The Current Regulatory Environment in Africa and the Future Role of the African Medicines Agency:

Contribution of the ECOWAS Region

FOREWORD

The publication of the book titled **"The Current Regulatory Environment in Africa and the Future Role of the African Medicines Agency: Contribution of the ECOWAS Region"** is timely in view of the imminent start of operations of the African Medicines Agency (AMA)

This ten chapter, research-based, book focuses on the ECOWAS Regional Harmonization (ECOWAS-MRH) Initiative. It begins with a good overview of the current regulatory environment in Africa before examining the performance of seven active national medicines regulatory agencies in the ECOWAS region. It compares the regulatory review models and timelines of the ECOWAS Regional Medicines Harmonisation (MRH) Initiative and discusses in detail the importance and potential contribution of WHO Maturity Level 3 (ML3) agencies towards the operationalisation of AMA. The book documents the challenges faced by national regulatory agencies as well as the pharmaceutical industry and concludes with suggestions for improved transparency, predictability and reliability in regulatory decision making in Africa.

The authors deserve commendation by for their diligence in not just documenting activities within the ECOWAS-MRH Initiative but in also assessing the possible impact on the regulatory landscape in Africa. The discussion on the role of WHO-ML3 agencies towards the operationalisation of the AMA aligns with the continental strategy for the AMA which includes leveraging African expertise as well as building on existing initiatives especially those within the African Medicines Regulatory Harmonisation Initiative including those harmonization initiatives within the eight Regional Economic Communities in Africa. Even though the studies that formed the basis for the book were conducted in the ECOWAS region, the findings are generally applicable to all 55 countries in Africa.

The African Medicines Agency is a key African institution established by treaty to enhance the regulation of medical products in Africa. One of its key aims is the promotion and strengthening of medicines regulatory harmonisation across Africa. It will do so by coordinating ongoing regulatory harmonisation initiatives, building capacity amongst member states and by sharing best practices. This book therefore provides timely expert information for consideration and possible adoption during the operationalisation of the AMA.

This book is a useful regulatory science manual, and the authors are encouraged to disseminate its findings widely in both scientific and professional journals. They are

entreated to collaborate with stakeholders to assess the feasibility or repeating some of the studies in other regions in Africa.

This book is a must-read for all those with interest in medicines regulation in Africa.

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PREFACE

National regulatory authorities (NRAs) are responsible for the regulation of medicines and for ensuring patients' access to the safe, good quality and effective medicines. The need for both effective and efficient regulatory systems has been identified and the importance of strengthening regulatory processes and the regulatory performance of NRAs is fully appreciated by all stakeholders. The drive for the operationalisation of an African Medicines Agency is dependent not only on national regulatory authorities, but also on the expertise of the regional initiatives in the African continent.

Against this background, there was an opportunity to evaluate the regulatory review models and the regulatory performance of the seven active agencies in the ECOWAS-MRH Region as well as the ECOWAS-MRH Regulation Harmonisation Initiative. Research into the challenges faced by the ECOWAS-MRH Initiative by both the agencies and the pharmaceutical Industry and the possibilities for an improved regulatory review process was conducted through a series of studies. The results from this research have for the first time provided a baseline against which the performance of ECOWAS-MRH initiative may be measured as well as the agencies that provide a work-sharing regional opportunity.

The outcomes from these studies have yielded a number of key recommendations within several major areas including the measuring and monitoring of the regulatory review processes in the region, the risk-based evaluation of medicines, reliance and the models of review, Good Review Practices as well as quality decision-making practices and the successes and challenges faced by these agencies in the low to middle income countries in Africa

One of the authors has over fifteen years of experience of working with the FDA GHANA programme in Africa and as such has an extensive knowledge of the regulatory environment in this important continent. The other two authors have, over the past four decades worked closely with the pharmaceutical industry, mature regulatory agencies and those in the emerging economies to provide guidance and validated tools that relate directly to the World health Organisation's Global Benchmarking Tool (WHO GBT) in order to enhance regulatory performance and reach the next maturity level as assessed by the WHO GBT.

Such was the importance of this work that the authors were encouraged to produce this research in a format that would be accessible to a wider audience. This book presents a seminal piece of work, together with key recommendations that may contribute

towards improved transparency, predictability and reliability in regulatory decision-making as well as tangible outcomes to expedite patients' access to medicines in the ECOWAS-MRH Region.

It is hoped that this research will inform areas of improvement that may be prioritised to underpin the success of the African Medicines Agency as it moves towards its operational goal. This work, we believe, will be of benefit to the Pharmaceutical Industry to help build trust in the continent which in turn may stimulate investment in Africa. In addition, we hope that these studies together with the methodologies and tools used, as well as the recommendations made, may be of value to other regulatory authorities within the emerging economies and will serve as a blueprint, providing practical solutions to support initiatives for regulatory reform.

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CHAPTER 01

OVERVIEW OF THE CURRENT REGULATORY ENVIRONMENT IN AFRICA

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SUMMARY

- The West African Health Organization in collaboration with the 15 NMRAs in West Africa established the ECOWAS-MRH initiative. The main objective of this initiative was to enhance patients' access to quality, safe and efficacious medical products in the sub-region.
- Products which are jointly assessed by the ECOWAS-MRH initiative include the following; essential medicines as listed by the WHO, antiretrovirals, antimalarials, medicines for tuberculosis, reproductive health, neglected tropical diseases, medicines for public health emergencies, WHO-prequalified products, stringent regulatory authorities- registered products, biological products including vaccines.
- These products, upon successful completion of the joint assessment, can then be processed within 60days through an NMRA's registration procedure for a marketing authorisation to be issued. Submissions to the joint assessment procedure are expected to be processed between approximately 120 and 226 calendar days.
- From available literature effective and efficient regulatory strategies that are found in a regional medicines harmonization regulatory initiative should be identified and published for other NMRAs and MRH initiative to learn and implement the same accordingly.
- Reviews are a key component of the scientific basis for regulatory decisions whilst good review practices are a key component of good regulatory practices; which is a requirement of every regulatory authority. Regulatory authorities are encouraged to improve their review processes as this will in turn improve the performance of their regulatory systems.
- An ideal benefit-risk assessment model should incorporate multi-criteria decision analysis (MCDA) in the systematic approach. It should be noted that an ideal benefit-risk assessment model is a complementary resource in quality decision making practices by the NMRAs and manufacturers
- Presently benefit risk assessment is not carried out in any of the agencies in ECOWAS, and since it is fundamental to the review of new medicines, it should be incorporated into the regulatory review processes.
- Presently the agencies in the ECOWAS region do not appear to have implemented quality decision-making practices; due to its importance to efficient and effective NMRAs, this will be addressed in this research.
- As part of this research, the views of both regulators and manufacturers regarding the effectiveness and efficiency of the ECOWAS-MRH will be collated and presented. This will enable stakeholders have a current detailed view of the ECOWAS-MRH initiative.

BACKGROUND

Regulating medical products

The World Health Organization (WHO) has in its constitution, which was signed in 1946, that "the enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being without distinction of race, religion, political belief, economic or social condition". It also includes that "Governments have a responsibility for the health of their peoples which can be fulfilled only by the provision of adequate health and social measure" (WHO, 2024a).

Since medicines form the core of a health care system to assure the health of the public, governments set up national medicine regulatory authorities (NMRAs) with the primary objective to ensure the quality, safety and efficacy of medical products that are available in a country. The importance and benefits of establishing strong national medicines regulatory authorities have been documented in the literature. It is worth noting that the requirements for an effective NMRA include government support, adequate technical, human and financial resources. It is expected that the NMRA will have in place an adequate management system, sufficient regulations, good regulatory practices as well as an effective and efficient regulatory review system. Additionally, the NMRA should cooperate with all stakeholders, namely, manufacturers, regulators, health care providers and patients. Furthermore, NMRAs are also encouraged to collaborate with other NMRAs. (WHO, 1999a; Ratanawijitrasin et al, 2002; WHO, 2003a; Rago et al, 2008; WHO,2010a; Barton et al, 2019; Yenet et al,2023).

In spite of the above, Yenet et al (2023) have reported that over 30% of the global population do not enjoy reliable access to medicines possible due to inefficient health systems and specifically in Africa about 60% of the population is not served with reliable access to medicines. They also reported that due to the lack of timely access of antimalarials, antituberculosis and anti- retrovirals about 1.6 million African patients died from malaria, tuberculosis and HIV/AIDS in the year 2015.

According to the WHO (2003a) "NRAs must be responsive to the needs of the general public, and effective and efficient in discharging their duties. Any deficiency or delay in decision-making may enable harmful medicines to reach the market or lead to shortages of vital medicines and thus endanger lives. It may be helpful for an NMRA to be dynamic so as to always meet the needs of the public as well as during pandemics. The WHO (2003a) accurately stated that "The problems of ineffective regulation transcend national borders and have global implications". It is therefore logical that in

this research the regulatory systems of individual countries are initially assessed and then this can be followed with the assessment of the sub-region.

Registration of Medicines

In the recent study by Yenet et al (2023), *inefficiencies in drug registration* were reported to impact on the availability of medicines in Africa. It is estimated that Africa imports about 80% of its medicines (Yenet et al, 2023), and it is expected that all medicines are registered in accordance with the regulatory requirements and review process in force in the relevant importing country (WHO, 2010a). In view of this the effectiveness and efficiency of an NMRA can be assessed based on the timelines it employs to review applications for marketing authorization. The review of applications for marketing authorization, also referred to as registration by an NMRA, presents opportunities for the NMRAs to deploy efficient regulatory strategies to execute its mandate for the benefit of all its stakeholders including manufacturers and patients.

There is a recommendation in the literature that "an optimal drug registration approach for Africa should reliably evaluate safety, efficacy and quality of drugs for African use. It should include African expertise, contribute to building African regulatory capacity and ultimately, expedite African access by reducing duplicative and sequential reviews by different regulators" (Moran et al, 2011). This research is focused on regulatory systems and activities of NMRAs in West Africa that are relevant for granting marketing authorization for new active substances, generic pharmaceutical medicines and biological products.

A review of the resources available for performing the marketing authorization function will be conducted at both the country and sub-regional levels. Due to the limited human resource reported in the literature to be present in the NMRAs, the benefits of having a reliable computerized system to keep record and track applications for marketing authorizations and ultimately enhance efficiency of the NMRAs will be emphasized (WHO, 1999a, Yenet et al,2023).

Strengthening regulatory systems

Countries need effective and efficient NMRAs to ensure that all medicines are duly registered, which means that their safety, quality and efficacy are assured. As part of the WHO's support to low and middle-income countries (LMICs), an assessment of 26 NMRAs in Africa was conducted prior to the year 2010. The following were included as part of the key findings of the assessment of the NMRAs; there was a pressing need to strengthen their regulatory capacity, there were variations in efficiency of their

regulatory strategies, there were no quality management systems in place, information on decision-making was minimal, there were variations regarding assessment of dossiers, there was insignificant capacity to assess dossiers of new active substances, there were application backlogs and long timelines for assessment, while the time for detailed dossier assessment was inadequate. Furthermore, most of the NMRAs did not have sufficient assessors and safe storage space to handle dossiers, few of the NMRAs had an electronic medicine registration system and this impacted on the accountability and transparency of the registration process. None of the NMRAs published any public assessment reports at the time. The WHO concluded that "the lack of mechanisms and procedures that would enable NMRAs to benefit from the scientific assessments and inspections carried out by other well-resourced and established regulators is a major concern, as most of the authorities in the region have limited human resources and scientific expertise" (WHO, 2010a) For the next steps, it was recommended that WHO should support NMRAs in Africa to obtain the requisite resources to address the key findings and also to conduct self-assessments (WHO, 2010a).

The WHO has developed the WHO Global benchmarking tool for the evaluation of a national regulatory system for medical products (WHO, 2023a). As a result of assessments by the WHO the NMRAs of Ghana, Nigeria and Senegal have achieved maturity level 3 (ML3) in 2020, 2022 and 2024 respectively. This implies that these three countries in West Africa have stable, well-functioning and integrated NMRAs. Presently there only eight NMRAs in Africa that have achieved maturity level 3, and in addition these include Tanzania, Egypt, Zimbabwe, Rwanda and South Africa. There is therefore the need for the remaining NMRAs to learn from these ML3 agencies and endeavour to achieve higher maturity levels (WHO, 2023b; WHO, 2024c).

REGULATORY HARMONISATION

The United States Food and Drug Administration refers to the alignment of technical requirements for the regulation of pharmaceuticals by different regulatory authorities as harmonisation. The benefits of harmonisation include removing duplication of time and resources for regulatory processes and thereby enhancing access to quality medical products (Barton et al, 2019; USFDA, 2020a).

Medicines regulatory harmonisation (MRH) started many years ago as a collaboration between the medicine's regulatory authorities and pharmaceutical manufacturers of the United States of America, European Union and Japan for their regulatory and industrial benefits respectively and also to improve public health. This collaboration resulted in the establishment of the International Conference on Harmonization of

Technical Requirements for the registration of pharmaceuticals for human use (ICH). The ICH was specifically concerned with new active substances. The World Health Organization was subsequently welcomed as an observer to the ICH. The NMRAs in low and middle-income countries (LMICs) look to the WHO to customize the ICH technical requirements to suit generic pharmaceuticals which out-number new active substances in their jurisdictions. It is believed that NMRAs in developing countries felt confident to introduce submission of dossiers in the common technical document (CTD) format for marketing authorization applications after the successful introduction of the relevant CTD guidelines and its implementation by the WHO prequalification programme (Rago et al, 2008; Reggi, 2017)

Medicines regulatory harmonisation has been documented as an important strategy to improve regulatory review processes which could enhance access to medicines. When regulatory harmonisation of medicines is implemented in a region, manufacturers provide the same documentation to the regional body and the outcome of the scientific assessment is upheld by all countries in the region. This ultimately leads to quicker access of medicines by patients and in some cases results in less expensive medicines as the regulatory burden is reduced for the manufacturers (WHO, 2024a).

In order for patients in Africa to reap the benefits of medicines regulatory harmonisation, the African Medicines Regulatory Harmonization Initiative (AMRHI) was launched 12years ago with the support of the World Health Organization. One of the objectives of the initiative was to establish a medicines regulatory harmonization initiative among the national medicines regulatory authorities (NMRAs) in sub-regional levels (Ndomondo-Sigonda et al, 2023; WHO, 2024a). Looking into the future of medicines regulation Rago et al (2008) aptly stated that "There is likely no alternative for more harmonisation (international, regional and sub-regional) of regulatory requirements and work-sharing (together with information sharing) between different national regulatory authorities".

The ECOWAS-MRH Initiative

The West African Health Organization (WAHO) was established by a protocol signed in Abuja in 1987 by the Heads of State and Government of the Economic Community of West African States (ECOWAS) to be responsible for the health of the people in the sub-region (WAHO,2021a). The ECOWAS is a regional economic community in Africa, consisting of fifteen member states all of which are located in West Africa. The member states are Benin, Burkina Faso, Cape Verde, Cote d'Ivoire, Gambia, Ghana, Guinea, Guinea Bissau, Liberia, Mali, Niger, Nigeria, Senegal, Sierra Leone and Togo. As

of 2020, the population of ECOWAS was estimated to be about three hundred and eighty-three million persons (Conway et al, 2020).

According to Article III of the protocol, *"The objective of the West African Health Organization shall be the attainment of the highest possible standard and protection of health of the peoples in the sub-region through the harmonization of the policies of the Member States, pooling of resources, and cooperation with one another and with others for a collective and strategic combat against the health problems of the sub-region"* (Conway et al, 2020). It is not surprising that the African spirit of 'In unity is strength' strongly resonates in the above objective and in the mission of ECOWAS which include among others harmonisation of regional policies (WAHO,2021a). Three main international languages are shared among the 15 member states- English, French and Portuguese, making it very convenient for nationals in different countries in the sub-region to communicate with each other and with the rest of the world.

The WAHO, with its headquarters located in Bobo-Dioulasso, Burkina Faso, and recognized by the Member States and the rest of the world as the Health Authority of ECOWAS has more important political, social and economic advantages when compared with the other health systems available in the individual Member States to enable it achieve the above objective. In March 2000, WAHO started its operations as the Health Authority of the 15 Member States. The WAHO has been guided in its operations since 2003 by three strategic plans covering the following periods: 2003–2007; 2009-2013 and 2016-2020. Whilst an assessment report on the implementation of the 2016-2020 strategic plan is not available at this time, it is worth noting that assessment of the 2009-2013 strategic plan showed that issues regarding harmonisation of health policies, legislation and standards had seen some significant progress (Conway et al, 2020). As part of the next steps, it was recommended that harmonisation of regional policies with emphasis on facilitation, regulation, coordination, advocacy and cooperation with other relevant health institutions as well as local production of medicines should be considered (WAHO,2021b).

The 2016-2020 strategic plan of WAHO aimed at achieving the three strategic goals: promotion of priority health policies and programmes in the ECOWAS region, strengthening strategic partnerships for health and building the institutional capacity of WAHO. The strategic plan also sought to address the situation in the sub-region where issues regarding governance of health systems, health financing, availability of medicines and pandemics account for the high morbidity and mortality in West Africa (WAHO,2021b).

In 2017 WAHO in collaboration with the NMRAs in West Africa established the ECOWAS-MRH initiative. The main objective of this initiative was to enhance patients' access to quality, safe and efficacious medical products in the sub-region. In 2018 expert working groups consisting of staff of the NMRAs and a steering committee consisting of the Heads of the NMRAs were put in place to develop and approve respectively the guidelines, a harmonised CTD and other documentation to be deployed for this initiative.

In the ECOWAS-MRH initiative, products which are jointly assessed include the following; essential medicines as listed by the WHO, antiretrovirals, antimalarials, medicines for tuberculosis, reproductive health, neglected tropical diseases, medicines for public health emergencies, WHO-prequalified products, stringent regulatory authorities-registered products, biological products including vaccines. These products, upon successful completion of the joint assessment, can then be processed within 60days through an NMRA's registration procedure for a marketing authorisation to be issued. An NMRA is identified to act as coordinator for a period of two years to handle submissions and liaises between WAHO and applicants. Submissions to the joint assessment procedure were processed between approximately 120 and 226 calendar days (ECOWAS, 2021).

From available literature effective and efficient regulatory strategies that are found in a regional medicines harmonization regulatory initiative should be identified and published for other NMRAs and MRH initiative to learn and implement the same accordingly (Ndomondo-Sigonda et al, 2023). This research, therefore aims to evaluate the regulatory review process of the ECOWAS-MRH initiative and that of the participating countries with the goal of improving the evaluation process and enhancing patients' access to medicines within the ECOWAS and beyond.

GOOD REVIEW PRACTICES

"The extent to which a regulatory authority can achieve timeliness of the review (i.e. completion within a specified time frame), as well as predictability, consistency, transparency, clarity, efficiency and high quality, can have a significant impact on public health (for example, in relation to patient's access to important medical products, as well as costs to both government and applicants)" (WHO, 2015a)

Standard operating procedures, templates and other standard best practices which facilitate consistent, transparent, efficient and timely review of dossiers submitted for marketing authorizations are in line with good review practice (GRevPs) guidelines (Liberti et al, 2013; WHO, 2015a).

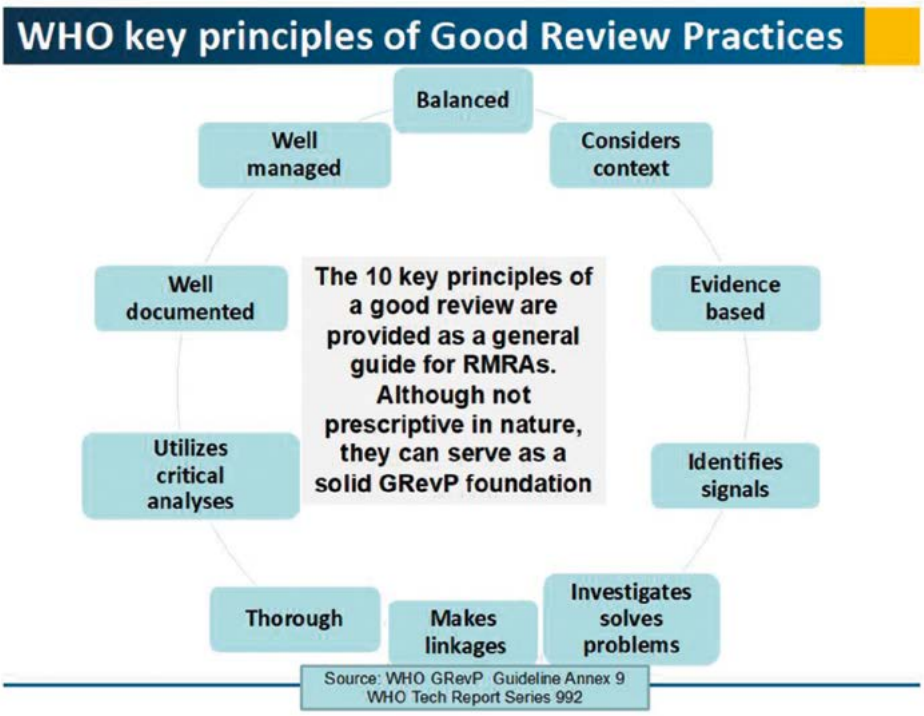
Reviews are a key component of the scientific basis for regulatory decisions whilst GRevPs are a key component of good regulatory practices; which is a requirement of every regulatory authority. Regulatory authorities are encouraged to improve their review processes as this will in turn improve the performance of their regulatory systems. The 10 key principles of a good review (Figure 1.1) have been provided by the WHO with reference to the GRevP parameters that should be implemented by a regulatory authority (WHO, 2015a). Of course, a quality review facilitates a quality decision by a regulatory authority (Liberti et al, 2013).

To be effective and efficient with their reviews, NMRAs are encouraged to implement the key principles of good review practices (WHO, 2015a).

BENEFIT RISK ASSESSMENT

There are variations in the decisions made on the same marketing authorization application submitted by the same manufacturer to different NMRAs, additionally for new active substances decisions are made with regard to uncompleted/on-going studies on safety, quality and efficacy. This is primarily due to different medicines

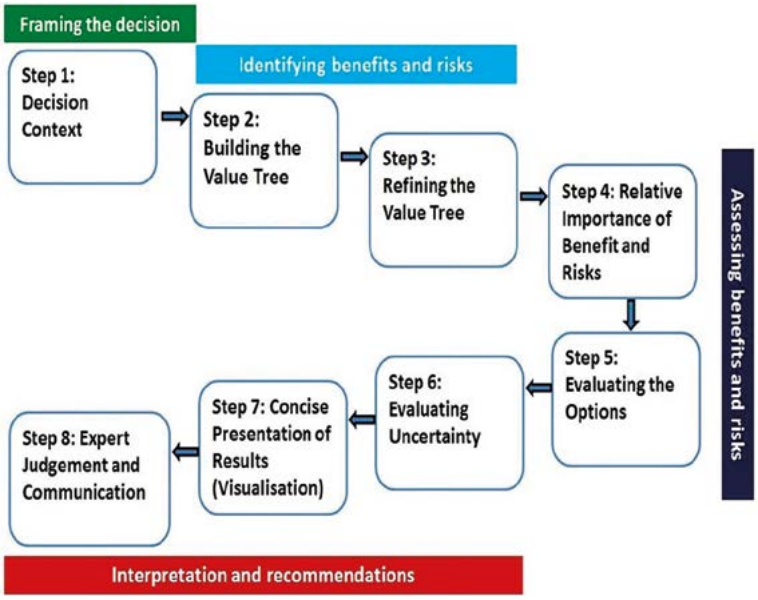
Figure 1.1. The WHO key principles of good review practices.



regulations which are used as references in different NMRAs. In order to reduce or eliminate these variations, it is important that a systematic approach using a widely accepted model for benefit-risk assessment of medicines is utilized by NMRAs and manufacturers in all regulatory review processes (Mussen et al, 2007; Mussen et al 2008). An ideal model should incorporate multi-criteria decision analysis (MCDA) in the systematic approach. The minimum criteria that an ideal model should satisfy include; ability to improve the regulatory review process of the NMRA, ability to consider the data provided by the manufacturer and also other available and relevant data, as well as the ability to be applied throughout the life-cycle of medicines (Mussen et al, 2007). Multi-criteria decision analysis is a requisite for an ideal model as it gives a balanced consideration to the several benefits and risks that may affect a decision. It should be noted that an ideal benefit-risk assessment model is a complementary resource in quality decision making practices by the NMRAs and manufacturers (Mussen et al, 2007; Mussen et al, 2008; Sullivan et al, 2023).

Walker and others (2014) have developed a universal/harmonised methodology for benefit-risk assessment (UMBRA) (Figure 1.2) for the use by both regulators and manufacturers to facilitate transparent decision-making. This framework was developed having considered the existing different frameworks like the FDA 5 -step benefit-risk framework and EMA PrOACT-URL(Problem, Objectives, Alternatives,

Figure 1.2. The UMBRA 8-step benefit-risk framework.



Consequences, Trade-offs, Uncertainty, Risk Tolerance, Linked decisions) framework which are used by the USFDA and EMA respectively as well as the BRAIN (Benefit-Risk Assessment in New and Old Drugs) and the PhRMA BRAT (Pharmaceutical Research and Manufacturers of America Benefit-Risk Action Team) which are used by the pharmaceutical industry. Presently benefit risk assessment is not carried out in any of the agencies in ECOWAS, since it is fundamental to the review of new medicines, it should be incorporated into the regulatory review processes.

QUALITY DECISION-MAKING PRACTICES

Regulatory authorities are responsible for making decisions on medicines during their life-cycle based on evidence. Such evidence may be incomplete initially; however, it evolves during the life-cycle of the medical product. It is therefore of value for the NMRA to have a structured and systematic framework to facilitate the decision-making process and subsequently facilitate its communication to its stakeholders, which is an enviable mark of the efficiency of an NMRA (Goetghebeur et al, 2008). Goetghebeur and others aptly presented the importance of quality decision-making practices by stating that "frequent controversy surrounding drug coverage variation across jurisdictions with similar levels of economic development, values and political systems highlights a need for rational and transparent approaches to decision-making."

