to pursue development, peace, security, economic growth, and to improve the quality of life in the southern African region through regional integration. SADC's cooperative medicinal product registration program, named as Zambia, Zimbabwe, Botswana, Namibia work Sharing Initiative (ZaZiBoNa), is a positive local work sharing initiative on the continent. It encourages a template to accelerate entry to good-quality medicines through sharing evaluation and inspection provisions. Medicinal products are granted registration in the member countries where the application is submitted. With agreements, the post-approval applications can also be handled via the same cooperative mechanism.

As member of the Southern African Development Community (SADC) and the Africa Union Development Agency - New Partnership for Africa's Development (AUDA-NEPAD), SAHPRA is expected to emerge as role model for the African region and become a reference country in the broader region. SAHPRA's footprint in the continent is instituting it as one of the leading regulatory bodies in region's healthcare product regulatory environment. This would result in bolstering the authority and sincerity of Africa as a whole on the worldwide response to concerns regarding healthcare products safety and availability [43, 69, 44].

7.4. Benefiting the Regulatory System

Constructing on and strengthening the regulatory system can be inspired by leading practices elsewhere. In addition to the benefits covered already (backlog, inspections compliance, evaluation processes, legislation development, universal health coverage, performance enhancements and improvements in pharmacovigilance) some of the areas where cooperative measures are either under progress or could be explored further are the following [55, 21, 29, 58, 59, 60, 62, 63, 46, 66, 67, 69]:

1. An approach to apply regulations for medical devices and its establishment licensing are being achieved through coordination with the South African National Accreditation System (SANAS) and similar internationally recognized institutions.

2. Liaison with and visits to various regulators across the globe is helping to shape up the structural and operational aspects of the agency, including scope of activities, resource management, budget and funds management, global and regional collaborations, and registration processes.

3. SAHPRA started a pilot training initiative in coordination with local universities in pharmaceutical and life sciences. This will not only produce a pool of evaluators but will also create insights about the new regulatory framework of SAHPRA.

4. The position and acceptability of proprietary names for medicinal product registration developed by other major regulators can have a lot of influence and should take care of local aspects regarding local acceptability.

8. How Local Challenges Handling can be Eased with Global Approach

SAHPRA has lot of challenges on a local level and may require a local customization of solution. However, a lot of the challenges would require a strategy proven or workable at global level. Some of these challenges and potential solutions through global collaborative/partnership mechanisms are [6, 7, 11, 24, 70, 34, 41, 42, 53, 65, 68, 49, 69, 48]:

8.1. Cannabis and Codeine Challenge

SAHPRA as a nimble regulator needs to be proactive in handling the regulatory framework through collaborative partnerships with other regulators and federal departments. This year SAHPRA participated in the session of United Nations Office on Drugs and Crime (UNODC) Commission on Narcotic Drugs held in Vienna.

8.2. Diseases of High Concern and Essential Medicines

SAHPRA needs to create collaborative constructs to launch innovative treatments into pilot programs to tackle diseases of high concern and burden, predominantly TB, HIV, cancer, etc. Similarly, efforts would be required to ensure access to essential medicines. The ZaZiBoNa initiative has this as a priority objective.

8.3. Electronic Format and Digitization

SAHPRA should look to work further on the electronic formatting and overall digitization of regulators' work aspects through partnership ventures and participation in a task force rather than working in isolation, to make use of synergies and be cost-effective.

8.4. Charging Fee for Backlog

Like other major regulators, SAHPRA is not exception if it asks to provision special fees to clear and prioritize the backlog. Other regulators, when needed, have made provisions of fee to special services, but this must be performance driven.

8.5. Public Consultation on Guidance Documents

Like the global leading practices, SAHPRA should raise its reputation by bringing more and more work for public/industry consultation. This shall help in receiving valuable inputs and also clarifying the intentions and alert for expectations.

8.6. Provisions for Abridged Evaluation

SAHPRA as an observer of the European Pharmacopoeia accepts certificate of suitability to European Pharmacopoeia (CEP) like European countries and some other international regulators. This reduces the burden of evaluating the Active Pharmaceutical Ingredient part if the CEP is available with the manufacturer.

8.7. Aligning with Global Traceability Standards

South Africa is intent on enhancing the traceability of medicinal and healthcare products across the supply chain. This will increase security, visibility, and availability of medicinal and healthcare products. For this, SAHPRA has collaborated with donor regulators, including the United States Agency for International Development (USAID) implementation of GS1 standards. The legislations for these provisions can be developed by collaborating and learning from established regulators like USFDA. Furthermore, as the supply chain is a multinational aspect, it cannot be protected without partnership and information exchange.

8.8. Partnership with Industry and Regulators in Pandemic like Corona Virus Disease 2019 (COVID-19)

The novel coronavirus, COVID-19, pandemic is going to have faraway effects on public health. Also, it has impacted the manufacturing business across the globe. The solution for a global problem impacting locally can also be through global approaches. SAHPRA has been ensuring continuity of supply of medicinal products and medical devices. It is in constant communication with other regulators and industry to ensure that safe, effective quality medicines and devices are available. Moreover, SAHPRA is working closely with NDOH in bringing awareness and spreading information related to pandemic, preventions, and treatment.

9. Conclusion

SAHPRA has come a long way and achieved good progress in its initial operation. There is noticeable momentum in the organization, working approaches, policies, communication, and engagement with stakeholders. There are numerous challenges inherited or forthcoming that would require a lot of focus and efforts from SAHPRA. However, there are also opportunities for SAHPRA to raise its reputation as a global level regulator that is organized and effective in managing healthcare products regulations and related processes. Collaboration is key to solving problems, and SAHPRA is expected to succeed in responding to challenges and opportunities. The reorganization of the South Africa health products regulator into SAHPRA was a worthy move.

10. Declaration of Conflicting Interest

The authors declare that there is no conflict of interest.

11. Article Information

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