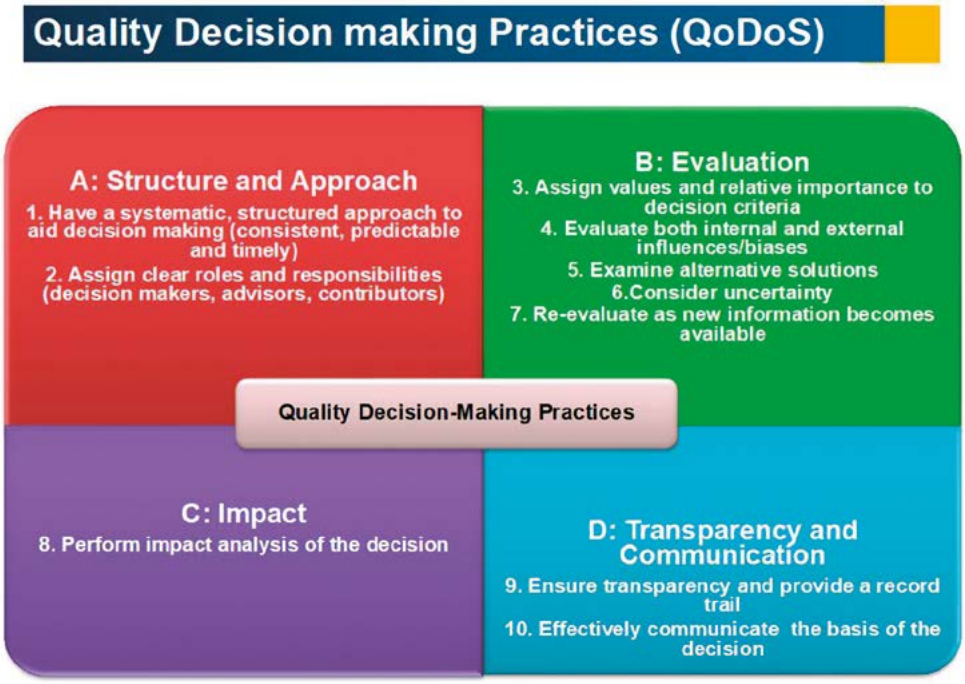
Goetghebeur and others (2008) summarized the four key stages of decision-making as; firstly submission of marketing authorization application dossier/documentation to the NMRA, secondly assessment of dossier and submission of report to a decision-making committee, thirdly decision (approve, defer or reject) made on marketing application and finally publishing a public assessment report to communicate the decision.

Decision-making incorporates both scientific/technical and value judgement. Whilst it can be stated that structures for scientific/technical judgements are usually available in the NMRAs, the same cannot be stated for value judgement. Multi-criteria decision analysis (MCDA) has also been noted as a vital resource to be used to achieve the value judgement component of decision making by the NMRAs (Goetghebeur et al, 2008).

A Quality of Decision-Making Orientation Scheme (QoDoS) (Figure1.3) can be used to facilitate quality decision making by manufacturers and regulators (Liberti et al, 2015a).

Presently the agencies in the ECOWAS region do not appear to have implemented quality decision-making practices; due to its importance to efficient and effective NMRAs, this will be addressed in this research.

Figure 1.3. Quality of Decision-Making Orientation Scheme.



RELIANCE

The relevance of this research will be considered understated if it does not cover the 'hot topic' of reliance as "regulatory reliance is a 21st century best regulatory practice" (Drago et al, 2022)

"The WHO supports reliance among regulators to make the best use of available resources and expertise. This principle allows leveraging the output of others whenever possible while placing a greater focus at national level on value-added regulatory activities that cannot be undertaken by other authorities" (WHO, 2021a).

In 2008, it was reported that manufacturers had little or no interest in the production of medicines to be used in the treatment of neglected tropical diseases however due to the establishment of facilitated regulatory pathways, the WHO has become a pacesetter by recognizing the assessment carried out by other stringent regulatory authorities (SRAs) and listing such products on its website accordingly. This real example of reliance is worth emulating by other NMRAs in order to make medicines which have been assessed by SRA to be readily available in LMICs. (Rago et al, 2008; WHO, 2021a). It is hoped that the African Medicines Agency will fully embrace the concept of reliance just like the WHO.

Saint-Raymond et al (2022) following their review of the reliance approaches that were deployed by regulators to collectively facilitate timely access of vaccines during the COVID-19 pandemic, were right by stating that "Reliance is key to effective access and oversight of medical products in case of public health emergencies".

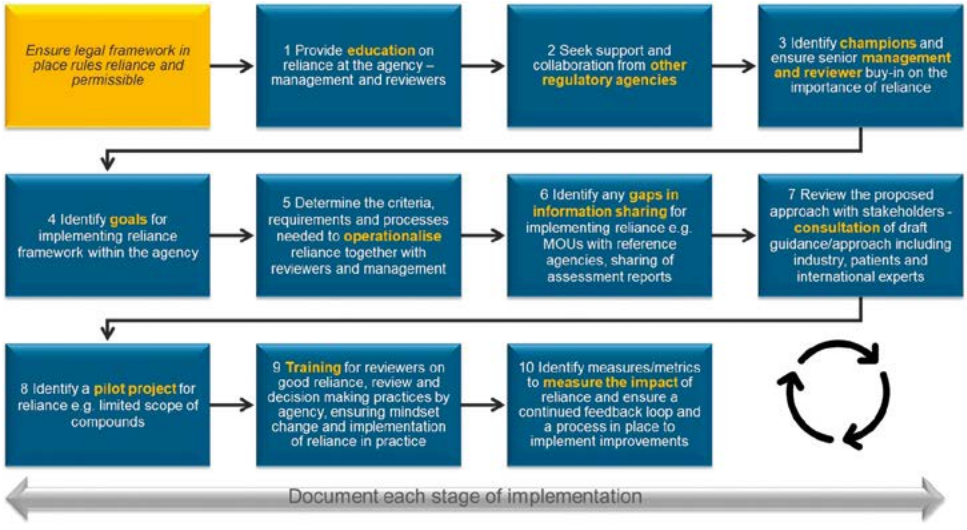
"The purpose of the Good Reliance Practice (GRelP) is to promote a more efficient approach to regulation, thereby improving and expediting access to quality-assured, effective and safe medical products" (WHO, 2021a). The 10-step process in reliance is illustrated in Figure 1.4

DISCUSSION

"The sixty-seventh World Health Assembly resolution 67.20 recognized that inefficient regulatory systems themselves can be a barrier to access to safe, effective and quality medical products" (Azatyan, 2023).

Medicines regulatory harmonisation is a regulatory option to enhance patients' access to medicines in West Africa. This is because on the contrary, regulatory fragmentation results in reduced access to quality medicines arising from longer timelines and increased cost of registering medicines in sub-saharan Africa. The removal of regulatory barriers by encouraging harmonisation as well as reliance tends to promote efficiency thereby making it an incentive for applicants to pursue this route (Barton et al, 2019; Ndomondo-Sigonda et al (2023).

Figure 1.4. The 10-step process in reliance.



Some authors are of the view that greater stakeholders' (NMRAs, manufacturers and patients) commitment and involvement in medicines regulatory harmonisation and innovation in sub-Saharan Africa will enhance patients' access to medicines in Africa (Barton et al, 2019). Ndomondo-Sigonda et al (2023) accurately reported that "industry has important insights" from their recent study. It appears that the ECOWAS-MRH initiative though relatively new, has been predominately run by the regulators with minimal or no input from the industry. This is somewhat a departure from the history of regulatory harmonisation in that both regulators and manufacturers worked together for their mutual benefit.

There is an urgent need to provide all the technical and financial support to the other NMRAs in the sub-region to enable them to work to attain at least WHO maturity level 3. This will enable these countries to assist in diligently assessing submissions, share the workload of Ghana and Nigeria, complete assessments on time, speed up the issuance of marketing authorizations and ultimately enabling manufacturers to expedite patients' access to medicines.

As part of this research, the views of both regulators and manufacturers regarding the effectiveness and efficiency of the ECOWAS-MRH will therefore be collated and presented. This will enable stakeholders have a current detailed view of the ECOWAS-MRH initiative.

According to the literature, some decision-making frameworks have been developed and others are in their various stages of development; however, they require validation in order to be accepted by the global community. Other frameworks have been found to be complicated to use and could increase the workload of the NMRAs, thereby reducing the efficiency of the NMRAs (Goetghebeur et al, 2008). It has been reported in the literature that the decision-making processes of most NMRAs are not well structured to facilitate communicating decisions to the public in order to promote transparency (Goetghebeur et al, 2008).

"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. Divergent regulatory decisions can be better communicated using structured frameworks" (Liberti et al, 2013)

It is recommended that an ideal decision-making framework should be able to simplify the decision-making process of the NMRAs. This when implemented will promote transparency and accountability and also enable stakeholders to appreciate the rationale for and ultimately accept sound regulatory decisions (Goetghebeur et al, 2008).

As "benefit-risk assessment is an integral part of FDA's regulatory review of marketing applications for new drugs and biologics" this research will present a strong case to encourage NMRAs in Africa to incorporate a structured benefit-risk assessment framework in making their regulatory decisions (USFDA, 2022a).

As the WHO recognizes reliance to be an "option to facilitate good quality regulatory decision" (Azatyan, 2023) and there is also an expert opinion that " reliance approaches facilitate regulatory approvals and allow a more efficient use of resources, ultimately serving patients by facilitating earlier access to quality assured, safe and effective medicines" (Saint-Raymond, 2022) this research will make strong recommendations to NMRAs in LMICs to implement GRelP in order to enjoy all the associated benefits.

"If implemented effectively, good regulatory practices can result in consistent regulatory processes, sound regulatory decision-making, increased efficiency of regulatory systems and better public health outcomes" (WHO TRS 1033, 2021)

Looking ahead, this research supports the view of Saint-Raymond et al (2022) that "the WHO initiative for the establishment of the WHO Listed authorities will also create opportunities for reliance, as it will clearly define which regulatory authority can be relied upon and for which specific regulatory function".

CHAPTER 02

THE REGULATORY REVIEW PROCESS IN THE ECOWAS REGION: THE CASE OF THE FDA GHANA

SUMMARY

The summary of the study is as follows:

- This study aimed to assess the current regulatory review process of the Food and Drugs Authority (FDA) Ghana by identifying key milestones, target timelines, good review practices and quality decision-making practices and evaluating the overall regulatory performance from 2019 to 2023, as well as the challenges and opportunities for improvement.
- The FDA Ghana representatives completed the Optimising Efficiencies in Regulatory Agencies (OpERA) questionnaire, including data identifying the milestones and overall approval times for all products registered by the FDA Ghana from 2019-2023.
- Of the products approved from 2019 to 2023, 5% were new active substances processed by full or abridged review pathways.
- Regardless of the review model used, the highest median decision time for new active substances was 374 calendar days; this was in 2021 due to the impact of the pandemic.
- Guidelines, standard operating procedures and review templates were in place and the majority of indicators for good review practices were implemented. Several quality decision-making practices were implemented, although currently there is not a systematic structured approach.
- The FDA Ghana monitors regulatory performance and currently meets its target timelines. To achieve World Health Organization Maturity Level 4 status, an electronic tracking system, benefit-risk assessment framework and template and the publication of assessment reports are recommended.

INTRODUCTION

Ghana National Medicines Regulatory Authority

Medical products, which include medicines, vaccines and medical devices form a core component of a national healthcare system. Ensuring the availability of high-quality, safe and effective medical products through the establishment of effective and efficient national medical regulatory authorities (NMRAs) is a country's responsibility to protect public health and safety (Ndomondo-Sigonda et al, 2017). The Food and Drugs Authority (FDA) Ghana is the national medicines regulatory authority legally mandated by Parts 6,7 & 8 of the Public Health Act 2012 (Act 851) to safeguard the safety, quality and efficacy of food and medical products in Ghana. The FDA Ghana's vision is to "protect the health and safety of people in Ghana and to be a global centre of excellence for food and medical product regulation" (Ministry of Health, 2012; FDA Ghana, 2022).

The Food and Drugs Authority was established as the Food and Drugs Board (FDB) in 1997, following the enactment of the Food and Drugs law (PNDCL 305B) in 1992. The law was updated by the Food and Drugs (Amendment) Act 523 in 1996. The FDB operated as an authority of the Ministry of Health in Ghana to regulate medicinal products for human and veterinary use, medical devices, household chemical substances, cosmetics as well as food. Following the establishment of the FDB, the authority was transformed into the Food and Drugs Authority (FDA) upon the enactment of the Public Health Act 2012 (Act 851) (FDA Ghana, 2022).

Currently in Africa, the NMRAs in Ghana, Tanzania, Nigeria, Egypt, Zimbabwe, Senegal, Rwanda and South Africa are the only agencies to have achieved the World Health Organization Global Benchmarking Tool (WHO GBT) maturity level 3 status. On a scale of 1 to 4, the WHO GBT maturity level measures how stable, well-functioning and integrated a country's regulatory systems performs. The common regulatory functions of an NMRA are registration and marketing authorisation, regulatory inspection, licensing of manufacturing and storage facilities, post-market surveillance, vigilance, quality control and clinical trials oversight. It is the case in most countries that medical products are first registered before they can be made available to patients (WHO, 2022a; WHO, 2022b; WHO,2024c).

Ghana, one of 15 countries in West Africa, has a population of about 31 million, with a median age of 21.5 years and a life expectancy at birth of 64.1years (GSS, 2021; Worldometer, 2022; The World Bank, 2022). In West Africa, the FDA Ghana is respected by other NMRAs, as a result of its regulatory standing in the region.

2

A robust NMRA supports the national healthcare system by ensuring the availability of safe, high-quality and effective medicines to patients, thus it is imperative that the FDA Ghana undergoes routine performance evaluation to ascertain its effectiveness and efficiency in discharging its mandates (Dansie et al, 2019; Ball, 2016). The WHO GBT has been used to assess NMRAs for regulatory-system strengthening and it is expected that when all the benchmarks are achieved and maintained, the regulatory capacity of an NMRA will be enhanced to deal with health emergencies, including pandemics (WHO, 2019a). The GBT evaluates the overarching national regulatory systems, which include registration and marketing authorisation, market surveillance and control, regulatory inspection, vigilance, licensing establishments, clinical trial oversight, laboratory testing, and national regulatory authority lot release (Khadem et al, 2020).

The aim of this chapter was to evaluate the regulatory review process of the FDA Ghana with the view to identifying the challenges and opportunities for improvement.

STUDY OBJECTIVE

Since the regulatory review process and performance of Ghana FDA had not been evaluated to date, this study would form a baseline for the authority moving forward.

As the FDA Ghana has achieved WHO GBT maturity level-3 status and is also an active NMRA in the Economic Community of West African States-Medicines Regulatory Harmonisation (ECOWAS-MRH) initiative, its strengths and opportunities for improvement will serve as a valuable reference for other NMRAs that are striving to achieve higher maturity levels.

The objectives of this study were to:

1. Assess the current regulatory review process of the FDA Ghana
2. Identify the key milestones and target timelines achieved in the review process
3. Evaluate the overall performance for the review models and different product types approved in Ghana during the period 2019 –2023.
4. Assess the authority's compliance with good review practices and quality decision-making practices employed in the review process.
5. Identify the challenges and opportunities for an enhanced regulatory review process in Ghana, with a view to expediting patients' access to lifesaving medicines.

METHODS

Data Collection Process

The review processes and practices within the FDA Ghana were assessed using the Optimising Efficiencies in Regulatory Agencies (OpERA) questionnaire which was developed by the Centre for Innovation in Regulatory Science (CIRS) for the assessment of regulatory review processes in emerging economies (McAuslane et al, 2009). This questionnaire is a unique regulatory-strengthening tool that enables all critical information necessary to assess a regulatory authority's performance to be documented systematically (Centre for Innovation in Regulatory Science, 2020). It can be utilised to monitor regulatory performance, enable comparisons with other regulatory authorities in order to evaluate good regulatory practices as well as to encourage the systematic monitoring of regulatory processes. The questionnaire was completed by senior assessors of the FDA Ghana and verified by the responsible Directors and agreed by the Chief Executive Officer.

The questionnaire consists of six parts:

Part 1: Organisation of the agency - this documents information on the structure, organisation, and resources of the authority.

Part 2: Types of review models - this identifies the different types of review models (verification, abridged, full) used to assess applications for marketing authorisation, including the extent to which applications are evaluated with regard to how an authority might rely on the results of assessments and reviews carried out by a reference authority.

Part 3: Key milestones in the review process - this captures information on the key milestones in the review process as well as providing a validated process map, which includes receipt of the dossier, validation and screening, questions to the sponsor and the final decision on approval or refusal of a product for registration. Data were collected for new active substances (NASs) and generics during the period 2019–2023.

Part 4: Good Review Practices (GRevP) - this enables the evaluation of how quality is built into the regulatory review process by examining activities that have been adopted to improve the consistency, transparency, timeliness and competency of the review process.

Part 5: Quality Decision-Making Practices - this explores information on the quality of the decision-making practices and whether the authority has measures in place to ensure that quality decisions are made about the data obtained during the registration process.

Part 6: Concluding observations-this provides the authority's own perception of its unique positive qualities and the major impediments it faces in carrying out the review of new medicines and making them available to meet patients' needs.

RESULTS

The results are presented in the following sequence: organisation of the authority; types of review models; key milestones in the review process; good review practices-building quality into the regulatory process, quality decision-making practices and concluding observations.

Part I - Organisation of the authority

The FDA Ghana is an authority of the Ministry of Health. It has a staff capacity of 683 across all the 16 regions of the country. The authority has 26 reviewers comprising 25 pharmacists and one scientist, who holds a PhD in Pharmaceutical and Biological Chemistry. These reviewers are responsible for the scientific assessment of marketing authorisation applications.

The FDA regulates medicinal products for human and veterinary use as well as medical devices and in-vitro diagnostics. The authority's scope of activities includes registration and marketing authorisation, market surveillance and control, regulatory good manufacturing practice (GMP) inspection, vigilance, licensing establishments, clinical trial oversight and laboratory testing.

The authority sets target timelines for the scientific assessment of applications as well as for the overall timeline for the review and decision of such applications. A Certificate of a Pharmaceutical Product (CPP) is a requirement only for products manufactured outside the country and must be provided before authorisation is issued. Questions to sponsors are batched at fixed points in the review procedure.

In addition, the authority recognises medical urgency as a criterion for accelerating the review process for qualifying products. Quality, safety, and efficacy are reviewed sequentially for generics since each assessor has been equipped with the technical expertise to conduct full assessment for each generic application. In the case of NASs, quality, safety and efficacy are reviewed in parallel, since assessors have some

limitations with regard to the specialised expertise required to conduct full assessment; the different modules of the dossier for NASs are therefore reviewed in parallel by different assessors who have the different requisite expertise. Price negotiation is not considered as part of the review and authorisation process.

For sample testing, the focus is on checking quality in the marketplace, therefore, it does not delay decisions on marketing authorisation applications. The authority recognises the value of continuous quality improvements in increasing transparency, improving the overall consistency and predictability of the regulatory process. As part of its quality management system, the authority has adopted several quality improvements tools to ***monitor and improve the quality of its review process.

Standard operating procedures have been implemented as part of measures to enhance the quality of the process, whilst assessment templates are used to standardise the format and content of written reports. Transparency with stakeholders is central to the overall regulatory process at the FDA Ghana. Application fees are charged based on the type of marketing authorisation application (NASs and generic medicines). Applicants are encouraged to contact the Agency (via telephone or email) during product development, pre-submission and assessment with the possibility of meetings where necessary. The Agency does not however charge a fee to provide scientific advice.

This section of the results has addressed objective 1 (to assess the current regulatory review process of the FDA Ghana) and objective 5 (to identify the challenges and opportunities for an enhanced regulatory review process in Ghana), with a view to expediting patients' access to life-saving medicines.

Part II - Types of Review Models

The FDA Ghana carries out three types of established regulatory reviews namely verification, abridged and full. Within each review category, there is a consideration for an additional priority/fast track review application when the need for rapid assessment is required for patients' access to medicines.

A verification review is applied based on the recognition of an authorisation by a reference or benchmark authority such as the WHO. The verification process is used to validate the status of the product and ensure that the product for local marketing conforms to the authorised product. The letter of authorisation from the WHO prequalification programme is accepted by the FDA Ghana as evidence of a positive

WHO prequalification. The dosage form, strength, ingredient(s), indication(s), dosage, warnings, and precautions must be identical to the authorised product. A completed dossier in the Common Technical Document (CTD) format, including data for all modules must be submitted.

An abridged review is applied on the pre-requisite that the product has been previously approved by a stringent regulatory authority such as the United States Food and Drug Administration (US FDA), United Kingdom Medicines and Healthcare products Regulatory Agency (UK MHRA), Health Canada or those reviewed by the European Medicines Agency (EMA) centralised registration procedures. An abridged assessment is carried out in relation to the benefit-risk assessment of the product under local conditions. In these reviews, the dosage form, strength, ingredient(s), indication(s), dosage, warnings and precautions must be identical to the authorised product and a complete dossier in the CTD format, including identical data for all modules must be submitted.

A full review is carried out by the authority in all other situations since it is capable of carrying out a full assessment of quality, pre-clinical (safety), and clinical (efficacy) data. Information on prior registration elsewhere may be a pre-requisite to final authorisation and the dosage form, strength, ingredient(s), indication(s), dosage, warnings and precautions must be identical to the authorised product. A completed dossier in the CTD format including data for all modules must be submitted.

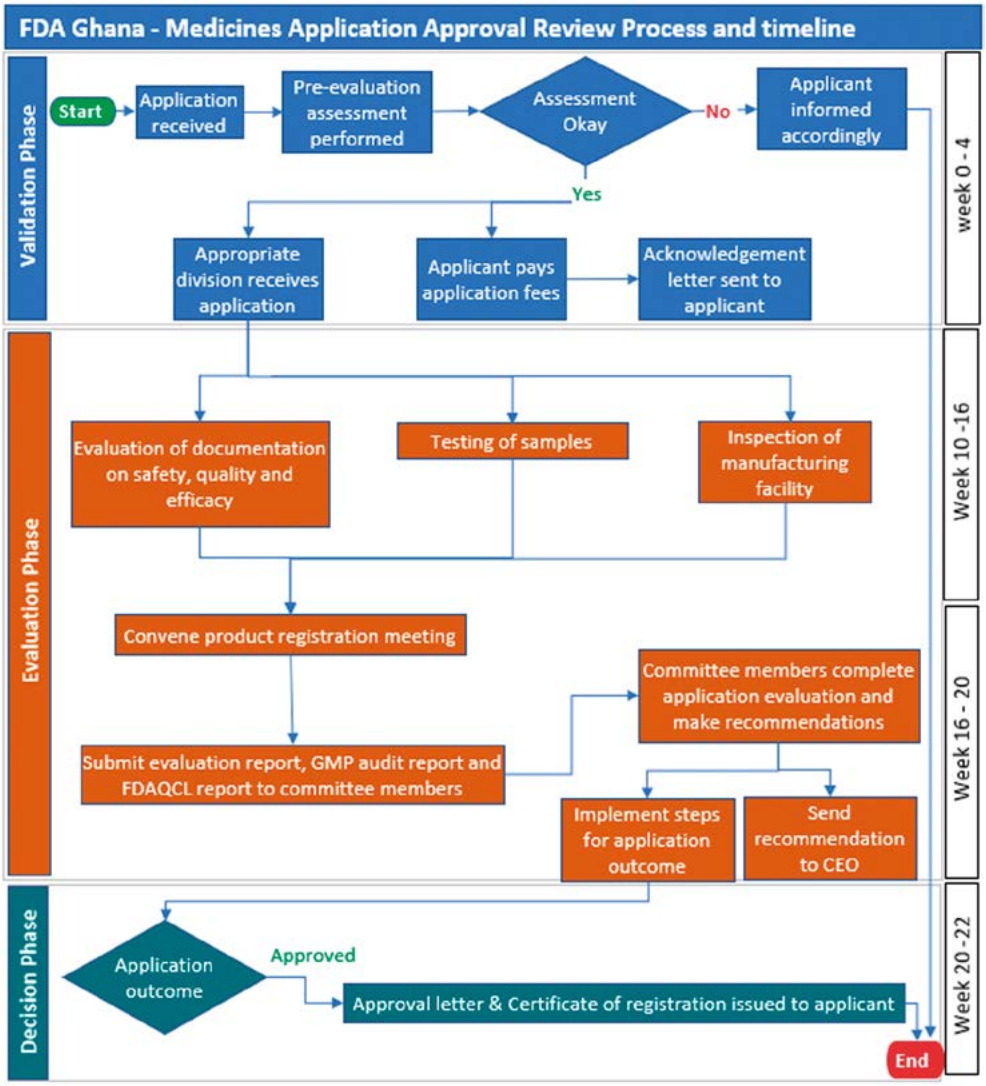
Priority/Fast track review applications, where there is a need, are considered within the same category of applications. A rapid assessment is carried out to obtain pharmacological, marketing/commercialisation, pharmacovigilance and clinical trials information. A completed dossier in the CTD format, including full data for all modules must be submitted.

This section of the results has addressed objective 1 (to assess the current regulatory review process of the FDA Ghana) and objective 5 (to identify the challenges and opportunities for an enhanced regulatory review process in Ghana), with a view to expediting patients' access to life-saving medicines.

Part III - Key milestones in the review process

A map of the review process and timelines for applications by the FDA Ghana is provided (Figure 2.1) showing the three phases in the review process, namely validation, evaluation and decision.

Figure 2.1. Regulatory Review Process Map for Ghana showing target times in calendar days.



The Map represents the review and authorization of a product that goes to approval after one review cycle.

The review process is presented in a format that correlates with the key milestones in the review procedure. It should be noted that the process map is a simplified representation of the main steps in the full review of an application and represents the review and authorisation of a product that is approved in the first cycle. The map

does not include a second cycle for products approved subject to the submission of additional data nor does it include the steps that follow the refusal of an application, such as hearings or appeals.

The key points in the review procedure by the FDA Ghana include receipt and validation, scientific assessment including review by the Product registration committee and authorisation. A detailed description of the keys points is presented in Figure 2.1.

Validation phase. Within a month of receipt of the submission in the common technical document (CTD) format for marketing authorisation, the application is validated for completeness and acceptance is formally recorded. A new application is held in a queue before the start of scientific assessment. Priority products are, however, taken out of the queuing system. Applications are assessed on a first in first out (FIFO) basis unless the product meets the classification criteria for expedited review process as set out in the FDA's guidelines for registration of pharmaceutical products.

An application is classified as priority and may be expedited if the product is for any of the following reasons; public health programmes (including HIV/AIDS, malaria, tuberculosis, reproductive health, neglected tropical diseases, expanded programme of immunization), paediatrics, Ministry of Health tender purposes, WHO prequalification-Collaborative registration process and any other disease conditions as may be determined by the FDA from time to time). The timeline for processing priority applications is three months. The FDA Ghana does not regard the backlog of applications as a problem, as the technical capacity of assessors enables them to process applications efficiently.

Evaluation phase: The scientific assessment is carried out by technical staff of the authority who are assigned to review the quality, safety, and clinical documentation. Questions are collected into a single batch and sent to the sponsor. An applicant can hold meetings with the authority staff following the receipt of questions from the authority that arise during the assessment. There is no "clock stop", therefore the overall review and decision time includes the time taken by the applicant to respond. Evaluation of dossier (documentation on safety, quality and efficacy), laboratory analysis of samples and inspection of manufacturing facility are conducted, and the respective reports are presented to a high-level committee, referred to as the Drug Registration Committee for review. The Drug Registration Committee meets each month and makes final decisions to grant or refuse marketing authorisations.

Decision phase: This authorisation procedure is dependent on sample analysis and inspection of the manufacturing facility, which are conducted in parallel with the scientific review. The procedure is duly completed following the issuance of a certificate of registration for the product.

Summary of applications registered from 2019 – 2023

There was a successive annual increase in the number of products approved in the period from 176 in 2019 to 235 in 2020 to 362 in 2021 to 925 in 2022; there was however a reduction in 2023 where 597 approvals were recorded. The observed increased trend is mainly attributed to an 80% reduction of marketing authorisation application fees in January 2020 to $240, $360 and $300 per annum for generic medicinal products, new chemical entities and biological products, respectively. Along with the 80% decrease in application fee, a verification fee of 0.80% of the CIF (Cost, Insurance and Freight) value was introduced for imported regulated products.

Applicants preferred this option since they only had to pay comparatively a small application fee at the time of applying for marketing authorisation and then pay the verification fee at the time of importing each consignment of the product into the country. More importantly, the Agency is able to increase its revenue with this approach. This is therefore a win-win strategy for the Agency and the Industry. This enabled sponsors to submit more applications at a lower cost and consequently resulted in an increase in the number of marketing authorisations granted.

Characteristics of new active substances registered between 2019- 2023

During the period 2019-2023, 106 NASs were registered by the FDA Ghana (Table 2.1). Whilst the highest number of NASs were registered in 2022 the least number of approvals was recorded in 2023.

The majority of the products (NASs and generics) were reviewed using the full review model whilst a relatively few applications were reviewed using the abridged model.

Characteristics of generics registered between 2019-2023

During the period 2019-2023 a total of 2,149 generic products were registered by the FDA Ghana (Table 3.1). Whilst the highest number of generics were registered in 2022 the least number of approvals was recorded in 2019.

In general, the generics reviewed by the verification pathway were for the treatment of HIV/AIDS, malaria, tuberculosis, diarrhoea, COVID-19 related therapies and

Table 2.1. Characteristics of products registered between 2019-2023.

Characteristic		Approval Year					
		2019	2020	2021	2022	2023	2019 – 2023
Overall		176	235	362	925	597	2295
Review Type	Verification	3	0	0	12	3	18
	Abridged	3	7	14	61	60	145
	Full	170	228	348	852	534	2132
Priority Review	Yes	18	29	68	129	84	328
	No	158	206	293	796	513	1966
	Unknown	0	0	1		0	1
Compound Type	New Active Substance	20	18	23	28	17	106
	Generic	156	217	339	889	548	2149
	Pre-qualified generic	0	0	0	8	32	40

Please note that differences exist between the numbers in this table and the n numbers in the follow graphs. This is due to a small number of negative durations calculated where milestones provided were not in chronological order.

reproductive therapeutics. The review types and numbers reflect the large volumes of generic applications compared with NASs originating from low- and middle-income countries (LMICs) (Thambavita et al, 2018).

Overall decision timelines for registered products

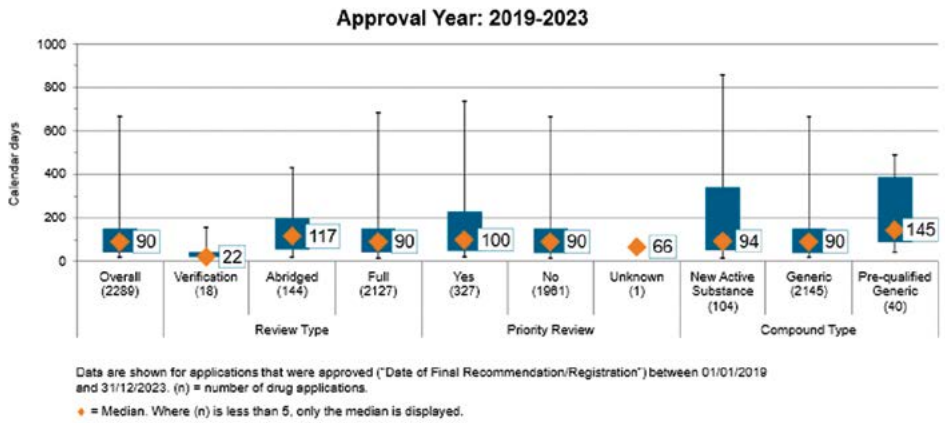
The overall timelines for all products (combined NASs and generics) over the period 2019-2023 are shown in Figure 2.2.

During this period, the overall median approval time was 90 days. With regard to the review type, the median approval time was 22 days (verification), 90 days (full) and 117 days (abridged). This demonstrates the range in approval times, with the diamond representing the median value, the box the range between the 25th and the 75th percentile, while the whiskers represent the outliers, which are the 5th and 95th percentiles. This visual representation fully describes the regulatory burden for the FDA Ghana. Not surprisingly, the median value for the 2145 generic products was also 90 calendar days, while the median value for the 104 NASs was 94 calendar days. These review times were within the target decision timeline of 266 calendar days (as per the FDA Ghana website).

Overall decision timelines for new active substances

The overall decision time for NASs registered between 2019-2023 are displayed in Figure 2.3. During this period, the median decision times for ranged from 56 calendar days (16 NASs) in 2023 to 374 calendar days (23 NASs) in 2021. It is of interest to note that during 2021, overall approval time was the highest and this was due to the impact of the covid pandemic.

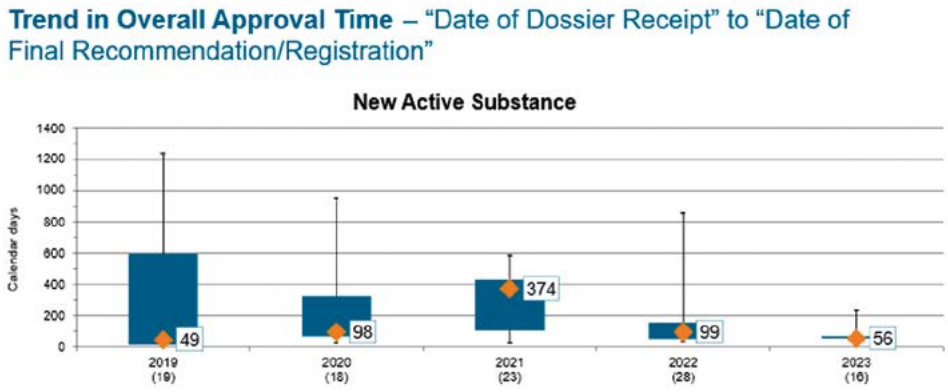
Figure 2.2. Overall decision times for all products between 2019 – 2023.



Data are shown for applications that were approved ("Date of Final Recommendation/Registration") between 01/01/2019 and 31/12/2023. (n) = number of drug applications.

♦ = Median. Where (n) is less than 5, only the median is displayed.

Figure 2.3. Overall decision times for new active substances from 2019 – 2023.



Data are shown for applications that were approved ("Date of Final Recommendation/Registration") between 01/01/2019 and 31/12/2023. (n) = number of drug applications.

♦ = Median. Where (n) is less than 5, only the median is displayed.

Overall decision timelines for generics

The overall decision time for generics registered between 2019-2023 are displayed in Figure 2.4. The overall decision time for generic products during the period 2019-2023 encompassing the three different regulatory pathways (verification, abridged and full) are shown in Figure 3.4. The majority of products were subject to full review within consistent decision times of 175 calendar days in 2019 (152 generics) and 175 calendar days in 2020 (217 generics) and reduced to 56 calendar days (548 generics) in 2023.

The overall decision time for all product applications during the period 2019-2023 encompassing the different product categories (NASs, generics and prequalified generics) are shown in Figure 3.5. Except for 2019 when the median approval time was 161 days, the median approval time showed improvement with a progressive decrease in the median time from 173 days in 2020 to 57 days in 2023.

Figure 2.4. Overall decision times for generics from 2019 – 2023.

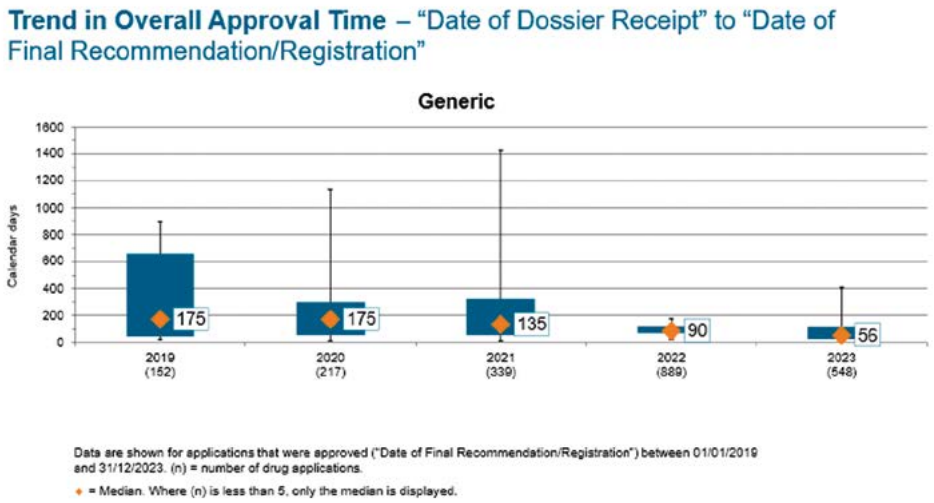
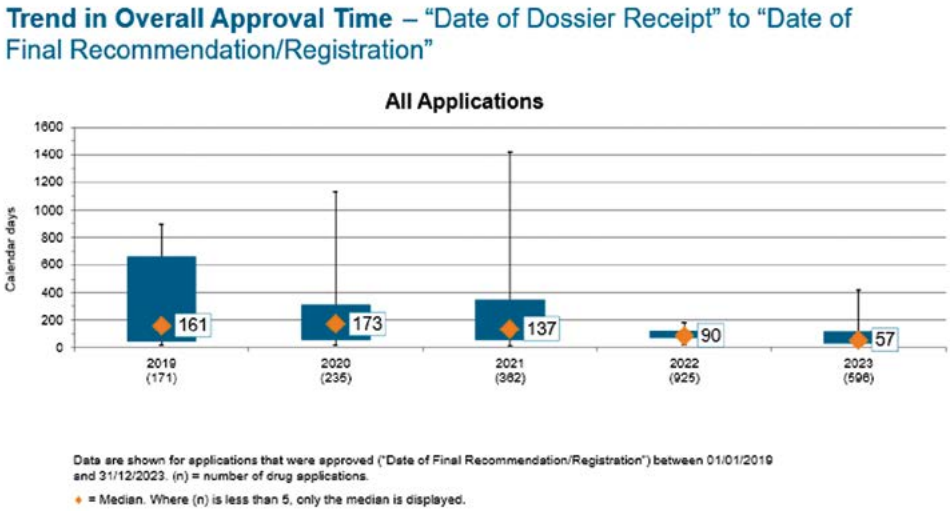


Figure 2.5. Overall decision times for all product applications from 2019 – 2023.



This section of the results has addressed objective 1 (to assess the current regulatory review process of the FDA Ghana), objective 2 (to identify the key milestones and target timelines in the review process), objective 3 (to evaluate the overall performance for the review models as well as the different product types approved in Ghana during the period 2019 to 2022) and objective 5 (to identify the challenges and opportunities for an enhanced regulatory review process in Ghana), with a view to expediting patients' access to life-saving medicines.

Part 4 - Good Review Practices (GrevP) - building quality into the regulatory process

The authority has implemented some quality measures in the review and authorisation of medicinal products as summarised in Table 2.2.

Quality and Transparency Measures

Ensuring quality and transparency in a pharmaceutical regulatory system improves patients' access to quality, safe and effective medicines. (Paschke et al, 2018). FDA Ghana identified three important measures as necessary for the management of quality and these include measures for ensuring consistency and increasing transparency and achieving stakeholder satisfaction. FDA Ghana achieved International Organization for Standardization (ISO) 9001:2015 certification in June 2017, affirming the FDA Ghana commitment to meeting international process standards to help provide quality products and services. This certification is assiduously maintained by the authority and there is a dedicated department with staff involved in assessing and/or ensuring quality in the registration process which is carried out annually under the supervision of the Deputy Chief Executive Officer.

Official guidelines to assist the industry are available, in English, through the authority website and on request by stakeholders.

Pre-application scientific advice is given to applicants and discussions are held with reference to the applicable guidelines, which ensures consistency in the information shared with applicants. Applicants are encouraged to engage with the Agency early in the product development process to assure there is clarity on needed data points and components in the dossier.

A pool of internal assessors is available to review dossiers and to provide detailed assessment reports, clinical opinions on the product and technical advice to the authority**.**

Table 2.2. Status of implementation of good review practices by the FDA Ghana.

Indicator	Status	Comments
Quality measures		
Internal quality policy	✓	The agency however considers that the existing GRevP framework could be improved since the quality system is still evolving
Good review practice system	✓	
Standard operating procedures (SOPs) for guidance of assessors	✓	
SOPs for the product registration committee consulted during the review process	✓	
Assessment templates	✓	The elements that are in the agency's assessment template include: drug substance, drug product, comments on ;label and questions for sponsors
Assessment report	✓	The agency prepares assessment reports (AR) in English. The agency does not share AR with other regulatory authorities. The agency does not put its AR on its website Sponsors do not get a full copy of the AR.
SOP for completing the assessment report	✓	
SOPs for any other procedures in the regulatory review process (e.g., validation)	✓	
Dedicated quality department	✓	
Scientific committee	✓	
Shared and joint reviews	✓	
Transparency and communication parameters		
Feedback to industry on submitted dossiers	✓	
Details of technical staff to contact	✓	
Pre-submission scientific advice to industry	✓	
Official guidelines to assist industry	✓	
Industry can track progress of applications	✓	
Summary of grounds on which approval was granted	✓	
Approval times	✓	
Advisory committee meeting dates	✓	
Approval of products	✓	
Continuous improvement initiatives		
External peer review	x	External peer reviews are not carried out when an NAS application is assessed, and there are no plans to introduce these within the next two years.
Internal peer review	✓	Internal peer reviews are carried out when an NAS application is assessed.
Internal tracking systems	x	
Review of assessors' feedback	✓	
Reviews of stakeholders' feedback	✓	
Training and education		
Training programme for assessors	✓	
International workshops/conferences	✓	
External courses	✓	
In-house courses	✓	
On-the-job training	✓	
External speakers invited to the authority	✓	
Induction training	✓	
Sponsorship of post-graduate degrees	✓	
Placements and secondment in other regulatory authorities	✓	

Key

✓ Formally implemented

✓ Informally implemented

x Not implemented

The Drug Registration Committee, which is an internal Committee in turn reviews all applications by reviewing the assessment reports, GMP audit reports and sample testing and makes decisions on the granting of marketing authority to the authority.

In order to improve the quality of applications and the scientific review, the following measures have been implemented:

The authority participates in the West African Health Organization (WAHO) regional harmonization initiative and has conducted shared or joint reviews with other regulatory authorities. There are formal measures in place to ensure consistent quality during the review through the WAHO Joint Assessment and this work-sharing process has had a positive impact on the work of the authority in general. In addition, bilateral and multilateral information-sharing agreements are in place with other jurisdictions with a collaborative procedure and are part of participation in the WHO Prequalification procedure and the WHO PQ-NMRA Collaborative Review Process.

The authority assigns high priority to being open and transparent in its relationships with the public, health professionals and the pharmaceutical industry. The authority is driven by three incentives for assigning resources to activities that enhance the openness of the regulatory system. This includes the need to provide assurances on safety safeguards, to increase confidence in the system and to efficiently meet and address the healthcare of the population. The FDA Ghana informs the public about authority regulatory activities by providing information on approved products on their website. Companies can follow the progress of their applications by telephone and e-mail contact, and they are also given detailed reasons for rejection of their applications. There is no electronic system for registering and tracking sponsor applications; however, there are plans to introduce such a system by the end of 2025.

Continuous Improvement Measures

The FDA Ghana has addressed the training and continuing education needs of assessors by modelling WHO recommendations that have been adopted by the EMA and the Federal Institute for Drugs and Medical Devices (BfArM), often providing training in collaboration with other mature agencies. The authority acknowledges the importance of having measures in place to continually improve the review process (Obeidat et al, 2014) and one important strategic measure is to ensure that assessors acquire international technical expertise to order to process applications in an efficient manner. The authority also participates in international workshops and training programmes (Gordon, 2009).

This section of the results has addressed objective 1 (to assess the current regulatory review process of the FDA Ghana), objective 4 (to evaluate how the quality of the process of decision making is built into the regulatory review process of medicines) and objective 5 (to identify the challenges and opportunities for an enhanced regulatory review process in Ghana), with a view to expediting patients' access to life-saving medicines.

Part 5 - Quality Decision-making practices

The authority implements certain aspects of the quality decision-making practice framework as the basis to approve or reject a marketing authorisation application, as summarised in Table 2.3.

The FDA Ghana has measures in place to minimise the impact of subjective influences/ biases on the authority's decision-making process to either approve or reject a marketing authorisation application. The roles and responsibilities of the regulator, manufacturers and national and international stakeholders have been defined and communicated on the authority's website.

The FDA Ghana is making progress to have a systematic, structured approach to quality decision-making practices and to periodically measure the impact of its decision to approve or reject a marketing authorisation application.

This section of the results has addressed objective 1 (to assess the current regulatory review process of the FDA Ghana), objective 4 (to evaluate how the quality of the process

Table 2.3. FDA Ghana Quality Decision-Making Practices.

Practice	Implemented into framework		Adhered to in practice	
	Fully	In progress	Fully	In progress
1. Have a systematic, structured approach		✓		✓
2. Assign clear roles and responsibilities (decision makers, advisors, information providers)	✓		✓	
3. Assign values and relative importance to decision criteria	✓		✓	
4. Evaluate both internal and external influences/biases	✓		✓	
5. Examine alternative solutions	✓		✓	
6. Consider uncertainty	✓		✓	
7. Re-evaluate as new information becomes available	✓		✓	
8. Perform impact analysis of the decision		✓		✓
9. Ensure transparency and provide a record trail	✓		✓	
10. Effectively communicate the basis of the decision	✓		✓	

of decision making is built into the regulatory review process of medicines) and objective 5 (to identify the challenges and opportunities for an enhanced regulatory review process in Ghana), with a view to expediting patients' access to life-saving medicines.

Part 6 – Concluding observations

The effectiveness and efficiency of the FDA Ghana review procedures and decision-making practices for medicinal product applications are enhanced by the continuous professional training of staff and the continuous internal audit of review processes as well as the development of published timelines for all the critical stages of the review. However, insufficient data for a product, unsatisfactory GMP compliance or substandard dossier submission can inhibit the timely approval of medicinal products by the authority.

This section of the results has addressed objective 1 (to assess the current regulatory review process of the FDA Ghana), objective 4 (to evaluate how the quality of the process of decision making is built into the regulatory review process of medicines) and objective 5 (to identify the challenges and opportunities for an enhanced regulatory review process in Ghana), with a view to expediting patients' access to life-saving medicines.

DISCUSSION

The WHO has recently reported that globally only about 30% of medicine regulatory authorities are performing to the basic, minimal standard expected of a regulatory authority. In view of this, the WHO is exploring various solutions to address this problem. One of these is the introduction of a WHO-listed Authorities (WLA) programme for regulatory authorities. When fully instituted - after an interim transitional period of five years - it will apply to NRAs who have achieved an overall ML3 accreditation by WHO (this is required to be eligible for WLA consideration) and who have, in addition, achieved ML4 either overall or in specific Global Benchmarking Tool modules for which the NRA wishes to be recognised as an WLA. Finally, the NRA will need to have demonstrated its ability to maintain this level of performance to WHO's satisfaction for a stated period. When fully implemented, this will signal to the global community that such WLA agencies are those on whom agencies can rely as reference agencies with confidence, if they choose. Currently eight countries in Africa (Egypt, Ghana, Nigeria, Rwanda, Senegal, South Africa, Tanzania and Zimbabwe) have national medicine regulatory agencies that have reached ML3 status (i.e., eligible for WLA, when the programme is fully implemented) [WHO, 2023b].

The authority employs the three established regulatory review models for assessing marketing authorisation applications. The extent to which quality, safety and efficacy data are assessed depends on the review model. The first and final milestone dates in the review process are the receipt of the application and the registration approval date. Currently, there is not an electronic tracking system in place and therefore the obvious challenges associated with a manual system are evident in the data collection processes. The FDA Ghana is taking steps to build quality into the regulatory process but has not yet started publishing public assessment reports on its website. It is hoped that publishing these assessment reports, including steps taken in the assessment process, will provide details on the time spent at each milestone of the process. After this, recommendations for ways to address possible delays in the review process can be implemented to achieve the overall regulatory goal of enhancing patients' access to quality, safe and efficacious medicines.

If manufactured and used appropriately, generic medicines can have major medical and economic benefits for the healthcare of a nation. It has been reported that generic medicines constitute about 90% of prescriptions in the United States and this has reduced healthcare cost by 2.2 trillion dollars as a result of using generics instead of new active substances (USFDA, 2022b). This study has demonstrated that generic medicines (including biosimilars) constituted 91% of medicines approved by the FDA Ghana from 2019 to 2021. These medicines are processed faster than NASs, mainly because of their relatively simpler clinical requirements. FDA Ghana has also developed adequate technical capacity to assess these generic applications. Due to the demand for generic medicines in LMICs, most NMRAs dedicate significant resources to evaluate applications for marketing authorisations quickly so that the healthcare system can enjoy these cost-saving benefits (Thambavita et al, 2018). Additionally, these generics products can often be assessed by pharmacists rather than physicians (bioequivalence and manufacturing quality) as is reflected in the FDA Ghana where 25 of the 26 internal reviewers are pharmacists.

It was also reported that the average time between generic drug application submission and approval in the United States was about six months and ten months for priority review and standard review respectively (Thambavita et al, 2018; USFDA, 2022b). The approval timeline for generics was 175 working days and 180 calendar days for Australia and Canada respectively (Thambavita et al, 2018; USFDA, 2022b). Therefore, the median approval times for generics approved in Ghana, which was in the range of 81 to 181 calendar days was comparable to the approval timelines in the United States, Australia and Canada.

RECOMMENDATIONS

The following recommendations for FDA Ghana were identified from the study:

- Product-specific guidelines should be provided to help applicants comply with the registration requirements and obtain approval after one review cycle.
- An electronic tracking system should be implemented to enable the authority and applicants to track applications for marketing authorisations.
- Annual training workshops should be arranged for manufacturers to help them with submission of fully completed dossiers to facilitate the review process and decrease approval timelines.
- Efficient ways should be explored to review marketing authorisation applications for NASs that are assessed via the full review pathway.
- A comparison with other stringent regulatory authorities should be carried out to identify best practices.
- Public assessment reports for all marketing authorisation applications should be made available.
- A systematic and well-structured quality decision-making practice framework should be implemented.
- The FDA Ghana should make clear that its timelines are for review and decision on a product not for review and approval of a product. In addition, that Ghana FDA should report its performance metrics in terms of agency time and industry time and assure all performance timelines are clear as to whether they apply to the agency or the industry.

CHAPTER 03

GOOD REGULATORY REVIEW PRACTICES: THE CASE OF THE FDA GHANA

SUMMARY

- Good review practices (GRevPs) consist of processes, procedures, culture and the overall philosophy of a regulatory agency and these should be adopted into the daily review activities of the regulatory agency. The aim of this study was to assess and compare the good review practices of the Food and Drugs Authority of Ghana to identify opportunities for improvement.
- Reviewers of the FDA Ghana completed an established, structured and multi-dimentional questionnaire for the assessment of GReVP by the agency.
- Twenty-seven of the 30 assessors took part in the study of whom 19 (70%) reported that GRevPs have been implemented and fully adopted across the agency. The study participants provided details indicating the reasons why they believe quality measures had been implemented within the FDA Ghana. The three most common reasons were to be more efficient, ensure consistency and to minimize errors. However, most of the respondents believed that the current GRevPs framework could be improved. Additional training to learn and understand how GRevPs are to be used and incorporated into daily work were indicated to be of value.
- The majority (24 - 90%) of the participants reported that the FDA Ghana has a consistent method for documenting those practices that need to be improved by GRevPs and a mechanism has been established to facilitate the updating of the GRevPs. In general, the importance of GRevPs was well understood by the assessors, however the study showed that target timelines were not well followed at both the department and agency levels.
- This study has evaluated Good Review Practices and their implementation within the FDA Ghana. It has provided a baseline for the FDA Ghana's knowledge, attitudes and practices as well as areas for improvement. As a result of having a baseline it is now possible to work towards achieving an improvement in the regulatory performance of the FDA Ghana as it prepares to become a WHO listed authority.

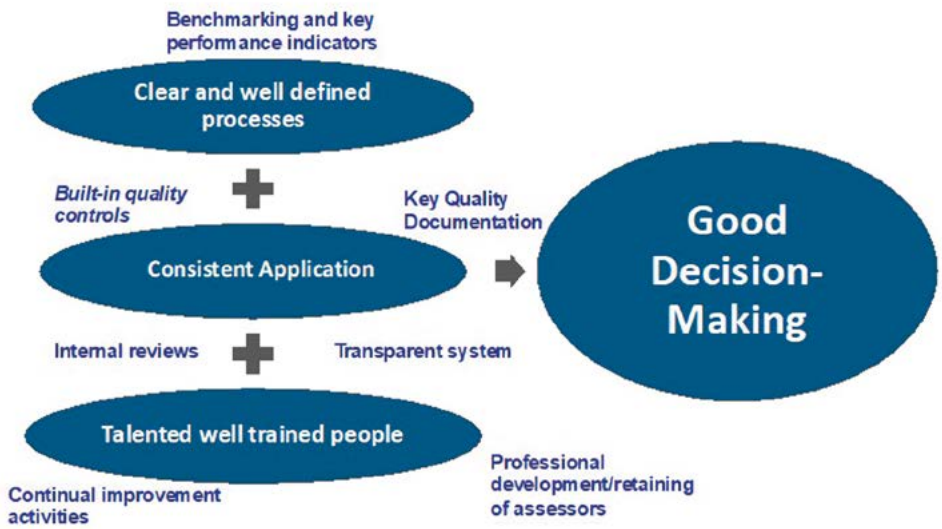
INTRODUCTION

In 2020, the Ghana Food and Drugs Agency achieved the World Health Organization's maturity Level 3 status with regards to its medicines regulatory system. "Level 3 indicates that the system is well-functioning and integrates all required elements to guarantee its stable performance" (WHO, 2020a). According to the World Health Organization, regulatory authorities are increasingly seeking ways to improve their performance and ensure the quality of their regulatory systems. Good Review Practices (GRevPs) are an integral part of overall good regulatory practices and focus on the medical product review aspect of the regulatory work" (WHO TRS No. 992, 2015a).

"Documented best practices for any aspect related to the process, format, content and management of a medical product review" are defined by the World Health Organization as Good Review Practices (WHO TRS No. 992, 2015a). However, GRevPs do not only consist of defined processes and procedures, but also include behaviours, management action, culture and an overall philosophy. These concepts should be understood and adopted into the daily review activities of a regulatory agency rather than just indicating the existence of GRevPs (Figure 3.1).

Earlier on in 2015 the WHO reported that "several regulatory authorities have introduced ways of monitoring and improving their review process through structured approaches or by moving towards stepwise implementation of GRevPs". Additionally, it stated that "regulatory authorities actively manage the process of reviewing medical product

Figure 3.1. Key measures essential for Good Regulatory Review Practice.



applications in order to maximize both the potential for a positive public health impact and the effective and efficient use of review resources" (WHO TRS No. 992, 2015a).

The extent to which implementation of GRevPs can affect patients' access to medical products has been documented in the literature (WHO TRS No. 992, 2015a). Some of the important benefits of GRevPs are consistency, transparency, efficiency and timeliness of product review. According to the WHO "implementation of GRevPs helps to achieve these outcomes by ensuring that those involved in the review process have the critical thinking skills and tools needed to optimize scientifically sound, evidence-based decisions" (WHO TRS No. 992, 2015a). After almost a decade of the WHO report it is timely that this study aims to evaluate the implementation of GRevPs by the FDA Ghana. It is hoped that other similarly matured and maturing regulatory authorities would benefit from building such a system into their review processes, as an attempt for this to become more effective and efficient in the management of their reviews.

STUDY OBJECTIVES

The study objectives were to:

1. Identify the current perspective of the assessors of the FDA Ghana in the use of GRevPs.
2. Provide a baseline on the FDA Ghana's knowledge, attitudes, practices, as well as identify areas for improvement.
3. Explore the processes and procedures currently in place that relate to GRevPs.
4. Determine how these procedures relate to the continuous process improvement within the FDA Ghana.

METHODS

In a 2022 study which was conducted to evaluate the regulatory review process of the FDA Ghana, two representatives of the agency provided information regarding the implementation of Good Review Practices by the agency by completing the established and structured tool, Optimising Efficiencies in Regulatory Agencies (OpERA). Information on the following GRevP indicators; quality measures, transparency and communication, continuous improvement and training and education was subsequently provided (Owusu-Asante et al, 2023).

Questionnaire technique

The questionnaire consists of 17 different types of questions intended to establish a baseline with respect to the staff of the agency's knowledge, attitude and practice regarding GRevPs. The overall objective was to determine whether GRevPs were

embedded into the processes and the culture while the agency moves forward in building both its capability and capacity. The questions were designed to elicit whether the participants understood the development, adoption and implementation of GRevPs. Satisfaction with the framework and process for the implementation of GRevPs for identifying these practices was also assessed. The questionnaire was also designed to enable the understanding of how the participants evaluated the implementation of these practices in terms of achieving the agency's goals as well as supporting regulatory review activities. Finally, the participants were asked to state how well implementation of GRevPs were being evaluated at both the departmental/individual and agency levels including how they could be improved.

RESULTS

For the purpose of clarity, the results are presented in three parts, as follows: Part I – Knowledge - this includes how GRevPs have been implemented within the agency, how do GRevPs improve performance and how important they are to both the department/individual and the agency in general; Part II – Practice -this includes the adoption of GRevPs, their implementation and maintenance as well as identifying the assessors understanding as to how the agency ensures that GRevP is embedded into their review practices; and Part III – Attitude - this includes satisfaction with the framework and process for the implementation of GRevPs, how do individual staff rate the implementation of GRevPs in terms of achieving the agency's goals and their support of review activities. What aspects still require GRevPs and what could be done to improve their implementation and how well they are followed both at the departmental/individual and agency levels.

Part I - Knowledge

Twenty-seven out of 30 (90%) assessors from the Health Products and Technology Division of the FDA Ghana completed the GRevP-specific questionnaire for the assessment of Good Review Practices by the agency.

According to nineteen (70%) of the respondents GRevPs have been developed and fully adopted across the agency (Figure 3.2). This supports the findings in the previous study (Owusu-Asante et al, 2023) that guidelines, standard operating procedures and review templates were in place and the majority of indicators for good review practices were implemented.

Respondents provided details indicating the reasons why they believe quality measures had been developed within the FDA Ghana (Figure 3.3). The three most common

Figure 3. 2. Extent to which GRevPs are in development in the agency.

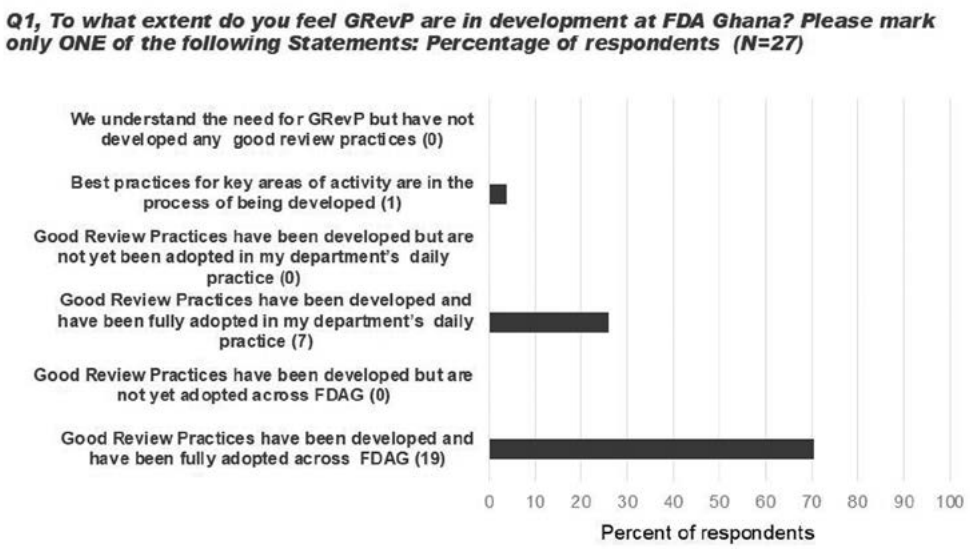
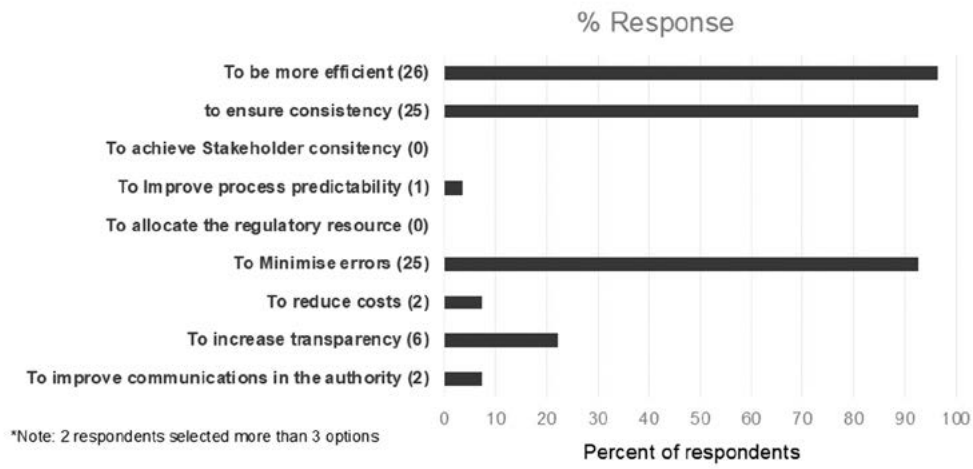
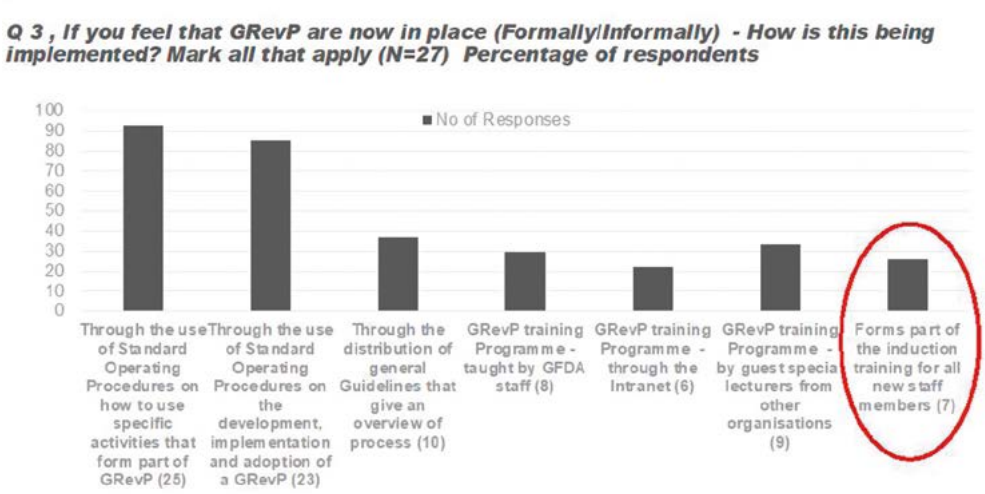


Figure 3.3. Reasons for introducing quality measures in the agency.



reasons were to be more efficient, ensure consistency and to minimize errors. Twenty-six respondents (96%) indicated that the main reason for introducing GRevPs was to be more efficient, while twenty-five respondents (93%) rated equally consistency and minimising errors as key factors. However, increasing transparency, reducing cost and

Figure 3.4. How GRevPs are implemented in the agency.



improving communication within the agency were selected by very few respondents as important reasons for introducing quality measures in the agency (Figure 3.3).

Part II - Practice

Twenty-five study participants (93%) responded to the question "In your view, how has FDA Ghana adopted GRevPs?", 24 (88%) of the respondents indicated that GRevPs have been formally adopted through the use of standard procedures, training and compliance monitoring. Twenty-five (93%) of the participants responded that GRevPs were being implemented through the use of standard operating procedures on how to use specific activities that form part of GRevP. Seven (26%) of the participants who believed GRevPs were in place formally or informally, thought that they are implemented as part of the induction training for all new staff members (Figure 3.4).

According to 27 (100%) of the participants, as GRevPs were rolled out, they were made available to the reviewers to adopt into their daily review activities. The department archives, trains and encourages the consistent use of updated GRevPs. This is the main mechanism that is used to ensure the adoption of GRevPs as standard processes. Ten (37%) participants indicated that staff were formally tested (oral or written) on their understanding of what GRevPs are and how they should be used.

Part III - Attitude

The study participants were asked several "attitude related questions" in order to achieve an understanding of their satisfaction with the framework and process

for the implementation of GRevPs. Twenty-five (93%) respondents believed that the existing GRevPs framework for FDA Ghana could be improved with only two indicating that they were satisfied with the current framework. Most of the respondents commented that the GRevPs system is in an evolving phase within the Agency and believed that additional training would be a value to understand how GRevPs should be incorporated into their daily work.

Twenty-five (93%) of the participants rated the process for the implementation of GRevP within the FDA Ghana as satisfactory. GRevPs have been implemented based on best practices identified through the collective experience of FDA Ghana and the reviewers. Two participants stated that while systems are being put in place and implemented, improvements could be made to make procedures more robust. All the participants indicated that there are still best practices that need to be implemented into the FDA Ghana GRevPs. This includes target timelines, feedback from companies, ability to track the review process, feedback from patients, feedback from staff/assessment teams were among the key areas that the agency needs to implement as part of good review practices.

The assessors acknowledged that the implementation of good review practices help to improve the following goals namely quality of the review, quality of the management of the review, consistency of the review, efficiency of the review through standardization, transparency of the review, clarity throughout the review process including critical review and decision activities and conflict or dispute resolution and the timeliness of the review process. Additionally, the respondents were of the view that the GRevP implemented within the agency are achieving these goals satisfactorily.

With regard to review principles and procedures, 20 (75%) of the participants believed that the FDA Ghana's GRevP provide strong guidance to help them do the following tasks effectively: review processes and methodologies (decision-making) and also multidisciplinary-based decision making. Twenty-two (80%) of the participants believed that some guidance is available for science-based decision, risk control methodology and continuous training of high-quality staff (Figure 3.5).

With regard to case management, 24 (90%) of the participants believed that the FDA Ghana's GRevP provide strong guidance to help them do the following tasks effectively namely internal meetings and communication with sponsors. Twenty-two (80%) of the participants believed some guidance is available for conflict and dispute resolution and also quality control (Figure 3.6).

Sixteen (60%) of the study participants indicated that there is no formal or informal mechanism currently in use to ensure GRevPs are actually adopted and used consistently. However, 21 (78%) of the participants indicated the main mechanisms that are being used are through mentoring by supervisors, by training and follow-up by training teams or people assigned to make sure that these GRevPs are implemented.

Figure 3.5. How do GRevP help to meet the agency's goals with regard to review principles and procedures.

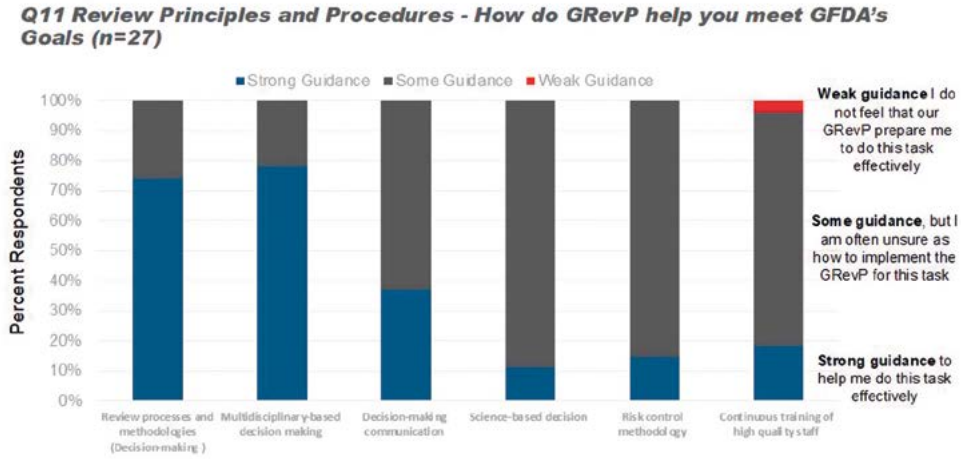
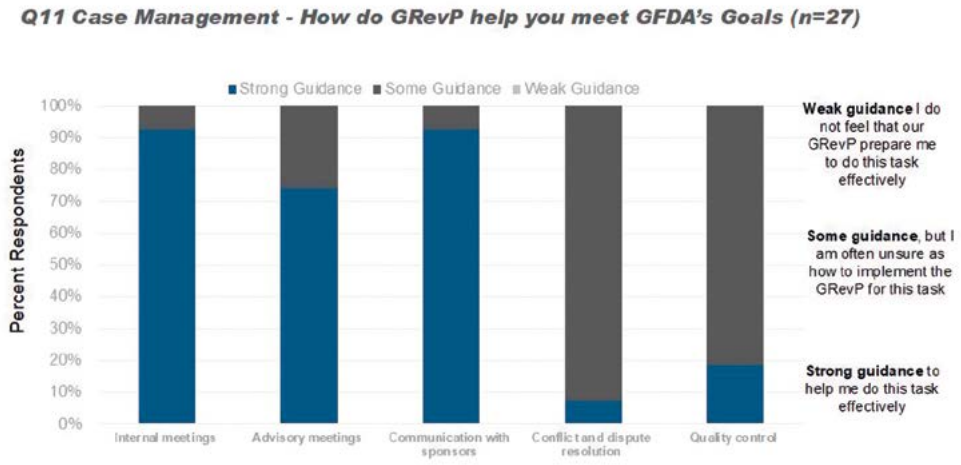


Figure 3.6. How do GRevP help to meet the agency's goals with regard to case management.



Some of the study participants suggested the following tasks that they could do at individual levels to improve the way GRevPs are implemented:

- *"Attend courses and training sessions with practical activities' regarding GRevP to enhance my knowledge"*
- *"Intentionally use the GRevP guidelines in my line of work"*
- *"Self-assessments, collaborating with other team members, undertaking continuous professional development courses"*
- *"Reading, reviewing and following standard operating procedures that outline review steps, expectations and best practices"*
- Some of the participants suggested the following issues that their senior managers could do to improve the way GRevPs are implemented:
- *"Periodically train staff either orally or written on GRevP"*
- *"Increase the number of training programs with regards to GRevP"*
- *"'Consistent training, and monitoring as well as continuous feedback to enhance the development of good review practices"*
- *"Continue to impact knowledge on the ways to effectively embark on quality assessment of dossiers"*
- *"Implement a review checklist and template to promote consistent documentation and version control, make it easier to track and retrieve information"*

According to 24 (90%) of the participants the statement which best represents how GRevPs are maintained/improved within the department and within FDA Ghana in general is 'a consistent method for documenting those practices that need to be improved by GRevPs has been established which also follows the updating process'.

A gap analysis of the importance of GRevPs for the department/individual and how closely these were followed up showed that the study participants perceived that all aspects of GRevPs were important. However, the internal audit process, quality department, quality policy, target timelines, assessment templates, feedback from patients and ability to track the process were considered to be very important. It was noted that the practices are mostly in parallel with perception for most aspects of GRevPs, but that regarding target timelines the median value showed that there is considerable difference between perception and practice. (Figure 3.7).

A gap analysis of the importance of GRevPs for the agency and how closely these were followed showed that participants perceived that all aspects of GRevPs were important. It was however noted that the practices are mostly in parallel with perception for most aspects of GRevPs, however with regard to target timelines and quality department,

Figure 3.7. Gap Analysis re Department.

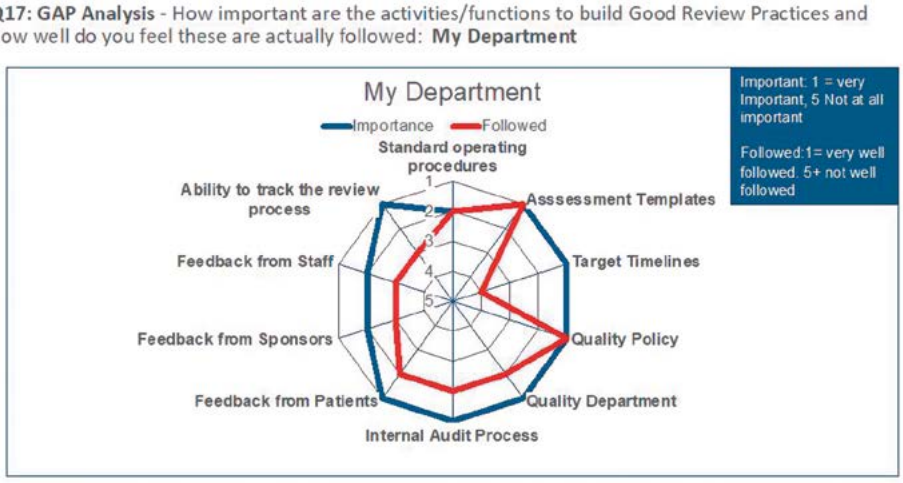
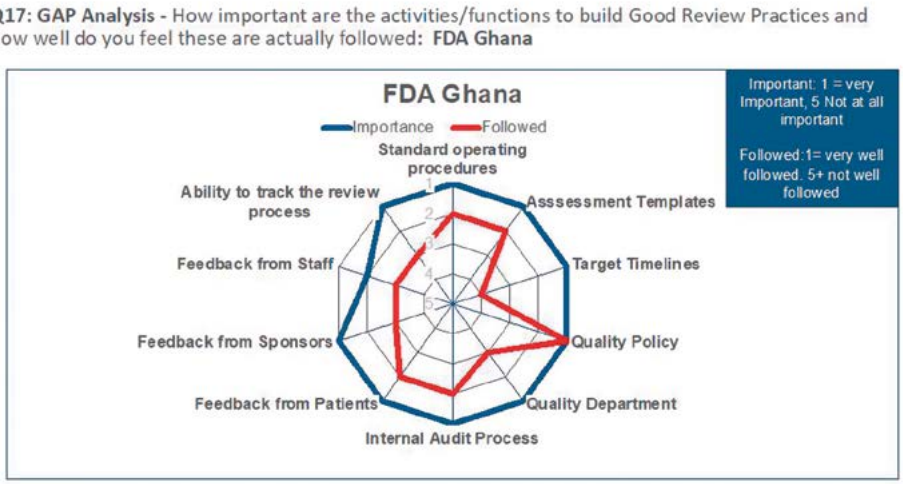


Figure 3.8. Gap Analysis re Agency.



the median values showed considerable differences between perception and practice. Lastly, it was remarkable that the quality policy was so well followed by the agency (Figure 3.8).

DISCUSSION

In this study, the strategies and measures that are in place within the FDA Ghana for developing and maintaining the quality in the review processes have been assessed. The results provide valuable insights into the perception of the assessors within

the FDA Ghana, and a baseline has been established regarding the current knowledge, practices, and attitudes within the agency together with an understanding of the contribution of existing processes and procedures that support GRevP for their continuous improvement.

The knowledge base of the FDA Ghana with respect to the role and purpose of good review practices was rated as good, and this serves as the foundation of implementing GRevP and impacts the practices and attitudes of staff of the FDA Ghana. This is aptly presented by the World Health Organization that 'capacity needs to be built on what exists' (WHO, 2001a). The FDA Ghana may therefore consider building a solid GReVP system based upon its current knowledge profile.

According to the literature 'guidelines, standard operating procedures and review templates are the building blocks for Good Review Practices in addition to other measures which also have an impact on the quality of the review process such as having a formal framework to apply quality decision-making practices' (Al-Essa and Al-Bastaki, 2024). This therefore justifies the need to have all the requisite GRevPs in place in order to progress to the implementation of quality-decision making practices by the agency. From this study these five areas need further development: target timelines, feedback from companies, ability to track the review process, feedback from patients, feedback from staff/ assessment teams.

It appears that two out of the five areas namely, ability to track the review process and target timelines are interlinked. The contributions of implementing target timelines to enhance patients' access to medicines cannot be overemphasized as it is being able to track the review process and ensure compliance with the timelines. There is adequate documentation in these areas in the literature (Al-Essa et al, 2015; Darrow et al, 2020; Patel et al, 2020; Bujar et al, 2021)

According to the literature, the extent to which GRevPs are implemented can affect patients' access to medical products. It is therefore appropriate that feedback from patients, companies and staff/assessment teams form part of the agency's Good Review Practices (WHO TRS No. 992, 2015a; Ndomondo-Sigonda, 2023; Kabir,2024). In some countries, patients are directly involved in decision-making processes of regulatory authorities through patient associations (Mühlbacher et al, 2016; Richards, 2016)

Lowe et al (2016) reported that 'Patients have been invited by regulators such as the FDA, the European Medicines Agency, and the National Institute for Health and Care Excellence to provide their perspectives and advice during decision making'

It is acknowledged that mentoring and on-the-job training would be valuable to train new reviewers and making use of readily available in-house resources is considered a sustainable way to implement GRevPs (Liu, 2013).

Most of the respondents believed that the current GRevPs framework could be improved. However, additional training to learn and understand how GRevPs are to be used and incorporated into daily work has been indicated as a requirement (Liu, 2013).

It was remarkable that most of the participants offered several suggestions that they and senior management of FDA Ghana could do to improve the way GRevPs are implemented. These suggestions are worth considering by the FDA Ghana.

According to the majority of the participants the FDA Ghana has a consistent method for documenting those practices that need to be improved by GRevPs and a mechanism has been established to facilitate the process of updating them.

In general, the importance of GRevPs is well known by the respondents, however this study showed that target timelines are not well followed either by the department or agency levels. This gap has adverse implications regarding patients' access to medicines. From the literature 'gaps in individual regulatory agency capabilities together with the duplication in non–value added national regulatory requirements, particularly in low- and middle-income countries (LMICs), can slow down regulatory approvals and therefore impede patients' access to new medicines' (O'Brien et al, 2020). In view of this 'there is a pressing need to strengthen regulatory review systems in emerging market economies as highlighted by the World Health Organization (WHO). These diverse challenges may seem overwhelming to individual national regulators, in part because of the sheer number of initiatives by multiple stakeholders, combined with a lack of information on concise practical actionable measures that can have a positive impact on review efficiency' (O'Brien et al, 2020). It is hoped that the FDA Ghana will take the necessary steps to address the gaps that have been identified in this study in order to have an improved regulatory review system.

This study has evaluated Good Review Practices and their implementation within the FDA Ghana. It has provided a baseline for the FDA Ghana's knowledge, attitudes and practices as well as areas for improvement. As a result of having a baseline it is possible now to work towards achieving an improvement in the regulatory performance of the FDA Ghana as it strives to become a WHO listed agency.

RECOMMENDATIONS

The following recommendations were identified from this study:

- Formalise the full implementation of Good Review Practices within the agency which would continue to build quality into the review process to achieve consistent, predictable, transparent and timely regulatory review.
- Make provisions to involve patient advocacy groups in regulatory review activities.
- Endeavour to include feedback from pharmaceutical manufacturers in regulatory review activities
- Improve the transparency and consistency of the scientific review system by implementing a structured framework for decision making and benefit-risk assessment
- Enhance transparency and communication through the development of summaries of the basis of approval that may be made available in the public domain.

CHAPTER 04

THE IMPORTANCE OF THE WHO MATURITY LEVEL 3 AFRICAN NATIONAL MEDICINES REGULATORY AUTHORITIES: CONTRIBUTION TO THE OPERATIONALIZATION OF THE AMA

SUMMARY

- The World Health Organization (WHO) developed the WHO Global Benchmarking Tool (GBT) to assess and benchmark the drug regulatory systems and practices in national medicines regulatory authorities (NMRAs). The objective of this study was to identify strengths and opportunities for improvement by comparing the regulatory performance of the NMRAs in Egypt, Ghana, Nigeria, South Africa, Tanzania and Zimbabwe, all which have attained maturity level 3 status for medicines and /or vaccines, in order to enhance regulatory review processes and patients' access to medicines and/or vaccines.
- The NMRAs selected for this study completed a questionnaire that collected data and metrics that facilitated comparative studies among the NMRAs.
- This comparative study showed that similarities among these authorities also translated into their strengths. The study also revealed that the human resource capacity in African NMRAs is inadequate to fully execute regulatory mandates. Review process map comparison revealed the important observation that these NMRAs conducted labelling review early in the review process rather than at the end, to facilitate preparation of public assessment reports.
- The recently established African Medicines Agency should engage these maturity level-3 NMRAs to explore ways of benefiting from their experience and resources. It is hoped that by such engagement, these authorities will build on their strengths and address the identified gaps and recommendations in this study to achieve WHO GBT level 4 and that NMRAs who have not yet reached GBT 3 can also benefit from this study in order to reach higher maturity levels.

INTRODUCTION

Evaluation of National Medicines Regulatory Authorities

National medicines regulatory authorities (NMRAs) have been encouraged to benchmark themselves to satisfy stakeholders in public health that these institutions are being efficient, effective and transparent in executing their mandate to ensure the safety, quality and efficacy of medicines and medical products.

According to Magd and Curry "Benchmarking involves learning about your own practices, the best practices of others and then making a change for improvement that will enable you to meet or be the best in the world." (Magd et al, 2003). This definition is supported by others (NASEM, 2020; WHO, 2021c) The World Health Organization (WHO) has stated that regulatory system benchmarking ". . . implies a structured and documented process by which Member States can identify and address gaps with the goal of reaching a level of regulatory oversight commensurate with a stable, well-functioning and integrated regulatory system" (WHO,2021c). As part of the efforts to strengthen the regulatory systems on a global scale, the WHO developed the Global Benchmarking Tool (GBT). The GBT ranks NMRAs with regard to the maturity level of the regulatory system on a scale of 1 (lowest maturity level) to 4 (highest maturity level) across core regulatory functions (WHO,2019c). These core regulatory functions, which are applicable to medicines are national regulatory system, registration and marketing authorization, vigilance, market surveillance and control, licensing establishments, regulatory inspection, laboratory testing, clinical trials oversight and national regulatory authority lot release applicable to biological products (WHO,2021c).

Vaz and colleagues (2022) recently noted that in addition to inefficient regulatory systems, "the lack of maturity of the regulatory systems for medical products," impedes timely access to medicines. During the launch of the WHO plan "Delivering Quality-assured Medical Products for All 2019-2023," the WHO Assistant Director General for Medicines and Health Products established the link between access to quality medicines and the strength of an NMRA, commenting "true access and the health gains that come with it can only be achieved if globally, regionally and nationally, health products do what they are meant to do – prevent illness and improve people's health. They can only do that if sound regulatory systems are in place" (WHO, 2019b). The WHO also reported that NMRAs in developing countries have inadequate resources to regulate new active substances to be used for non-communicable diseases that are becoming prevalent in these countries, apart from being inadequately prepared

to manage pandemics through the deployment of facilitated regulatory pathways (Broojerdi et al,2020; WHO,2019b).

As of June 2024, six NMRAs in Africa have been listed as operating at maturity level 3 for medicines and/or vaccines, meaning that these authorities have "stable, well-functioning and integrated regulatory systems" (Anonymous, 2022; WHO, 2024). These NMRAs are the Egyptian Drug Authority (EDA) vaccines (producing); the Food and Drugs Authority of Ghana (FDA) medicines and vaccines (non-producing); the National Agency for Food and Drug Administration and Control of Nigeria (NAFDAC) medicines and vaccines (non-producing); the South African Health Products Regulatory Authority (SAHPRA) vaccines (producing; the Tanzania Medicines and Medical Devices Authority (TMDA) medicines and vaccines (non-producing); and the Medicines Control Authority of Zimbabwe (MCAZ) medicines and vaccines (non-producing) (WHO, 2023b; Anonymous, 2022).

Regional harmonization initiatives

Currently, the TMDA (Tanzania) which belongs to the East African Community (EAC) regional harmonization initiative and SAHPRA (South Africa) which is part of the Southern African Development Community (SADC) program are listed as observers representing Africa by the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) (ICH,2022). The EDA (Egypt) joined ICH as an observer in November 2021 and became a full member of ICH in June 2023, marking a significant milestone as the first regulatory member from Africa. NAFDAC joined ICH in June 2023 as an observer and is on the verge of becoming a full member of the Council based on the requirements that have almost been met (ICH,2024).

In 2014, the pharmaceutical markets in South Africa, Egypt, Algeria, Morocco and Nigeria were listed as the major markets in Africa, with a total market value of 70% (Rosenkranz et al, 2015). This highlights the benefits and importance of their listing by either the WHO or ICH in regional pharmaceutical markets in Africa. The other benefits that strengthened NMRAs and their respective countries as a result of their WHO GBT assessment have been elaborated by Guzman (Guzman et al,2020).

For NMRAs to benefit from benchmarking, these institutions should have a quality agenda or a benchmarking culture in place to continually improve their quality management systems by incorporating lessons from other institutions who have been proven to be comparatively more successful in providing efficient and effective services

to the public and stakeholders (Magd et al, 2003). Although access to regulatory data from some NMRAs may be a challenge; a risk-based framework can be used to identify the inadequacies present in a drug regulatory system (NASEM,2020).

According to a recent publication, less mature NMRAs that study more mature NMRAs within their region, improved their regulatory systems (Guzman et al, 2020). This is a very significant finding and should serve as an important platform to launch positive reforms in the regulatory landscape in the African region.

As the NMRAs in Africa that have achieved maturity level-3 status strive to achieve maturity level 4, such as have been accomplished by Saudi Arabia, the Republic of Korea and Singapore (WHO, 2022c), it is timely to conduct a comparative study to identify similarities and differences that exist in the regulatory systems of these level-3 NMRAs.

STUDY OBJECTIVES

The objectives of this study were to identify and compare the best practices from the African NMRAs operating at WHO GBT level 3 that should be implemented by other NMRAs as they strive to achieve WHO GBT higher maturity levels.

METHODS

Study participants

The EDA (Egypt), FDA Ghana, NAFDAC (Nigeria), SAHPRA (South Africa), TMDA (Tanzania) and MCAZ (Zimbabwe), which have been listed as NMRAs operating at maturity level 3 were selected for this study.

Data Collection

To facilitate comparison among the African NMRAs, each authority except for the EDA completed the Optimising Efficiencies in Regulatory Agencies (OpERA) questionnaire, which was designed by the Centre for Innovation in Regulatory Science (CIRS) (CIRS,2020) to collect data and metrics for the regulatory review process in the same document. Data for the EDA was collected and organized by a senior EDA staff member from publicly accessible information and the EDA website.

Questionnaire Technique

The questionnaire was divided into the following six modules:
Module 1: Organization of the authority – relating to the structure, organization, and resources

Module 2: Types of review models – relating to the review models used for scientific assessment of marketing authorization applications

Module 3: Key milestones in the review process – relating to the process map and key milestone dates to facilitate review of timelines

Module 4: Good review practices (GRevP): building quality into the regulatory process – relating to measures that have been implemented to achieve transparency, consistency, and timeliness in the regulatory process

Module 5**:** Quality decision-making processes – relating to measures that have been implemented to ensure that decisions that are made are in line with best practice

Module 6: Concluding observations – relating to the strengths and challenges from the view of the authority in carrying out its mandate.

RESULTS

For the purpose of clarity, the results are presented in six parts as follows; Part I: Organization of the authority; Part II: Types of review models; Part III: Key milestones in the review process; Part IV: Good review practices (GRevP); Part V: Quality decision-making processes, and Part VI: Concluding observations.

Part I: Organization of the authorities

All the authorities except for FDA Ghana, are organized as autonomous authorities to regulate medical products for human and veterinary use, medical devices, and diagnostics. The scope of regulatory activities include marketing authorizations/ product licenses, clinical authorization, post-marketing surveillance, regulation of advertising, laboratory analysis of samples and regulatory site inspections/ visits. Additionally, among other activities, the EDA manages medicine pricing, pharmaceutical establishment licensing, lot release, importation approvals and plans, and customs release in Egypt.

The staff to population ratio ranges from 1.76 staff per million (Tanzania) to 30 per million (Egypt). The authorities are generally funded from two main sources, namely application fees and government contribution. The financial contribution from government to the NMRAs varies from 12% (Tanzania), 22% (Ghana and Nigeria) to 70% (South Africa). Similarly, EDA is funded from two main sources: application fees and government contribution; however, the specific percentage of Egypt's budget allocated to the EDA is not explicitly detailed in the publicly accessible information. In Zimbabwe, the authority is self-funded entirely from fees.

Part II: Types of review models

The authorities mostly employ the three types of review models for the scientific assessment of medicines; the exceptions apply to Tanzania and Nigeria, which use two of the review models (Table 4.1). Type 1 (verification) is used by the authorities for WHO-Prequalified products and Marketing Authorisation for Global Health Products (MAGHP) procedure by Swissmedic. Type 2 (abridged) is used for products previously approved by a stringent regulatory authority (SRA) and type 3 (full) is used for all major applications. All the authorities have in place a priority/fast-track procedure for applications for diseases with unmet medical need when a rapid assessment is required to obtain additional pharmacological, marketing/commercialization, pharmacovigilance, and clinical trials information.

Table 4.1. Types of review models employed by the authorities

Review model	Egypt	Ghana	Nigeria	South Africa	Tanzania	Zimbabwe
Type 1 - Verification	√	√	√	√	×	√
Type 2 - Abridged	√	√	×	√	√	√
Type 3A – Full	√ *	√	√	√	×	√
Type 3B – Full	√ *	×	×	√	√	×

NB: If the agency can carry out a full assessment of quality, pre-clinical (safety) and clinical (efficacy) data, then information on prior registration elsewhere may still be a prerequisite to final authorization (Model 3A) or the review may be self-standing (3B) for all major applications.

*In EDA, reliance review is practiced for human pharmaceutical products through verification and abridged pathways, while reliance is practiced for biological products through two levels: reliance level 1 for products approved by the European Medicines Agency (EMA) and/or the U.S. Food and Drug Administration (FDA) with the submission of a complete unredacted assessment report from the reference agency, list of questions and answers exchanged between the applicant and the reference agency, including all annexes, a full Common Technical Document (CTD), CPP and sameness letter); and reliance level 2, which also applies to products approved by the EMA and/or FDA, however, the submission requirements include only the CTD, sameness letter, and CPP, but does not require an unredacted assessment report and list of questions and answers.

A CPP (Certificate of Pharmaceutical Product) is required before local authorization by the other authorities. For the EDA, the CPP must be valid and demonstrate that product is registered and marketed in one of the 24 reference countries determined and approved by the technical committee for Drug control or WHO-Prequalified products (EDA,2024). Additionally, a complete common technical document (CTD) module is required for all models. In case of non- reference products, products undergo scientific assessment first and must obtain scientific committee approval prior to submission for registration. A letter of authorization or the detailed assessment report from the WHO-Prequalification program are, however, accepted as evidence of authorization. For SAHPRA, evidence of authorization by other countries is also accepted in place of the CPP. Additionally for type 2 reviews, the authorities refer to the public assessment reports.

Part III: Key milestones in the review process

The authorities set targets for the time spent for review and approval (Table 4.2).

Questions to the sponsors/applicants are batched at fixed points in the review procedure. A map of the review process and authorization of a product that is approved on the first cycle for a typical NMRA with maturity level 3 status is provided in Figure 4.1 in a format that correlates with the key milestones of the review process. *Approved in one cycle* denotes that a second or further cycles were not required for products approved subject to the submission of additional data. Recording procedures allows the applicant's response time to be measured and differentiated from the overall processing time. Generally, there is no formal procedure before the start of the application procedure. In Ghana and Nigeria some formal contact may take place during pre-submission.

Receipt and validation procedures

In the first milestone for all authorities, the application is formally received and the date of receipt is recorded. The application is then checked for acceptability and completeness and if found to be satisfactory, it is accepted and then progressed to the next stage for review. The timeline for this stage ranges from 3 to 90 days across the authorities (Table 4.2).

In the EDA, marketing authorization for human pharmaceutical and biological products falls under separate central administrations within the EDA. The Central Administration of Biological and Innovative Products and Clinical Studies for Biological Products (BioInn) handles biological products, while the Central Administration of

Table 4.2. Comparison of authority target times in the regulatory review process

Key milestones	Egypt (working days)		Ghana (calendar days)	Nigeria (working days)	South Africa (working days)	Tanzania (working days)	Zimbabwe (calendar days)
	Human pharmaceuticals*	Biologicals*					
Receipt and validation	31	10 3 20	28	5	20	14	90
Scientific assessment	90 198	120	112	56	NCEs: 360; generics: 250	14	60
Applicant response time	90 renewed only once	60 renewed only once	12 monthsa	90	Clinical/ quality: 30; Inspect/ naming/ sched.: 10**	180	60
Expert Committee (s)	20	20	1	30	1-2	1	N/A
Authorization procedure	10	NS	30	30	30	30	60
Overall approval time	349	173	266	120	NCEs: 472; generic: 362	240	480

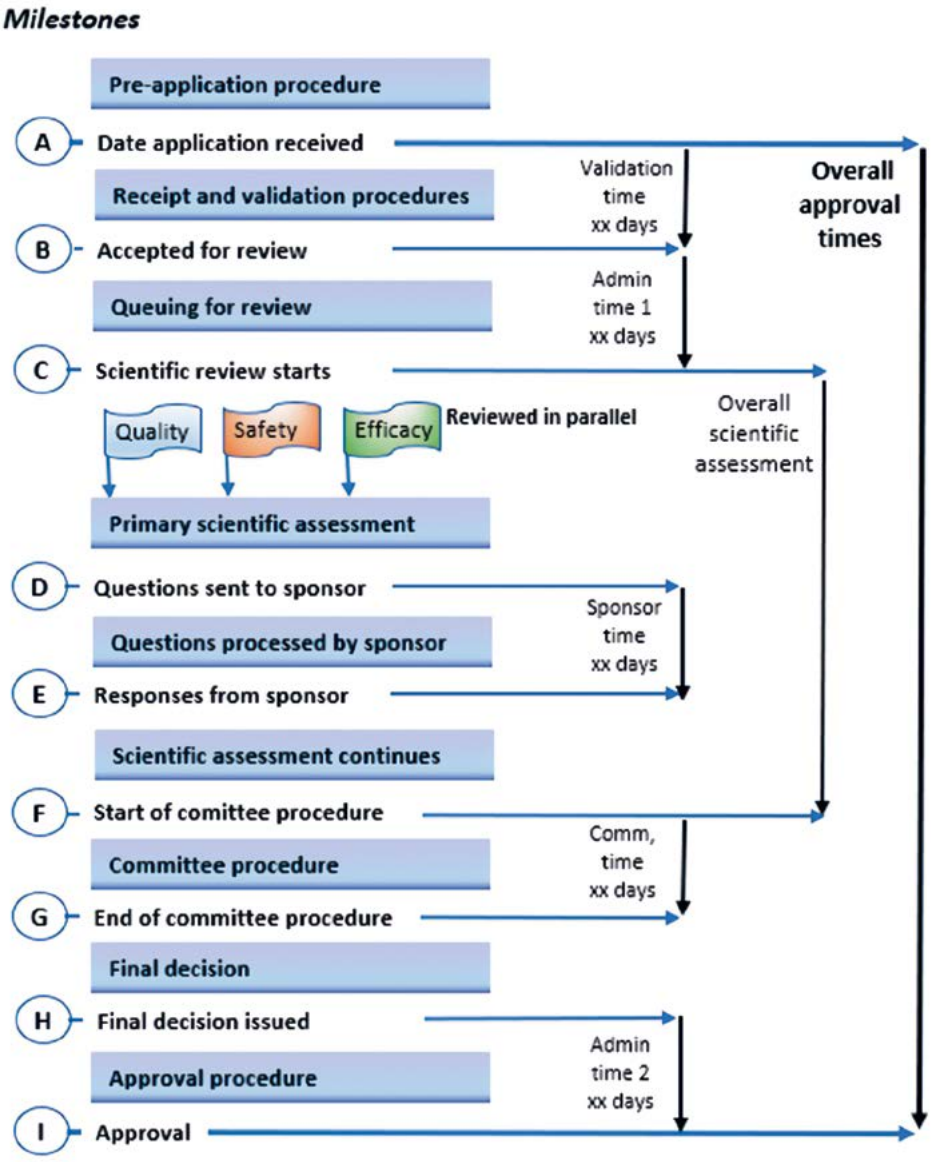
N/A=Not available. NS: not specified

[a] Not later than 12, 6, and 3months from the date of 1st, 2nd and 3rd deferrals respectively.

*EDA: Normal track target timeframe for locally manufactured human pharmaceuticals and imported biological products, which dominate the Egyptian market.

**Maximum 3 query rounds.

Figure 4.1. Status map of the review process and authorization of a product for a typical national medicines regulatory authority with WHO maturity level 3: with product approved on the first cycle (that is, does not include a second or further cycles for products approved subject to the submission of additional data) and in a format that correlates with the key milestones of the review process.



Pharmaceutical Products (CAPP) manages human pharmaceutical products. Each administration uses its own guidelines, timeframes, and operating procedures, with

some commonalities and specific differences. For both human pharmaceuticals and biological products, a registration request inquiry process is a mandatory and integral step in the marketing authorization procedure.

This step serves as a prerequisite and preliminary step for the submission of the complete application and file and functions as an action letter to facilitate subsequent stages of the submission process. The inquiry process assesses the product's eligibility for registration in the Egyptian market and helps regulate the number of products available under each active ingredient. For human pharmaceuticals, the process requires 31 working days due to the substantial volume of submissions, whereas, for biological products, it is completed within 10 working days. For human pharmaceuticals, a rolling submission is implemented for the local products, allowing the incremental submission of the registration dossier to accommodate the demands of the large local market.

After registration request inquiry approval, the first stage involves the submission and evaluation of naming, pharmacovigilance (PV), and pricing documents, with a target completion time of 90 working days. Upon completing this stage, the company is permitted to import raw and packaging materials for pilot batch production, enabling a six-month accelerated stability study and bioequivalence studies if required. The complete registration file must be submitted within 33 months from the approval of pricing or PV. A total of 198 days is allocated for the evaluation of the complete registration file. For biological products, the registration request inquiry takes 10 working days, and this step is also responsible for approving the proposed product name and granting the applicant permission to submit the pricing file to the pricing unit within 30 days of the request inquiry approval issuance. The biological products evaluation process encompasses 3 days: assigning a meeting for file submission, 20 days for screening and validation and 120 working days for complete file evaluation.

In Nigeria, new applications are held in a queue for approximately two weeks. The authority addresses its backlog by increasing the number of assessors, workspace and other resources, developing new and transparent assessment flow charts to depict good peer-review practice as well as working on product review performance metrics versus volume of applications received to improve the efficiency of the review process. In South Africa, new applications are held in queue for approximately one year.

In Tanzania, new applications are held in a queue for approximately two to eight weeks prior to scientific assessment. To address its backlog, the authority organizes joint assessment sessions every two months in which both internal and external

reviewers participate. Additionally, special sessions are organized regularly to ensure that applications are assessed on time. In Ghana, new applications are held in a queue for approximately two to six months. To address its backlog, the authority organizes assessment sessions on bi-monthly basis. In Zimbabwe, applications that have a positive outcome after screening join a queue for scientific assessments, which commences within 180 calendar days following the receipt of the application. Priority products are always taken out of the queue in all the above authorities.

Scientific assessment

A dossier in the CTD format, with all the five modules duly completed, is required for all types of scientific assessments in all the authorities. For a new application, the different sections of technical data (Quality, Safety, Efficacy) are reviewed in parallel. In Ghana and Nigeria, external experts are not involved with assessments, but in Tanzania, both internal and external experts carry out the scientific assessment. The timelines for scientific assessment ranges from 14 to 360 days (Table 4.2). Price negotiations are separated from the technical review and do not hold up the approval of products in any of the authorities.

Questions are collected into a single batch and sent to the sponsor after the initial assessment but before reporting to the Expert Committee(s). The scientific review ceases while questions are being processed by the sponsor; that is, a clock stop is applied. The timeline given to sponsors to provide responses to questions range from 30 to 180 days for all the authorities except for Ghana where applicants have 12, 6 or 3months to respond to first, second or third deferrals respectively (Table 5.2). In all the authorities, applicants can hold meetings with the authority staff to discuss questions and clarify issues that arise during the assessment. Expert committees are integrated into the internal/external scientific review procedures in the authorities. In some of the authorities studied, it is mandatory to follow the committee's recommendation whilst in other authorities, the committee acts only in an advisory capacity. The timeline for review by the expert committee ranges from 1 to 30 days (Table 4.2).

Authorization is not dependent on sampling analysis, although this does not apply to every application. Focus is rather on checking the product's quality in the marketplace so that requirements for analytical work do not hold up the marketing authorization. The analytical work is started in parallel with the scientific review. In the EDA, for human pharmaceuticals, sample analysis of the first received shipment is conducted after the issuance of the final marketing authorization license. This is unlike the case

for biological products for which the sample analysis before the issuance of final marketing authorization is mandated for all review types except, reliance level 1, where marketing authorization can be issued and the analysis can be deferred to the first shipment stage, prior to the product being placed on the market. For these products, conditional marketing authorization will be granted, allowing for analysis before the product's market introduction.

Authorization is also not dependent on a pricing agreement. The EDA requires information relating to pricing as part of its review process. A separate committee carries this out and pricing submission is requested before submission of the file for validation and evaluation and pricing certificate is a request before final marketing authorization issuance.

All negotiations regarding a product's safety, quality, and efficacy and the product information and labelling are carried out during assessment. The manufacturing facility's compliance with current good manufacturing process (cGMP) is also considered in the marketing authorization application decision. The sponsor is not informed of a positive scientific opinion before the authorization is issued. The time for this final stage ranges from 30 to 90 days.

Table 5.3 shows the number of generics and WHO-prequalified medicines approved in 2023 and the mean review times from receipt of application to approval according to type of review model employed.

It is reported above from the number of generics approved and mean review times that all the countries except Zimbabwe met their timelines in 2023 (Table 4.3). The respective data from Egypt was however not available.

Table 5.4 shows the number of new active substances and major line extensions approved from receipt of applications to approval, also according to type of review model used.

It is reported above from the number of new active substances approved and mean review times that all the countries except Zimbabwe met their timelines in 2023 (Table 4.4). The respective data from Egypt and Tanzania was however not available.

Part IV: Good review practices

A comparison of quality measures implemented by the authorities is provided in Table 5.5.

Table 4.3. Number of generics and WHO-PQ medicines approved in 2023 and mean review times from receipt of application to approval according to review model

National medicines regulatory authority	Generics approved, (n)	Mean review times	WHO-PQ approved, (n)	Mean review times
Egypt	N/A	N/A	N/A	N/A
Full				
Abridged				
Verification				
Ghana				
Full	534	56 days	0	N/A
Abridged	43	116 days	0	N/A
Verification	0	0	3	128 days
Nigeria	N/A	N/A	N/A	N/A
Full				
Abridged				
Verification				
South Africa	315 master applications		7 masters applications	
Full		240 working days		228 working days
Abridged		232 working days		167 working days
Verification		146 working days		n/a
Tanzania				
Full	359	85 days	12	79 days
Abridged	0	0	0	0
Verification	0	0	0	0
Zimbabwe				
Full	112	31 months	0	0
Abridged	40	24 months	0	0
Verification	0	0	5	10 months

WHO-PQ = WHO-prequalified.

Table 4.4. Number of NASs and MLEs approved in 2023 and mean review times from receipt of application to approval according to review model

National medicines regulatory authority	NAS approved, (n)	Mean review times, days	MLEs approved, (n)	Mean review times, days
Egypt				
Full	N/A	N/A	N/A	N/A
Abridged				
Verification				
Ghana				
Full	0	N/A	0	N/A
Abridged	16	116	0	N/A
Verification	0	N/A	0	N/A
Nigeria				
Full	0	0	0	0
Abridged	1	30	18	118
Verification	0	0	0	0
South Africa	48 master applications		2 master applications	
Full		246 working days		104 working days
Abridged		102 working days		n/a
Verification		32 working days		n/a
Tanzania				
Full	0	N/A	0	N/A
Abridged	0	N/A	0	N/A
Verification	0	N/A	0	N/A
Zimbabwe				
Full	24	33 months	0	0
Abridged	3	20 months	0	0
Verification	0	0	0	0

NASs = new active substances; MLEs = major line extensions.
N/A=not applicable

Table 4.5. Comparison of quality measures implemented by the authorities

Quality measures	Egypt	Ghana	Nigeria	South Africa	Tanzania	Zimbabwe
Internal quality policy	√	√	√	√	√	√
Good review practice system	√	√ (informally implemented)	√	√	√ (informally implemented)	√ (informally implemented)
Standard operating procedures for guidance of assessors	√	√	√	√	√	√
Standard operating procedures for the product registration committee consulted during the review process	√	√	√	√	√	Not specified
Assessment templates	√	√	√	√	√	√
Assessment report	√	√	√	√	√	√
SOP for completing the assessment report	√	√	√	√	√	√
SOP for any other procedures in the regulatory review process (e.g. validation)	√	√	√	Not specified	√	√
Dedicated quality department	√	√	√	√	×	Not specified
Scientific committee	√	√	√	√	√	√
Shared and joint reviews	√*	√	√	√	√	Not specified

* In July 2023, the EDA and the South African Health Products Regulatory Authority (SAHPRA) signed a Memorandum of Understanding (MoU) to establish the EDA-SAHPRA Work Sharing Initiative (WSI) for Registration. In October 2024, both authorities extended an invitation to industry partners to participate in the pilot phase of this initiative, scheduled to commence in 2025.

Table 4.6. Comparison of transparency and communication parameters implemented by the authorities

Parameter	Egypt	Ghana	Nigeria	South Africa	Tanzania	Zimbabwe
Feedback to industry on submitted dossiers	√	√	×	√	√	√
Details of technical staff to contact	√ (Informally)	√ (informally)	×	√	×	×
Pre-submission scientific advice to industry	√	√ (informally)	√	√ (informally)	√	√
Official guidelines to assist industry	√	√	√	√	√	√
Industry can track progress of applications	√* Manually	√	√	√ (informally)	√	√
Summary of grounds on which approval was granted	√	√	×	√	×	×
Approval times	√	√	√	√	√	√
Advisory committee meeting	√	√	√	√	√	√
Approval of products	√	√	√	√	√	√

Informally implemented= by custom and practice i.e., it has never been clearly defined or codified but over time has become the process. ×=Not implemented
* There is no electronic tracking system for applicants to monitor their application progress. Companies can communicate with EDA staff, track their applications, and obtain updates through email, online inquiry links, internal departmental phone lines, or pre-requested in-person meetings.

Table 4.7. Comparison of continuous improvement initiatives implemented by the authorities

Initiative	Egypt	Ghana	Nigeria	South Africa	Tanzania	Zimbabwe
External peer review	√	×	×	×	×	√
Internal peer review	√	×	√	×	×	√
Internal tracking systems	√	×	√	√ (informally)	√	√
Review of assessors' feedback	√	√	√	√	√	√
Review of stakeholders' feedback	√	√	√	√ (indirectly through Industry Task Group)	√	√

×=Not implemented. N/A= Not available.

Good review practices (GRevPs) relate to measures that have been implemented in order to achieve quality, transparency, consistency, and continuous improvement initiatives in the regulatory process. The authorities in this study put a high priority on building quality into their processes and have measures in place to monitor and improve the quality, overall consistency, transparency, and predictability of the regulatory process and achieve stakeholder satisfaction.

A comparison of training and continuing education as an element of quality showed that all the authorities have implemented the following: training program for assessors, internal workshops/conferences, external courses, in-house courses, on-the-job training, external speakers invited to the authority, induction training, sponsorship of post-graduate degrees and placement and secondments in other regulatory authorities.

Some of the authorities seek direct assistance of more experienced authorities in the development of standard operating procedures (SOPs) and guidelines - by using reference documents from WHO and European Medicines Agency (EMA), jointly develop and review some guidelines with the Federal Institute for Drugs and Medical Devices (BfArM), collaborate with West African Health Organization (WAHO), EAC and SADC and other authorities such as WHO, Medicines and Healthcare products Regulatory Agency (MHRA), European Directorate for the Quality of Medicines and Healthcare (EDQM) and BfArM in the training of assessors.

In addition, some of the authorities have the following in place; tools to build quality into the assessment process, internal mechanisms for quality management (internal audits and process audits), and external quality audits by an accredited certification body to improve the system. SAHPRA's strategy is to build capacity through recruitment and training, secondments to other regulatory authorities, and joint reviews with other regulatory authorities in order to carry out more of its assessments within the authority.

Part V: Quality decision-making practices

Quality decision-making practices relate to the decision-making frameworks in place that form the basis of the decision to approve or reject a marketing authorization application and measures available to minimize the impact of subjective influences/ biases on those processes. A summary of implementation of the ten Quality Decision-Making Practices (QDMPs) by the authorities is provided in Table 4.8. It is noted that these practices have been largely implemented into the framework of each authority. However, a formal assessment to periodically measure the quality of decision-making processes within the authority is only fully in place in Tanzania. The decision-making process of the other authorities for approving/rejecting a marketing authorization application could therefore be improved.

Part VI: Concluding observations

The effectiveness and efficiency of an authority's review procedure and decision-making processes for applications are mainly influenced by barriers and drivers. The following were identified by the authorities as key barriers: insufficient data on the product, unsatisfactory quality (chemistry, manufacturing and control) reports on the products, unsatisfactory good manufacturing practice compliance report, poor quality dossiers/regulatory submissions, inadequate number of competent assessors, lack of reliance policy and framework, slow turnaround times for recognized reference authorities to provide reports, inadequate support from industry, poor compilation of the technical information for product registration leading to consumption of considerable time for assessment., workload outweighing the available human resources, insufficient funding to support as many assessment sessions as possible and inadequacy of expertise in some areas such as biologicals.

The following key positive drivers were identified by the authorities: continuous professional training, continuous internal audit, development of published timelines, integrated quality management systems, competency of the assessors, implementation of good review practices., existence of a framework for registration

Table 4.8. A summary of implementation of the ten Quality Decision-Making Practices (QDMPs) by the authorities

Practice	Egypt		Ghana	
	Implemented into framework	Adhered to in practice	Implemented into framework	Adhered to in practice
Have a systematic, structured approach	√	√	√	√
Assign clear roles and responsibilities (decision makers, advisors, information providers)	√	√	√	√
Assign values and relative importance to decision criteria	√	√	√	√
Evaluate both internal and external influences/biases	√	√	√	√
Examine alternative solutions	√	√	√	√
Consider uncertainty	√	√	√	√
Re-evaluate as new information becomes available	√	√	√	√
Perform impact analysis of the decision	√	√	√ (In progress)	√ (In progress)
Ensure transparency and provide a record trail	√	√	√	√
Effectively communicate the basis of the decision	√	√	√	√

of new active substances (NASs), availability of guidelines for assessors, international guidelines and templates, collaborative agreements with ZaZiBoNa, WHO and other regulatory authorities, proper compilation and correctness of technical information for product registration, timely response of queries from sponsors and independence of the authority in the review process and decision making.

DISCUSSION

This comparative study of the regulatory systems and practices in the NMRAs that have achieved WHO maturity level 3 status has shown that some similarities exist, all of which translate into strengths for these NMRAs. This study also highlighted various differences or gaps and, with the exception of FDA Ghana, the ability of the NMRAs to carry out their regulatory mandate autonomously is the ideal starting point for them to become WHO listed authorities (Ndomondo-Sigonda et al, 2017).

Nigeria		South Africa		Tanzania		Zimbabwe	
Implemented into framework	**Adhered to in practice**	**Implemented into framework**	**Adhered to in practice**	**Implemented into framework**	**Adhered to in practice**	**Implemented into framework**	**Adhered to in practice**
√	√	√	√	√	√	√	√
√	√	√	√	√	√	√	√
√	√	√	√	√	√	√	√
√ (partially)	√ (partially)	√	√	√	√	√	√
√ (partially)	√ (partially)	√	√	√	√	√	√
√ (partially)	√ (partially)	√	√	√	√	√	√
√	√	√	√	√	√	√	√
√ (partially)	√ (partially)	Not specified	Not specified	√	√	√	√
√	√	√	√	√	√	√	√
√	√	√	√	√	√	√	√

This study has revealed that the human resource capacity in each of the African NMRAs is inadequate to carry out its regulatory mandate. The benefits of having the requisite human resources for optimal regulatory activities has been well documented in the literature (Ndomondo-Sigonda et al, 2017). Generally, the assessors in the NMRAs in Africa are pharmacists; however, unlike generics, the assessment of NASs covers Module 4 of the CTD dossier and requires the involvement of toxicologists or assessors who have the requisite skills to assess preclinical data/animal studies.

The number of such experts in Africa, though strongly suspected to be inadequate, is not in the public domain. This gap in human resources prolongs the timeline for assessing and registering NASs in lower- and middle-income countries (LMICs) and ultimately impedes patients' access to some NASs, which are assessed via the full assessment pathway by the NMRAs in Africa (Doua et al, 2014;Hill et al, 2004).

The NMRAs in Africa can learn directly from other regulatory authorities with regard to the innovative strategies that were deployed to issue timely marketing authorization for COVID vaccines during the pandemic. They may also have comparative strategies in place that would assist these NMRAs to process applications for NASs that require Africa as their gateway to the rest of the world (Doua et al, 2014;Hill et al, 2004). The fact that Nigeria does not use the type 2 review model and Tanzania does not use the type 1 review model may not be an issue at this time as long as the processing timelines are met for the related marketing authorization applications.

It is important to note that comparing the key stages and milestones in the review processes and authorization procedures of the NMRAs in Africa showed several similarities, typical of institutions that have attained the same maturity level. In the WHO Prequalification Team: Medicines (PQTm) procedure, review of product information is conducted in the last stage of the process prior to prequalification of a product, The rationale for reviewing the product information in the final stages of the prequalification process is two-fold; the first of which is to facilitate the preparation of the public assessment report, and the second is to ensure that the Summary of Product Characteristics (SmPC), Patient information leaflet (PIL) and product labels, which are major components of the public assessment report, reflect the final product information of the manufacturer, as approved by the authority. This approach by the WHO prequalification program facilitates timely issuance of public assessment reports (WHO, 2023c). This ideal practice prevents duplication of efforts and could make an NMRA efficient in allocating its resources to satisfy its stakeholders. Presently, it is only Tanzania that publishes public assessment reports, and therefore, it will be helpful for the other NMRAs to reconsider the stage at which the review of labelling information is carried out. This will help the NMRAs to publish public assessment reports in a bid to become more transparent to their stakeholders and meet an important criterion of attaining maturity level 4 (HSA, 2022).

To be more effective, NMRAs in Africa should institutionalize some of these additional meetings (scientific advice, early clarification, late clarification, and accelerated application hearing) with applicants in order to optimize the marketing authorization procedure. The queuing of applications in the NMRA review process is an opportunity for improvement. The NMRAs should consider learning about innovative regulatory pathways for NASs from the Republic of Korea and Singapore in order to attract new product applications, most of which are needed in Africa to address the continent's ever-increasing health needs.

Regarding good review practices, the absence of external peer review initiatives should be addressed, since such initiatives help to solve the problem of capacity building of the NMRAs. The NMRAs stand to benefit from the skills and expertise of external experts when they are involved with the review process.

It is commendable to note that these maturity level-3 authorities have implemented all the training and continuing education indicators. It appears that they have adopted a benchmarking culture to continually improve their regulatory systems by incorporating lessons from other institutions such as WHO, MHRA, EDQM, and BfArM) who have been proven to be comparatively more successful in providing efficient and effective services to the public and stakeholders (Magd et al,2003). This culture should be encouraged as the authorities stand to benefit from such collaborations to achieve "strong, efficient and sustainable regulatory systems" (WHO,2021b).

There were, however, some gaps observed with regard to implementation of the QDMPs by the authorities. Addressing these gaps would result in the NMRAs making progress toward the achievement of WHO GBT maturity level-4 status.

This study compared the drug regulatory systems and practices in the NMRAs in Africa that have achieved WHO maturity level 3 status. Although many similarities were observed, some differences or gaps were identified. It is hoped that the NMRAs in Africa, who have achieved maturity level 3, will build on their strengths, address the identified gaps, and implement the recommendations in this study in their WHO global benchmarking-journey to reach WHO maturity level 4.

RECOMMENDATIONS

The key recommendations from the study are as follows

- There should be collaboration amongst the NMRAs that have achieve WHO GBT maturity level-3 status. An expert working group consisting of assessors from these NMRAs can apply their relatively stringent standards in the assessment of NASs and the outcome of the assessment could be applied throughout the African continent through an innovative collaborative procedure. This collaboration will enhance access to much-needed NASs by patients in Africa.
- A mutual recognition procedure should be established to significantly reduce duplication in assessments and use resources more efficiently.
- The recently established AMA should engage these maturity level-3 NMRAs to explore ways that the AMA could benefit from their experience and resources, thereby supporting the effectiveness and efficiency of the AMA in achieving its overall goal.
- More capacity-building opportunities in regulatory science including training in non-clinical toxicity should be made available to NMRAs in Africa (Doua,2014; WHO,2023c; HSA,2022; WHO, 2021b; Moran et al, 2011).
- The regulatory review process of the NMRAs in Africa should be adjusted such that review of product labelling is conducted at the end of the review process and prior to the authorization of the application to facilitate the preparation of public assessment reports.
- Authorities should have a formal assessment to periodically measure the quality of their decision-making processes in place.
- The NMRAs should implement the nine principles in the Good Regulatory Practices guidance document- "legality, consistency, independence, impartiality, proportionality, flexibility, clarity, efficiency and transparency- as these are relevant to all authorities responsible for the regulation of medical products, irrespective of their resources, sophistication or regulatory model" (WHO, 2021b).

  The scope of this study was limited to the six NMRAs in Africa that have achieved maturity level 3 status as of June 2024. Subsequent to this Rwanda and Senegal have achieved maturity level 3 status. Going forward it would be helpful to obtain the respective data from these two additional NMRAs.

CHAPTER 05

COMPARISON OF GOOD REGULATORY REVIEW PRACTICES OF THE ECOWAS REGIONAL INITIATIVE

SUMMARY

- Good review practices (GRevPs) when implemented by national and regional regulatory agencies ensure the timely quality review of medicines for enhanced patients' access to safe, quality and efficacious innovative and generic products. It is important that, all aspects of GrevPs are continuously evaluated and updated in order to promote the continuous improvement of regulatory systems in the country and at regional levels. The aim of this study was to assess and compare the good review practices of the national medicines regulatory agencies (NMRAs) of Burkina Faso, Cote d'Ivoire, Ghana, Nigeria, Senegal, Sierra Leone and Togo, who are active participants of the ECOWAS-MRH initiative in order to identify opportunities for improvement.
- The Optimising Efficiencies in Regulatory Agencies (OpERA) questionnaire, was completed by each of the NMRAs which facilitated the assessment of the regulatory review processes which in turn affect good review practices.
- Except for Cote d'Ivoire and Nigeria which are autonomous, the other NMRAs namely Burkina Faso, Ghana, Senegal, Sierra Leone and Togo operate within the administrative structure of their respective Health Ministry, to regulate medical products for human use, medical devices and diagnostics. Apart from Togo, the agencies receive partial funding from their governments as well as from regulatory fees. The population in the seven countries varies from 8.6 million to 211.4 million.
- All the agencies had in place measures to achieve quality in their review processes although there were some remaining initiatives related to transparency and communication, continuous improvement as well as training and education, to be implemented by the NMRAs. It was noted from the findings that, Ghana had implemented nine of the ten quality decision-making practices into a framework while Togo and Cote d'Ivoire had implemented eight and seven of the quality decision-making practices into a framework respectively. Nigeria and Burkina Faso have implemented six and five of the quality decision-making practices into a framework respectively while Sierra Leone has partially implemented all ten quality decision-making practices. However, Senegal had not implemented any of the quality decision-making practices.
- The study compared the organization, good review practices and quality decision-making processes of the NMRAs that actively participate in the ECOWAS-MRH initiative. Though some differences were identified with regard to the organization of the NMRAs, a significant number of good review practice initiatives and quality decision-making practices were identified to be implemented to promote continuous improvement in the regulatory processes of the NMRAs.

INTRODUCTION

In 2015 the World Health Organization (WHO) issued guidelines on good review practices (GRevPs) for national and regional regulatory authorities for medical products to support the continual improvement of the effectiveness, efficiency and consistency. The review of medicines has been broadly defined by the WHO as "that part of the regulatory work that forms the scientific foundation for regulatory decisions on marketing authorizations. It requires a highly complex, multidisciplinary assessment of product data to ensure that products submitted for regulatory approval meet adequate scientific and evidentiary standards for safety, efficacy and quality" (WHO, 2015b; WHO,2015c).

Good review practices are defined by the WHO as "documented best practices for any aspect related to the process, format, content and management of a medical product review. The objective of GRevPs is to help achieve timeliness, predictability, consistency, transparency, clarity, efficiency and high quality in both the content and management of reviews. This is carried out through the development of guidelines, review tools (for example, standard operating procedures (SOPs) and templates) and reviewer learning activities (for example training courses, mentoring, orientation packages and discussion sessions). To promote continuous improvement, all aspects of GRevPs should be continuously evaluated and updated" (WHO, 2015b) This definition has been supported and expanded by the European Medicines Agency and the United States Food and Drug Administration (Al-Essa et al, 2024; USFDA,2018).

The ten key principles of a good review are that is balanced, considers context, evidence-based, identifies signals, investigates and solves problems, makes linkages, utilizes critical analyses, thorough, well-documented and well-managed activities, and guides regulatory agencies in their regulatory practices. Similarly, the benefits of implementing good review practices by national and regional regulatory agencies which include the timely quality review of medical products, enhances patients' access to safe, quality and efficacious medicines in individual countries and regions respectively (WHO, 2015b).

Due to the dynamic nature of the global regulatory landscape for medical products, it is necessary to assess the efficiencies of the relevant regulatory agencies available in the countries within the sub-region with a view to continually update the regulatory systems (Al-Essa et al, 2024).

According to Al-Essa et al (2024) "quality measures may be evaluated on a regular basis to determine their impact on the quality and speed of the drug approval process. Review of human resources and the workload must always be assessed and updated according to the needs, challenges and opportunities for improving regulatory review practices". Very useful insights on the implementation of quality measures by regulatory agencies have been provided by these same authors in their recent publication. Therefore, in addition to assessing the quality measures, human resources and workload, this study will also assess transparency and communication parameters, continuous improvement initiatives, as well as training and education programmes.

To highlight the regulatory importance of good review practices, it is reported in the literature that the Asia-Pacific Economic Cooperation (APEC) Regulatory Harmonization Steering Committee instituted the implementation of the 2020 Good Review Practices roadmap. Two international workshops were successfully organized by the Taiwan Food and Drug Administration including other objectives which addressed the building blocks of a regulatory review system in line with the roadmap. From the workshops it was noted that regulatory agencies associated the implementation of quality measures with efficient and transparent regulatory systems (Lin et al, 2015).

Lin et al (2015) reported that "there is a lack of uniformity in review practices for medical products among APEC economies, as each economy has different regulatory practices, levels of expertise and capacity". Also "the implementation of GRevP could be essential for strengthening the performance of regulatory agencies and enhancing mutual trust between economies in the APEC region". Similarly with regard to the ECOWAS- MRH initiative, there are seven NMRAs that are active in the assessment of applications for marketing authorization in the sub region. As all the 15 NMRAs in the ECOWAS region collaborate to implement this initiative, it is expected that assessing and improving the good review practices in the seven active NMRAs will in turn benefit all the NMRAs in the ECOWAS region (WAHO, 2021c).

According to the WHO "good communication is critical and has many advantages for regulatory agencies, applicants and the public. It can improve the efficiency of the development and review processes and thus ultimately speed up patients' access to quality medical products" (WHO, 2015b).

As a result of the successful assessment of good review practices of countries participating in the ZaZiBoNa and EAC -MRH initiatives, it is appropriate that the good review practices of countries participating in the ECOWAS-MRH initiative are assessed

and hence the implementation of this study (Sithole et al.,2021; Ngum et al., 2024a). This study is therefore aimed at assessing the good review practices of countries participating in the ECOWAS-MRH initiative and to communicate the findings to other regulatory agencies, stakeholders and the public and serve as a reference for future comparative analyses across the NMRAs in ECOWAS to establish best practices.

STUDY OBJECTIVES

The objective of this study which is one of a two-part series was to provide an insight into the implementation of good review practices of countries participating in the ECOWAS-MRH initiative. The other study will compare their review models and regulatory timelines.

METHODS

Study participants

All seven active NMRAs of the ECOWAS-MRH initiative namely, National Pharmaceutical Regulatory Agency-Burkina Faso, Autorite Ivoirienne de Regulation Pharmaceutique (AIRP)-Republic of Cote d'Ivoire, Food and Drugs Authority (FDA Ghana), National Agency for Food and Drug Administration and Control (NAFDAC)- The Federal Republic of Nigeria, Senegalese Pharmaceutical Regulatory Agency (l'Agence Senegalaise de Reglementation Pharmaceutique (ARP)- Republic of Senegal, Pharmacy Board of Sierra Leone (PBSL) and the Directorate of Pharmacy, Medicine and Laboratories-Togo, participated in this study between August 2021 and November 2023.

Data collection

The Optimising Efficiencies in Regulatory Agencies (OpERA) questionnaire, which had been validated by Rodier and colleagues (2020) of the Centre for Innovation in Regulatory Science (CIRS) was completed by each of the NMRAs. Completing the OpERA questionnaire facilitated the assessment of the regulatory review processes which affect approval times. Upon completion of the OpERA questionnaire, a country report specific to each NMRA was generated which enables the sharing and adoption of Good Review Practices. (Rodier et al, 2020)

The OpERA questionnaire consists of six modules: module 1 covers structure, organisation and resources of the agency; module 2 explores the review models used for the scientific assessment of medicines; module 3 identifies the key milestones in the review process; module 4 captures regulatory measures that have been built into the regulatory review process; module 5 explores the quality of decision-making

processes and module 6 documents the agency's perception of the key drivers and barriers that influence the effectiveness and efficiency of its review and decision-making processes.

RESULTS

For the purpose of clarity, the results of the study covering three out of the six modules are presented in the following three parts: Part I Organization of the agencies; Part II Good review practices (GRevP)-building quality into the review process; and Part III Quality decision-making processes.

Part I. Organization of the agencies

Within a span of three decades (from 1992 to 2022) the NMRAs of Burkina Faso, Cote d'Ivoire, Ghana, Nigeria, Senegal, Sierra Leone and Togo were established. With the exception of Cote d'Ivoire and Nigeria, which are autonomous, the other NMRAs operate within the administrative structure of the Health Ministry. All the agencies regulate medical products for human use, medical devices and diagnostics. The population in the seven countries varies from 8.6 million to 211.4 million. A summary of the human resources of the NMRAs is provided in Table 5.1.

All the agencies, with the exception of Togo, receive partial funding from their governments as well as from regulatory fees. Table 5.2 details the fees charged for the review of marketing authorization applications for new active substances (NASs) and generics, respectively.

Table 5.1. Comparison of the country population, size of NMRA and workload in 2022

Country	Burkina Faso	Cote d'Ivoire	Ghana	Nigeria	Senegal	Sierra Leone	Togo
Population (millions)	22.7	28.2	30.8	211.4	17.3	8.6	8.8
Number of Agency staff	64	71	683	2080	50+	200	30
Staff per million residents	2.8	2.5	22.2	9.8	2.9	23.3	3.4
Number of internal reviewers	34	15	26	44	37	15	4
% of Reviewers in agency	53	21	3.8	2.1	74	7.5	13.3

Table 5.2. Comparison of fees charged and source of funding in 2022

Country	Burkina Faso	Cote d'Ivoire	Ghana	Nigeria	Senegal	Sierra Leone	Togo
Source of funding	93% Government, 7% Fees	63% Government, 37% Fees	35% Government, 65% Fees	22.41% Government, 77.59% Fees, 5.5% International Partners	Government and Fees	90% Government, 10% Donor funds	100% Government-
Fees for review of new active substances (USD)	494	808	1080	1280	2511	750	327
Fees for review of generics (USD)	247	808	720	1280	1674	250	818

Part ll. Good review practices (GRevP) building quality into the review process

For the purpose of clarity, the documentation of review procedures that include general measures used to achieve quality, transparency and communication parameters, continuous improvement initiatives as well as training and education strategies that the agencies have in place, are presented as follows:

General measures used to achieve quality

A summary of the comparison of the quality measures implemented by the NMRAs within the ECOWAS region is provided in Table 6.3.

All the agencies have in place measures to achieve quality in their review processes namely; a good review practice system, an internal quality policy, standard operating procedures (SOPs) for the guidance of assessors, SOPs for the advisory and /or registration committee consulted during the review process, assessment templates, assessment report, SOPs for completing the assessment report, SOPs for any other procedures in the regulatory review process, a dedicated quality department, a scientific committee and also shared and joint reviews. It is only Togo that has a few of the quality measures which are informally implemented.

Transparency and communications parameters

A summary of the comparison of the transparency and communication parameters implemented by the NMRAs within the ECOWAS initiative is provided in Table 5.4.

It was noted that out of the nine listed parameters, Ghana and Sierra Leone have formally implemented seven and informally implemented the remaining two parameters. Burkina Faso, Cote d'Ivoire and Togo have also implemented six parameters. Nigeria and Senegal have formally implemented five and four parameters respectively.

Continuous improvement initiatives

Sierra Leone is the only country that has formally implemented all the five listed parameters in line with continuous improvement initiatives. Nigeria and Senegal have formally implemented four of the parameters. However, Cote d'Ivoire and Togo have informally implemented one and two parameters respectively. A summary of the comparison of the continuous improvement initiatives implemented by the NMRAs is provided in Table 5.5.

Table 5.3. Comparison of the quality measures implemented by the NMRAs

Indicator	NMRA						
	Burkina Faso	Cote d'ivoire	Ghana	Nigeria	Senegal	Sierra Leone	Togo
Good review practice system	✓	✓	✓	✓	✓	✓	✓
Internal quality policy	✓	✓	✓	✓	✓	✓	✓
Standard operating procedures (SOPs) for guidance of assessors	✓	✓	✓	✓	✓	✓	✓
SOPs for the advisory /registration committee consulted during the review process	✓	✓	✓	✓	✓	✓	×
Assessment templates	✓	✓	✓	✓	✓	✓	✓
Assessment report	✓	✓	✓	✓	✓	✓	✓
SOPs for completing the assessment report	✓	✓	✓	✓	✓	✓[a]	✓[a]
SOPs for any other procedures in the regulatory review process (e.g. validation)	✓	✓	✓	✓	✓	✓	✓[a]
Dedicated quality department	✓	✓	✓	✓	✓	✓	✓[a]
Scientific Committee	✓	✓	✓	✓	✓	✓	✓
Shared and joint reviews	✓	✓	✓	✓	✓	✓	✓

a = implemented but not formally documented

Table 5.4. Comparison of the transparency and communication parameters implemented by the NMRAs

	NMRA						
Indicator	**Burkina Faso**	**Cote d'ivoire**	**Ghana**	**Nigeria**	**Senegal**	**Sierra Leone**	**Togo**
Post-approval feedback to applicant on quality of submitted dossiers	✓	✓	✓	×	✓	✓	✓
Details of technical staff to contact	×	×	✓[a]	×	✓	✓[a]	✓[a]
Pre-submission scientific advice to industry	×	×	✓[a]	✓	×	✓	✓
Official guidelines to assist industry	×	✓	✓	✓	×	✓	✓
Industry can track progress of applications	✓	✓[a]	✓	✓	✓	✓[a]	✓[a]
Publication of summary grounds on which approval was granted	✓	✓	✓	×	×	✓	✓
Approval times	✓	✓	✓	✓	×	✓	✓
Advisory committee meeting dates	✓	✓	✓	×	×	✓	✓
Approval of products	✓	✓	✓	✓	✓	✓	✓[a]

a = implemented but not formally documented

Table 5.5. Comparison of the continuous improvement initiatives implemented by the NMRAs

	NMRA						
Indicator	**Burkina Faso**	**Cote d'ivoire**	**Ghana**	**Nigeria**	**Senegal**	**Sierra Leone**	**Togo**
External peer review	✗	✗	✗	✗	✗	✓	✗
Internal peer review	✗	✓[a]	✓	✓	✓	✓	✗
Internal tracking systems	✓[a]	✗	✗	✓	✓	✓	✓[a]
Review of assessors' feedback	✓	✗	✓	✓	✓	✓	✗
Review of stakeholders' feedback	✓	✗	✓	✓	✓	✓	✓[a]

a = implemented but not formally documented

Training and education strategies

A summary of the comparison of the training and education strategy implemented by the NMRAs is provided in Table 5.6. It was noted that Ghana and Sierra Leone have formally implemented all the nine listed initiatives. Senegal has formally implemented seven of the initiatives while Cote d'Ivoire has informally implemented seven of the initiatives. Burkina Faso and Togo have only implemented three initiatives:

Part lll. Quality decision-making practices

The NMRAs within ECOWAS-MRH are required to have a framework in place that forms the basis of the quality decision-making practices (QDMP) to approve or reject a marketing authorization application. The following ten principles should be implemented into the framework and also adhered to in practice: namely have a systematic, structured approach, assign clear roles and responsibilities(decision makers, advisors, information providers), assign values and relative importance to decision criteria, evaluate both internal and external influences/biases, examine alternative solutions, consider uncertainty, re-evaluate as new information becomes available, perform impact analyses of the decision, ensure transparency and provide a record trail and finally effectively communicate the basis of the decision.

It was noted from the study that Ghana has implemented nine of the ten quality decision-making practices into a framework and additionally these nine practices are also adhered to in practice. Togo and Cote d'Ivoire have implemented eight and seven of the quality decision-making practices into a framework respectively. Nigeria and Burkina Faso have implemented six and five of the quality decision-making practices into a framework respectively and additionally these practices are also adhered to in practice.

Sierra Leone has partially implemented all ten quality decision-making practices into a framework and has also partially adhered to the practices. Senegal has neither implemented quality decision-making practices into a framework nor adhered to these quality decision-making practices. A summary of the comparison of the quality decision-making practices implemented by the NMRAs is provided in Table 5.7.

DISCUSSION

This study compared the good review practices of countries participating in the ECOWAS-MRH initiative and identified opportunities for improvement.

This study which is similar to the SADC and EAC regional studies by Sithole et al (2021a) and Ngum et al (2024a) respectively was also designed to widely share

Table 5.6. Comparison of the training and education strategies implemented by the NMRAs

Indicator	NMRA						
	Burkina Faso	Cote d'ivoire	Ghana	Nigeria	Senegal	Sierra Leone	Togo
Training programme for assessors	✗	✓[a]	✓	✓	✓	✓	✗
International workshops/conferences	✗	✓[a]	✓	✓	✓	✓	✗
External courses	✗	✓[a]	✓	✗	✓	✓	✗
In-house courses	✗	✓[a]	✓	✗	✓	✓	✗
On-the-job training	✓[a]	✓[a]	✓	✓	✓	✓	✗
External speakers invited to the authority	✗	✓[a]	✓	✗	✗	✓	✓
Induction training	✓	✓[a]	✓	✓	✓	✓	✓[a]
Sponsorship of post-graduate degrees	✓[a]	✗	✓	✗	✗	✓	✓
Placements and secondment in other regulatory agencies	✗	✗	✓	✓	✓	✓	✗

Table 5.7. Comparison of the Quality Decision-Making Practices implemented by the NMRAs

Practice	Burkina Faso		Ghana		Nigeria		Cote d'Ivoire		Senegal		Sierra Leone		Togo	
	Implemented into framework	Adhered to in practice	Implemented into framework	Adhered to in practice	Implemented into framework	Adhered to in practice	Implemented into framework	Adhered to in practice	Implemented into framework	Adhered to in practice	Implemented into framework	Adhered to in practice	Implemented into framework	Adhered to in practice
Have a systematic, structured approach	√	√	√	√	√	√	√	√	NV	NV	√ (In progress)	√ (In progress)	√	√
Assign clear roles and responsibilities (decision makers, advisors, information providers)	√	√	√	√	√	√	√	√	×	NV	√ (In progress)	√ (In progress)	√	√
Assign values and relative importance to decision criteria	√	√	√	√	√	√	√	√	NV	NV	√ (In progress)	√ (In progress)	√	√
Evaluate both internal and external influences/biases	√ (In progress)	NV	√	√	√ (In progress)	√ (In progress)	×	×	NV	NV	√ (In progress)	√ (In progress)	√	√
Examine alternative solutions	√ (In progress)	NV	√	√	√ (In progress)	√ (In progress)	√ (In progress)	√	NV	NV	√ (In progress)	√ (In progress)	×	×
Consider uncertainty	×	NV	√	√	√ (In progress)	√ (In progress)	√	√ (In progress)	NV	NV	√ (In progress)	√ (In progress)	√	√
Re-evaluate as new information becomes available	×	NV	√	√	√	√	√	√	NV	NV	√ (In progress)	√ (In progress)	√	√
Perform impact analysis of the decision	×	NV	√ (In progress)	√ (In progress)	√ (In progress)	√ (In progress)	×	×	NV	NV	√ (In progress)	√ (In progress)	×	×
Ensure transparency and provide a record trail	√	√	√	√	√	√	√	√	NV	NV	√ (In progress)	√ (In progress)	√	√
Effectively communicate the basis of the decision	√	√	√	√	√	√	√	√	NV	NV	√ (In progress)	√ (In progress)	√	√

the regulatory good practices in the ECOWAS region to all stakeholders. This could enable manufacturers to be interested in investing more in the region for the ultimate benefit to patients.

It is of interest to note that out of the seven NMRAs, Nigeria and Ghana had the lowest percentage of reviewers in their agencies. It was also noted that Nigeria and Ghana had the highest contribution of their funds from regulatory fees. Coincidentally, Nigeria and Ghana have achieved WHO Global Benchmarking Tool maturity level-3 status signifying that they have stable, well-functioning and integrated regulatory systems. It can therefore be inferred that these two agencies are demonstrating efficiency in utilizing their human and financial resources to strengthen their regulatory systems. This could serve as a major learning point for other NMRAs who seek to make improvements to their regulatory systems.

The ratio of the staff per million residents in five of the agencies was less than 10, this was similar to that which was reported by Sithole et al, (2021) with regards to the SADC region; only two agencies had a staff per million residents' ratio of about twenty.

The situation in the ECOWAS region where most of the NMRAs are not autonomous also exists in the EAC and SADC regions and is reported as a major challenge, although relevant provisions have been made in the African Union Model Law to promote the autonomous NMRAs (Sithole et al (2021a) and Ngum et al (2024a)

Having assessed the regulatory good review practices of these NMRAs with regards to the implementation of quality measures, transparency and communication parameters, continuous improvement initiatives, training and education programmes, it was noted that the quality measures had been largely implemented by the NMRAs within the ECOWAS region. This comparison will serve as a useful reference for other NMRAs to implement the quality measures.

Comparison of the transparency and communication parameters implemented by the NMRAs also showed that there were still some of the parameters to be implemented by the agencies. There could therefore be an opportunity for the exchange of strategies in order for each of the NMRAs to implement all remaining parameters.

With regard to a comparison of continuous improvement initiatives implemented by the NMRAs, this study revealed that Sierra Leone was the only country that has fully

implemented all the initiatives at this time. There is therefore an opportunity for other NMRAs to learn from Sierra Leone accordingly. According to O'Brien et al, (2020) "Regulators may elect to use external experts from academia, external experts must have appropriate knowledge, skills and experience to conduct an assessment; have no conflicts of interest; meet pre-agreed deadlines and respect the confidentiality of data".

Comparing the training and education initiatives which have been implemented by the NMRAs showed that Sierra Leone and additionally Ghana could serve as a reference to the other NMRAs accordingly.

This study has therefore shown that resources are available in the ECOWAS region for the NMRAs to rely on as well as to improve their respective good review practices.

For the implementation of quality decision-making practices, since this study showed that none of the NMRAs had fully implemented the framework and had not also fully adhered to the practices, this can be considered to be a challenge that needs to be resolved.

This comparative study of the good review practices of countries participating in the ECOWAS-MRH region has highlighted both the similarities among the agencies and also the differences which should be addressed in order to improve the regulatory systems in these countries. The full implementation of GRevP should be essential for strengthening the performance of regulatory agencies and enhancing mutual trust between the NMRAs in the ECOWAS region.

RECOMMENDATIONS

The following are the recommendations for improving the good review practices of countries participating in the ECOWAS-MRH initiative.

- **Autonomy of Regulatory Agencies:** The NMRAs in the ECOWAS region should work towards achieving independence, enabling them to operate outside the administration of their respective Health Ministry
- **Regulatory Strengthening:** Consideration should be given to employing the services of external experts for the review of marketing authorization applications in view of the limited resources currently within some of the NMRAs in the ECOWAS region.
- **Performance Monitoring:** Agencies should have internal tracking systems to monitor the progress of marketing authorisation applications in order to meet their target timelines.
- **Transparency and Communication Strategies:** Agencies in the region would benefit from implementing additional good review practice measures as well as sharing of assessment reports with applicants and publishing approval times as well as the summary basis of approval.
- **Quality Decision-making Practices:** It is recommended that all agencies implement the 10 quality decision-making practices underpinned by initiating appropriate structured training.

CHAPTER 06

COMPARISON OF THE REGULATORY REVIEW MODELS AND TIMELINES OF THE ECOWAS REGIONAL INITIATIVE

SUMMARY

- Some of the best regulatory practices which are being implemented by NMRAs across the world include mutual recognition, reliance and other facilitated regulatory pathways. This is to improve the timely access to quality medical products. The WHO Prequalification programme serves as a ready reference with regard to its implementation of facilitated regulatory pathways to benefit low- and middle-income countries.
- The aim of this study was to assess and compare the review models and regulatory timelines of the national medicines regulatory authorities (NMRAs) of Burkina Faso, Cote d'Ivoire, Ghana, Nigeria, Senegal, Sierra Leone and Togo, in order to identify opportunities for improvement.
- The Optimising Efficiencies in Regulatory Agencies (OpERA) questionnaire, which had been validated by the Centre for Innovation in Regulatory Science (CIRS) was completed by each of the NMRAs. Completing the OpERA questionnaire facilitated the assessment of the regulatory review processes which affect good review practices.
- The agencies employ the three types of scientific review models. These are namely; verification review (type 1), abridged review (type 2) and full review (type 3). Five of the NMRAs deploy the fast track/priority review model. Under this pathway a rapid assessment is carried out to obtain pharmacological, marketing/commercialization, pharmacovigilance and additional clinical trials information. In Cote d'Ivoire, priority review is used by the agency for WHO prequalified medicines and SRA- approved medicines.
- The data requirements for the applications are essentially the same among the agencies. Applicants are required to provide a completed dossier in the ICH common technical format (CTD) to support an application for marketing authorization/registration irrespective of the review model to be deployed in processing the application. The extent of the scientific review is however dependent on the type of review model that is deployed in processing the application.
- This comparative study of the review models and regulatory timelines of countries participating in the ECOWAS-MRH initiative has highlighted both the similarities among the agencies and also the differences which are to be addressed in order to improve upon the regulatory systems in these countries.

INTRODUCTION

National regulatory medicines authorities (NMRAs) are mandated to assure timely access to quality, safe and efficacious medical products. This assurance is primarily achieved through a marketing authorisation/registration procedure established in each country. Ahonkai and others (2016) documented that "the mandatory individual review by multiple countries, each with its own regulatory authority, processes and capability challenges leads to increased complexity and long product approval timelines" leading to delays in making these products accessible to patients. (Alfonso et al, 2024; WHO, 2024d; Ncube et al, 2021; Sillo et al, 2020; Ahonkai et al, 2016; Kamwanja et al 2011)

According to available literature "an optimized regulatory process would contribute to improved access to quality health products." (Ahonkhai et al, 2016). Some of the contributory factors to long regulatory timelines in Sub-Saharan Africa have been identified as a "failure to leverage or rely on the findings from reviews already performed by competent authorities, disparate requirements for product approval by the countries and lengthy timelines by manufacturers to respond to regulatory queries." (Ahonkhai et al, 2016).

There is a discrepancy in regulatory review requirements mainly due to non-scientific additional factors potentially increasing the regulatory timelines and this appears to be challenging to manufacturers in making medicines available to patients (O'Brien et al, 2020).

A reputable multinational company has documented "ten pillars that represent the key hallmarks of strong regulatory review systems globally". Furthermore, it has clearly stated that "It is in the interest of all stakeholders to have effective and efficient regulatory review systems in place. From development and registration of new, innovative products for unmet medical need to the management of approved products through their life cycle, there is a pressing need to ensure streamlined regulatory review systems that result in safe and effective medicines for patients" (O'Brien et al, 2020).

To improve the timely access to quality medical products, some of the regulatory best practices which are being implemented by NMRAs across the world include mutual recognition, reliance and other facilitated regulatory pathways. (Yoffe, 2023; Liberti, 2022). The WHO Prequalification programme always serves as a ready reference with

regard to its implementation of facilitated regulatory pathways to benefit low- and middle-income countries.

In 2020, the United States FDA updated its generic drug application prioritization policy "to efficiently allocate limited agency resources to areas where priority review is most likely to meaningfully increase generic drug access and ensure fairness to applicants" (USFDA, 2020b). In Europe the EMA has in place a procedure to accelerate assessment of marketing authorisation applications which can impact public health (EMA, 2024).

The World Health Organization reported that the absence of well-functioning regulatory systems to facilitate timely access to quality, safe and efficacious medical products was clearly evident during the COVID-19 pandemic. (WHO, 2024e)

It is also reported that there is insufficient information publicly available to serve as reference on the differences and similarities that exist amongst NMRAs even at the global level and therefore makes it very challenging to achieve efficient national regulatory systems. Thoroughly investigating the critical components of regulatory systems will help to discover their current state and propose appropriate improvements to address any identified gaps. (Alfonso et al, 2024; O'Brien et al, 2020; Ahonkhai et al, 2016).

Ahonkhai et al (2016) proposed that future publications should pay attention to the outcome of implementation of various regulatory measures to achieve shorter timelines by the NMRAs in Sub-Saharan Africa.

The authors, Alfonso et al, (2024) accurately stated that "regulatory system strengthening via regional coordination could also support the operationalization of the newly formed continental agency, the African Medicines Agency (AMA)". Therefore, this study of the review models and regulatory timelines in ECOWAS is considered timely.

According to the WHO "good communication is critical and has many advantages for regulatory authorities, applicants and the public. It can improve the efficiency of the development and review processes and thus ultimately speed up patient access to quality medical products" (WHO, 2015a). NMRAs have been urged to share their best practices to enhance efficiency in the review process of medicines. (O'Brien et al, 2020).

As a result of the successful assessment of the review models and regulatory timelines of countries participating in the ZaZiBoNa and EAC -MRH initiatives, it is appropriate

that the review models and regulatory timelines of countries participating in the ECOWAS-MRH initiative are assessed and hence the implementation of this study (Sithole et al.,2021a; Ngum et al., 2024b). The study is therefore aimed at assessing the review models and regulatory timelines of countries participating in the ECOWAS-MRH initiative and to communicate the findings to other regulatory authorities, stakeholders and the public and serve as a reference for future comparative analysis across the NMRAs in ECOWAS to establish best practices.

STUDY OBJECTIVES

The objective of this study which is one of a two-part series provides an insight into the review models and regulatory timelines of countries participating in the ECOWAS-MRH initiative. The other study will compare their good review practices.

METHODS

Study participants

All seven active NMRAs of the ECOWAS-MRH initiative namely, National Pharmaceutical Regulatory Agency-Burkina Faso, Autorite Ivoirienne de Regulation Pharmaceutique (AIRP)-Republic of Cote d'Ivoire, Food and Drugs Authority (Ghana-FDA), National Agency for Food and Drug Administration and Control (NAFDAC)- The Federal Republic of Nigeria, Senegalese Pharmaceutical Regulatory Agency (l'Agence Senegalaise de Reglementation Pharmaceutique -ARP)- Republic of Senegal, Pharmacy Board of Sierra Leone (PBSL) and the Directorate of Pharmacy, Medicine and Laboratories-Togo, participated in the study between August 2021 and November 2023.

Data collection

The Optimising Efficiencies in Regulatory Agencies (OpERA) questionnaire, which had been validated by Rodier and colleagues (2020) of the Centre for Innovation in Regulatory Science (CIRS) was completed by each of the NMRAs. Completing the OpERA questionnaire facilitated the assessment of the regulatory review processes which affect approval times.

The OpERA questionnaire consists of six modules: module 1 covers structure, organisation and resources of the agency; module 2 explores the review models used for the scientific assessment of medicines; module 3 identifies the key milestones in the review process; module 4 captures regulatory measures that have been built into the regulatory review process; module 5 explores the quality of decision-making processes and module 6 documents the agency's perception of the key drivers and

barriers that influence the effectiveness and efficiency of its review and decision-making processes.

RESULTS

For the purpose of clarity, the results of the study will be presented in three parts: Part l) Metrics of NASs, generics and WHO prequalified generics received and approved in 2023; Part ll) types of review models and extent of scientific assessment and Part lll) key milestones in the review process.

Part l. Metrics of NASs, generics and WHO prequalified generics

A comparison of metrics of NASs, generics and WHO prequalified generics which were received and approved in 2023 is provided in Table 7.1

It is noted that a large number of generics were not approved by the agencies. This is very concerning and requires attention of both manufacturers and the regulators.

Mean approval times

Table 6.2 shows a comparison of mean approval times of NASs, generics and WHO prequalified generics in 2023.

Four out of the seven NRAs provided data regarding their mean approval times (calendar days) for NASs, generics and WHO-prequalified generics in 2023. Cote

Table 6.1. Comparison of metrics on NASs, generics and WHO prequalified generics in 2023

Country	Burkina Faso	Cote d'Ivoire	Ghana	Nigeria	Senegal	Sierra Leone	Togo
NASs							
Received	NS	23	26	NS	NS	4	NS
Approved	NS	23	17	1	NS	4	NS
Generics							
Received	NS	312	1189	NS	NS	550	NS
Approved	NS	90	577	729	NS	390	NS
WHO-prequalified generics							
Received	NS	21	3	NS	NS	2	NS
Approved	NS	21	3	8	NS	2	NS

NS-Not submitted

Table 6.2. Comparison of mean approval times (days) of NASs, generics and WHO prequalified generics in 2023

Country	Burkina Faso	Cote d'Ivoire	Ghana	Nigeria	Senegal	Sierra Leone	Togo
Full Review							
NASs	NS	240	56	0	NS	150	NS
Generics	NS	240	56	247	NS	150	NS
WHO PQ generics	NS	NA	NA	0	NS	75	NS
Abridged							
NASs	NS	NA	116	30	NS	75	NS
Generics	NS	NA	116	0	NS	53	NS
WHO PQ generics	NS	NA	NA	0	NS	30	NS
Verification							
NASs	NS	NA	NA	0	NS	53	NS
Generics	NS	NA	NA	0	NS	38	NS
WHO PQ generics	NS	NA	118	60	NS	30	NS

NS-Not submitted NA-Not applicable

d'Ivoire, reported the highest mean approval time of 240 calendar days for NASs that were processed via the full review pathway. Nigeria on the other hand reported the longest mean approval time of 247 calendar days with regard to generics that were processed via the full review pathway. For applications that were processed via the abridged review pathway, Ghana reported the highest mean approval time of 116 calendar days with regard to both NASs and generics. Finally for applications that were processed via the verification pathway, Ghana reported the highest mean approval time (Table 6.2)

Part II. Types of review models and extent of scientific assessment

The agencies employ three types of scientific review models. These are namely, verification review (type 1), abridged review (type 2) and full review (type 3).

The verification model is used for applications that have been authorized by one or more recognised reference or 'benchmark' agencies. The definition of a recognised reference agency is dependent on each NMRA. Notwithstanding, generally the recognised reference agencies are the World Health Organization (WHO), European Medicine

Agency (EMA), United States Food and Drug Administration (USFDA) and Swissmedic. The NMRA in the importing country 'verifies' that the product's quality, safety and efficacy in both the reference and importing countries are essentially the same. By employing this model, applications are reviewed within a short time, usually within 90 days.

The abridged model is used for applications that have been authorized by a recognized reference agency which requires an 'abridged' independent review of the quality data which may be relevant to the climatic conditions and also a benefit-risk assessment may also be undertaken with regard to its use in the importing country.

The full review model is used for applications that have not been authorized by a recognized reference agency and therefore requires a 'full' review of the product's quality, safety and efficacy.

In addition to the three types of review models defined above, the agencies have a fast track/ priority review model in place for prioritizing applications for unmet medical needs / public health programmes in each country (Table 6.3).

Verification review

Five of the NMRAs deploy the verification review model. Applications submitted through the WHO collaborative procedures and the MAGHP by Swissmedic are processed under the verification review model. The verification process is used to validate the status of the product and ensure that the product which is intended for local marketing conforms to the authorized product. In Nigeria and Sierra Leone applications which have been assessed by stringent regulatory authorities (SRAs), members of ICH and WAHO are also processed through the verification review model. Those agencies which have achieved WHO GBT maturity level 3 or 4 are recognized as reference agencies. In some instances a 'checklist' is used to confirm the completeness of the data. Unredacted assessment reports are required from these reference agencies (Table 6.3)

Abridged review

All the NMRAs deploy the abridged review model. In Ghana applications previously registered by an SRA (EMA, USFDA, MHRA and Health Canada) are assessed via the abridged review pathway. An abridged assessment is carried out in relation to the use of the products under local/ national conditions. In Togo products approved by SRAs and WHO prequalified medicines are assessed via the abridged review pathway. (Table 6.3)

Table 6.3. Review models employed and target timelines (calendar days)

Type of review model	Burkina Faso	Cote d'Ivoire	Ghana (excludes applicant time)	Nigeria	Senegal	Sierra Leone	Togo
Verification review (Type 1)	✓	✗	✓	✓	✓	✓	✗
Target	NA	NA*	90	90	90	NA	NA*
Abridged review (Type 2)	✓	✓	✓	✓	✓	✓	✓
Target	NA	NA	90	NA	NA	NA	NA
Full review (Type 3)	✓	✓	✓	✓	✓	✓	✓
Target	NA	NA	180	240	120	NA	NA
Fast Track/Priority Review	✓	✓	✓	✓	✗	✓	✗
Target	NA	NA	90	NA	NA*	NA	NA*

NA -Not available NA*-Not applicable

Full review

All the NMRAs deploy the full review model. The agencies are capable of carrying out full assessment of quality, pre-clinical (safety) and clinical (efficacy) data. Information on prior registration elsewhere may still be a pre-requisite to final authorization (type 3A) or the review may be 'self-standing' (type 3B). Generally, applications for medicines from non-ICH regions and non-WHO prequalified products are processed via this pathway.

Fast track/priority review

Five of the NMRAs deploy the fast track/priority review model. Under this pathway a rapid assessment is carried out to obtain pharmacological, marketing/commercialization, pharmacovigilance and additional clinical trials information. In Cote d'Ivoire, priority review is used by the agency for WHO prequalified medicines and SRA-approved medicines.

Data requirements and extent of assessment

A summary comparison of key features of the regulatory systems for processing applications for marketing authorization for medicines in the NMRAs is provided in Table 6.4. It is noted that there are several similarities in the regulatory systems of these agencies.

The data requirements for the applications are essentially the same among the agencies. Applicants are required to provide a completed dossier in the ICH common technical format (CTD) to support an application for marketing authorization/registration irrespective of the review model to be deployed in processing the application. Each agency sets targets for the time it spends on the scientific assessment of NASs and generic applications. Additionally, each agency has a target for the overall time for the review and approval of an application. Questions to sponsors are batched at fixed points in the review procedure. Each agency recognises medical urgency as a criterion for accelerating the review and approval process for qualifying products. Different sections of the technical data are reviewed in parallel rather than sequentially. Discussion of pricing is separate from the technical review and does not delay the approval of products. The focus of each agency is on checking quality in the marketplace and requirements for analytical work do not delay the marketing authorisation. With regard to differences which were noted, five of the agencies required submission of a WHO certificate of a pharmaceutical product (CPP) with the application or before authorisation is issued. In two of the agencies more than 25% within the agency review staff were physicians and recording procedures to allow the company response time to be measured and differentiated in the overall processing time were not available in Burkina Faso.

The extent of the scientific review is however dependent on the type of review model that is deployed in processing the application. Since all the NMRAs deploy the full review model, Table 6.5 shows a comparison of the extent of assessment of the scientific data.

Part lll Key milestones in the review process.

A typical NMRA with maturity level 3 status' map of the review process and authorization of a product that is approved on the first cycle (i.e., does not include a second or more cycles for products approved subject to the submission of additional data) and in a format that correlates with the 'key milestones' on the review process. (Figure 6.1)

A typical NMRA with maturity level 3 status' map of the review process and authorization of a product that is approved on the first cycle (i.e., does not include a second or more cycles for products approved subject to the submission of additional data) and in a format that correlates with the 'key milestones' on the review process is provided in Figure 6.1.

Table 6.4. Summary comparison of key features of the regulatory systems for medicines

Marketing authorisations	Burkina Faso	Cote d'Ivoire	Ghana	Nigeria	Senegal	Sierra Leone	Togo
Certificate of a Pharmaceutical Product (CPP): CPP is required with the application or before authorisation is issued	✓	×	✓	✓	✓	✓	×
Common Technical Document (CTD): CTD format is mandatory for applications	✓	✓	✓	✓	✓	✓	✓
Medical staff: More than 25% within the agency review staff are physicians	✓	×	×	✓	✓	✓	✓
Review times: The agency sets targets for the time it spends on the scientific assessment of NASs and generic applications	✓	✓	✓	✓	✓	✓	✓
Approval times: The agency has a target for the overall time for the review and approval of an application	✓	✓	✓	✓	✓	✓	✓
Questions to sponsors are batched at fixed points in the review procedure	✓	✓	✓	✓	✓	✓	✓
Company response time: Recording procedures allow the company response time to be measured and differentiated in the overall processing time	×	✓	✓	✓	✓	✓	✓
Priority reviews: The agency recognises medical urgency as a criterion for accelerating the review and approval process for qualifying products	✓	✓	✓	✓	✓	✓	✓
Parallel processing: Different sections of technical data reviewed in parallel rather than sequentially	✓	✓	✓	✓	✓	✓	✓
Price negotiation: Discussion of pricing is separate from the technical review and does not delay the approval of products	✓	✓	✓	✓	✓	✓	✓
Sample analysis: The focus is on checking quality in the marketplace and requirements for analytical work do not delay the marketing authorisation	✓	✓	✓	✓	✓	✓	✓

Table 6.5. Extent of scientific assessment for full review

Parameter	Burkina Faso	Cote d'Ivoire	Ghana	Nigeria	Senegal	Sierra Leone	Togo
Chemistry, manufacturing and control (CMC) data extensive assessment	✓	✓	✓	✓	✓	✓	✓
Non-clinical data extensive assessment	✓	✓	✓	✓[a]	✓	✓	✓
Clinical data extensive assessment	✓	✓	✓	✓	✓	✓	✓
Bioequivalence data extensive assessment	✓	✓	✓	✓	✓	✓	✓
Additional information obtained (where appropriate)	✓	✓	✓	✓	✓	✓	✓
Other agencies internal review reports	✓	✓	✓	✓	✓	✓	✓
Medical and scientific literature	✓	✓	✓	✓	✓	✓	✓

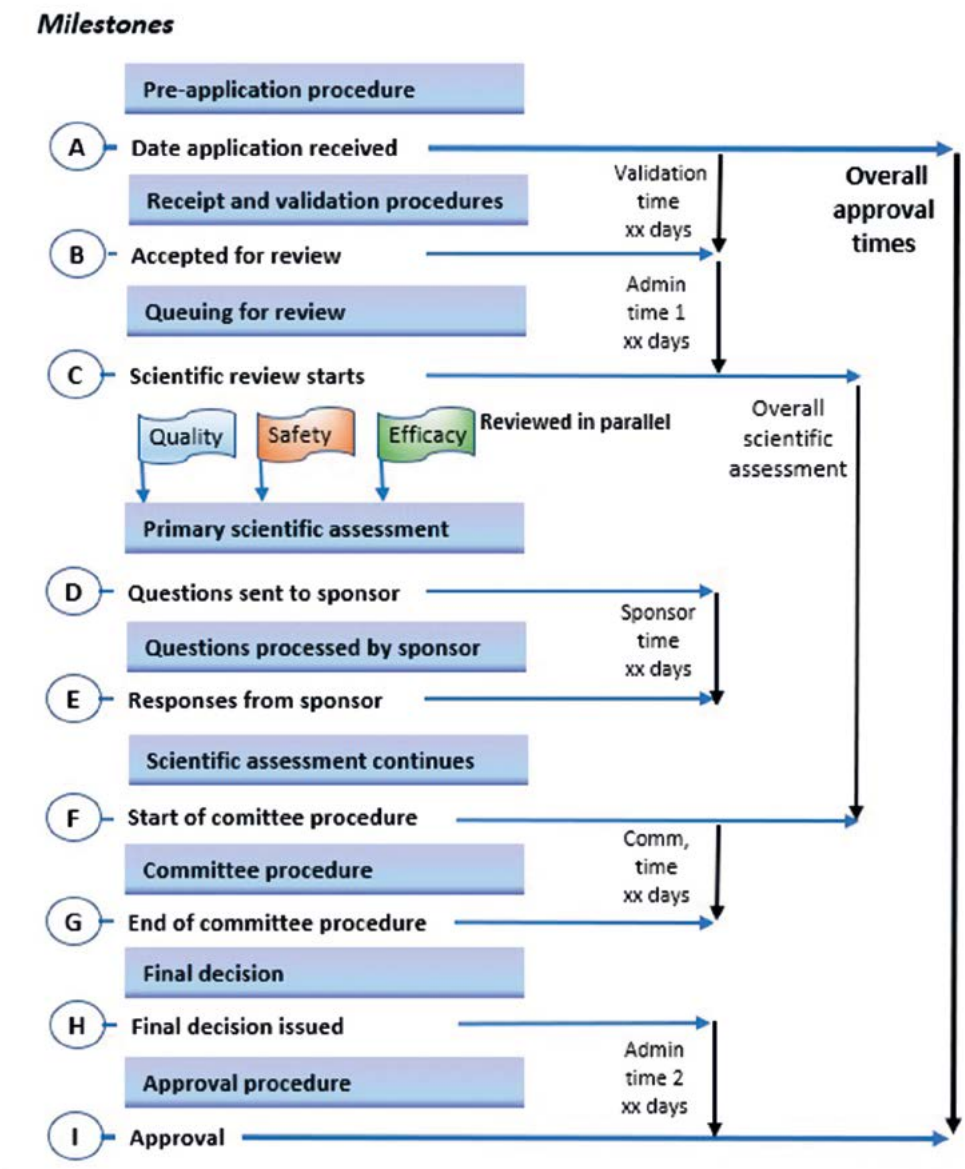
✓[a] Required for NAS but not generic products

It is noted that the NMRAs have identified similar key milestones in their full review pathways. These are namely receipt and validation; queuing; primary scientific assessment; questions to applicant; review by expert committee and approval procedure. Table 6.6 shows a comparison of targets for key milestones in the full (type 3) review process.

Receipt and validation

There is no formal procedure before the start of the application process. The receipt and **v**alidation process lasts from one day to 30 days. The variation in the time is dependent on the initial administrative and technical processes which are in place in

Figure 6.1. Key Milestones in the Review Process



the NMRAs. Applications are screened to ascertain their level of completeness in order to be processed for assessment. For incomplete applications a request for the missing data is sent to the applicant. The applicant is obliged to provide a satisfactory response with a stipulated time limit.

Table 6.6. Comparison of targets for key milestones in the full (type 3) review process (calendar days). NA=Not Available

Target	Burkina Faso	Cote d'Ivoire	Ghana	Nigeria	Senegal	Sierra Leone	Togo
Receipt and validation (A-B)	15	30	28	10	1	7	NA
Queuing (B-C)	14-56	14-56	14-42		NA	14-56	NA
Primary scientific assessment (C-D)	15	30	112	80	NA	NA	NA
Questions to applicant (clock stop) (D-E)	180	90	30	90	NA	42	90
Review by Expert Committee (G-H)	15	20-30	1	30	NA	7	1-2
Approval procedure (Admin)	<30	30-90	30	30	30-90	30	NA
Overall approval time (A-I)	311 (excludes applicant's time)	120 (excludes applicant's time)	180 (excludes applicant's time)	240 (excludes applicant's time)	120 (excludes applicant's time)	180 (excludes applicant's time)	120 (excludes applicant's time)

Queue time

Applications which are not eligible for the fast track/priority pathway are placed in a queue according to their review pathways to await their turn for the primary scientific assessment. The queue time varies from 14 to 56 days among the agencies. The queue time is dependent on the agency's workload and availability of assessors to conduct the primary scientific assessment. In Ghana samples of applications are sent to the FDA Ghana laboratory for analysis whilst the dossier is placed in a queue for assessment. Some of the agencies regard backlog as a challenge and try to address this by increasing the uptake of assessors, introducing smart approaches such as not duplicating effort on same dossier submitted by a different applicant from the same manufacturer and also implementing risk-based assessment. Additionally, some agencies work on product review performance metrics versus the volume of applications received to improve the efficiency of the review process.

PRIMARY SCIENTIFIC ASSESSMENT

The duration of the primary scientific assessment is from 15 to 112 days amongst the agencies. (Table 6.4) with the different sections of the technical data being reviewed sequentially rather than in parallel. The time spent on the assessment of dossiers is very much dependent on the technical expertise, knowledge and experience of assessors. The assessment is carried out by the agency's technical staff however some of the NMRAs use external experts to assess clinical and non-clinical data.

Questions to applicants

Following completion of the primary scientific assessment, questions are sent to applicants for response to be provided within a time frame which lasts from 30 to 180days. Depending on the NMRA, questions are collected into a single batch and sent either prior to the expert committee meeting or after the expert committee has reviewed them. In some NMRAs the applicant can hold meetings with the agency staff to discuss questions and queries that arise during the assessment. In some agencies the scientific review ceases while questions are being processed by the applicant, ie "clock stop" is applied.

Review by expert committee

A committee of experts is used in the review process, they are consulted after the agencies have reviewed and reported on the scientific data. The expert committee takes between 1 to 30days to review the application, dossier assessment and laboratory analytical report and makes a final decision on applications for marketing authorisation.

There is no additional step in the scientific review process after the Committee has given its opinion.

Authorisation procedure

The NMRAs take between 30 to 90 days to grant approval after receiving a positive outcome from the expert Committee.

DISCUSSION

This study compared the review models and regulatory timelines of countries that actively participate in the ECOWAS-MRH initiative in order to identify opportunities for improvement.

This study which is similar to the SADC and EAC regional studies by Sithole et al (2021) and Ngum et al (2024b) respectively also sought additionally to discover the similarities and differences amongst these NRAs as they work together to advance the course of the ECOWAS-MRH initiative.

The agencies generally utilize the standard review pathways and have also set realistic target timelines with regard to the limited resources available in West Africa. This is a significant observation for the NMRAs in that it indicates that these agencies are operating in similar ways as other recognized reference agencies (Ngum et al., 2024b). By implementing verification and abridged review pathways, it can be inferred that these agencies "leverage or rely on findings from reviews already performed by competent authorities" (Ahonkhai et al, 2016).

The issue of "disparate requirements for product approval by the countries" which was previously reported by Ahonkai et al (2016) appears to be non-existent as there were more similarities observed among the agencies regarding data requirements and extent of assessment of the scientific data. This is largely due to the fact the submission of documentation is in the common technical document (CTD) format.

The following differences were noted with regard to comparison of the key features of the regulatory systems for medicines; five of the agencies required submission of a WHO certificate of a pharmaceutical product (CPP) with the application or before authorisation is issued. In two of the agencies more than 25% within the agency review staff were physicians and had recording procedures which allowed the company response time to be measured and differentiated in the overall processing time which were not available in Burkina Faso. Submission of a CPP was also reported as a requirement in the SADC region (Sithole et al.,2021a; Ngum et al., 2024b).

There were differences reported in the targets for the key milestones in the full review process; and these ultimately led to differences in the overall approval times for medicines which were processed via the full review pathway.

It was reported that in the SADC region, 'countries with higher workloads had no targets for the scientific assessment or overall approval process' (Sithole et al.,2021b) This was not the case for ECOWAS as all the agencies has targets for the scientific assessment and for the overall approval process.

The study in the SADC region also suggested that resources could be optimized by the maturing agencies when reliance is placed on other mature agencies. This suggestion is worth replicating in the ECOWAS region to optimize resources within the sub-region (Sithole et al.,2021b).

This comparative study of the review models and regulatory timelines of countries participating in the ECOWAS-MRH initiative has highlighted both the similarities among the agencies and also the gaps which are to be addressed in order to improve the regulatory systems in these countries.

RECOMMENDATIONS

The key recommendations for improving review models and regulatory timelines of countries participating in the ECOWAS-MRH initiative are:

- **Publication of targets and timelines for key milestones**- Agencies should make their timelines for key milestones available to all stakeholders including the public. This will help to promote transparency in their regulatory processes.
- **The ECOWAS-MRH initiative should be recognized as a reference;** Agencies should process applications submitted via the ECOWAS-MRH procedure through the verification review pathway in order to expedite their approvals at the country level.
- **Publication of status of applications-** Agencies should consider publishing the status of all applications periodically. This will increase transparency in their regulatory work and also be of interest to all stakeholders especially manufacturers and patients.
- **Develop robust information technology systems**- Agencies should invest in robust IT systems to help in the tracking of applications to enable them to be efficient.
- **Explore smart ways to communicate to applicants**- Agencies should find innovative ways to effectively communicate with stakeholders to achieve their regulatory mandates on time.

CHAPTER 07

THE WEST AFRICAN MEDICINES REGULATORY HARMONIZATION INITIATIVE: THE VIEWS OF THE ECOWAS MEMBER COUNTRIES

SUMMARY

- The West Africa Health Organization launched the West Africa Medicines Regulatory Harmonization Project (WA-MRH) in 2017 with the overarching objective to improve the availability of high-quality, safe and effective medicines and vaccines by the 15 countries in the Economic Community of West African States region. Although this project has made significant progress towards the realisation of its goals, challenges still remain. The aim of this study was to evaluate the effectiveness and efficiency of the WA-MRH, examine what challenges are being encountered and identify strategies that would strengthen the process for realising the initiative's goals.
- The Process Effectiveness and Efficiency Rating (PEER) questionnaire was used to collect data from assessors representing the seven active NMRAs in the joint assessment procedure that identified the benefits, challenges and recommendations for improving the performance of the WA-MRH project.
- The benefits of the joint assessment procedure included time savings to manufacturers resulting from submitting one dossier and the same response package to multiple countries resulting in access to the several African markets within the same timeframe. Additionally, some of the NMRAs have been able to strengthen their technical capacity as a result of this initiative. Key challenges to the project include the lack of a robust information technology system that would enable dossier tracking and constraints in human resources needed to support dossier submissions and the assessment process.
- This study identified the strengths of the WA-MRH initiative as well as strategies for improvement and achievement of its objectives. The centralised submission of a dossier and its tracking is key to the regulatory assessment process. This research has demonstrated that amongst other considerations, a robust information technology system, coupled with the necessary human resource capacity would greatly enhance the effectiveness and efficiency of the WA-MRH initiative.

INTRODUCTION

The national medicines regulatory authorities (NMRAs) in Africa are challenged to judiciously utilise their limited human, technical and financial resources to ensure access to safe, high-quality and efficacious medicines in the presence of high disease burden and inadequate local pharmaceutical manufacturing on the continent (WHO, 2014a; WHO, 2010b).

To help address these challenges in Africa, the African Medicines Regulatory Harmonization (AMRH) Initiative was launched in 2009 to collaborate with the Regional Economic Communities to establish mechanisms to harmonize regulatory activities in the various regional blocks. Subsequently in 2010, a report on 26 national medicine regulatory authorities (NMRAs) in sub-Saharan Africa which had been assessed over an eight-year period was published by the World Health Organization (WHO) (WHO, 2010b).

Not surprisingly, the common challenge reported was inadequate regulatory capacity. To deal with this challenge, the West African Health Organization and its economic partners took a bold decision in 2014 to initiate medicine regulatory harmonization in West Africa under the leadership of WAHO. As part of the preparations for the implementation of the West African harmonization programme, a Steering Committee, consisting of the heads of medicine regulatory agencies in the 15 countries in West Africa was established in 2015 to provide the much-needed high-level regulatory support required for the initiative to be successful. Following this, in November 2017 the West African Health Organization (WAHO), launched the West Africa Medicines Regulatory Harmonization Project (WA-MRH) under the AMRH, to improve the availability of high-quality, safe and effective medicines and vaccines in the Economic Community of West African States (ECOWAS) (WA-MRH, 2021).

According to the Director General of the West African Health Organization (WAHO), "that is why we have agreed to jointly register and regulate medicines produced locally and imported into the region with the aim of reducing the time of registration and improving access to medicines as well as ensure better regulatory oversight." (Daniel, 2019). This remark referred to the challenges with technical and financial resources and also the differences in the official national languages in the ECOWAS region (Daniel, 2019). Between March 2018 and February 2019, harmonised guidance documents which were required to facilitate the initiative were developed by technical working groups, and then authorised by the Steering Committee (WA-MRH, 2021).

In the current operating model of the WA-MRH initiative, an NMRA serves as a lead coordinator for a two-year period and receives, validates and arranges for the assessment of the dossiers and additionally communicates with applicants and the WA-MRH secretariat, which is based in the WAHO. There are 11 steps in the WA-MRH joint assessment procedure which include: expressions of interest; pre-submission meeting; submission and dossier validation; technical evaluation (Phase I); joint evaluation by the expert working group (EWG) and technical partners (Phase I); joint good manufacturing practice inspection and quality control; technical evaluation (Phase II); joint evaluation by expert working group and technical partners (Phase II); technical evaluation (Phase III); final joint evaluation by EWG and technical partners; and validation by WA-MRH Steering Committee (WA-MRH, 2021)..

A flow chart of the WA-MRH joint assessment procedure is provided (Figure 8.1). In summary, it takes 120 and 226 calendar days for a high standard-completed dossier and a dossier with a one-time list of questions to go through these 11 steps, respectively (WA-MRH, 2021).

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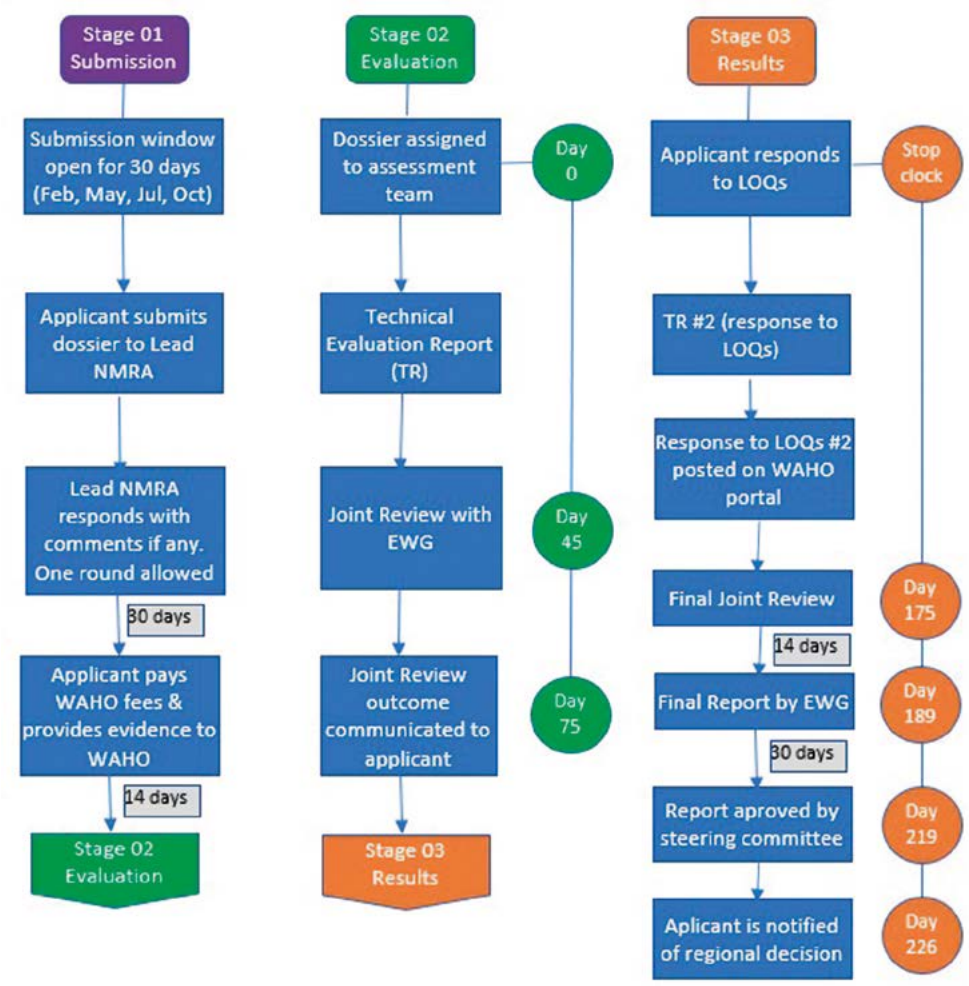
Since 2019, seven NMRAs in West Africa have participated in joint assessments of submitted applications for registration of medicines and the outcomes of these assessments have been taken as a basis for the regulatory decisions in the 15 NMRAs in the ECOWAS region. It is important to note that in the ECOWAS region, the NMRAs of Ghana and Nigeria obtained WHO-GBT maturity level-3 status in April 2020 and April 2022 respectively, a level that indicates a stable and well-functioning regulatory system (WA-MRH, 2021; WHO, 2022d).

There is a drive within regulatory agencies to re-engineer their processes to meet stakeholders' expectations in a timely manner. This timeliness, being central to assessing the efficiency and effectiveness of any system, can be regarded as the motivation for the regular evaluation of the processes, which is to ensure that the strengths of the system are sharpened whilst identified redundancies are eliminated to realise stakeholder expectations.

Following the successful assessment of the ZaZiBoNa and EAC-MRH initiatives in 2021 and the launch of the African Medicines Agency, it is timely that the WA-MRH initiative is assessed at this time and hence the implementation of this study. (Sithole et al, 2022a; Ngum et al 2022a). This study aimed to assess the effectiveness and efficiency of the West Africa Medicines Regulatory Harmonization Initiative by the member countries.

Figure 7.1. The WA-MRH joint assessment process.



STUDY OBJECTIVES

The objectives of this study were to

1. Obtain the views of the individual medicines' regulatory authorities of the WA-MRH initiative about the performance of the programme to date
2. Identify the challenges experienced by individual authorities throughout the life cycle of the WA-MRH initiative
3. Determine the strengths and weaknesses of the initiative
4. Identify the ways of improving the performance of the work-sharing programme
5. Envisage the strategy for moving forward

METHODS

Study Participants

All seven active NMRAs of the WA-MRH initiative namely, National Pharmaceutical Regulatory Agency-Burkina Faso, Autorite Ivoirienne de Regulation Pharmaceutique (AIRP) - Republic of Cote d'Ivoire, Food and Drugs Authority (Ghana-FDA), National Agency for Food and Drug Administration and Control (NAFDAC) -The Federal Republic of Nigeria, Senegalese Pharmaceutical Regulatory Agency (l'Agence Senegalaise de Reglementation Pharmaceutique -ARP) -Republic of Senegal, Pharmacy Board of Sierra Leone (PBSL) and the Directorate of Pharmacy, Medicine and Laboratories - Togo, participated in the study between January and June 2022.

Data Collection

The Process Effectiveness and Efficiency Rating (PEER) questionnaire, previously developed and validated by Ngum and colleagues to evaluate the performance of the East African Community joint assessment procedure (Ngum, 2022), was used to collect the study data. The PEER questionnaire consists of five parts as follows: authority resources, benefits of the WA-MRH initiative, challenges of the WA-MRH initiative, improving the performance (effectiveness and efficiency) of the work-sharing programme and strategy for moving forward.

The representative person and the head of the NMRA from each country were responsible for completing and approving each questionnaire respectively. Semi-structured interviews using a checklist were carried out with each authority to validate their responses to the questionnaire. The interviews provided flexibility and a further opportunity for the respondents as they were able to give open-ended answers to some questions. Some sections of the questionnaire were clarified, challenges in completing the questionnaire were discussed, the benefits of the study acknowledged and the participants reviewed the final study report. To ensure confidentiality, the questionnaire was marked as confidential and this was reinforced during the interviews.

The checklist used is as follows:

YOUR VIEWS ON THE PEER QUESTIONNAIRE

Please answer the following questions to help us improve the WA-MRH PEER questionnaire:

1. Did you find the questions clear and straightforward to respond?

Yes ☐ No☐

2. Did you find the response options relevant to the heading of each section (A to E)?

Yes ☐ No☐

3. Did you find the questions relevant to the aims and objectives of the study?

Yes ☐ No☐

4. Did you find the questions relevant to your authority and WA-MRH work sharing initiative?

Yes ☐ No☐

5. Did you find any relevant questions missing?

Yes☐ No☐

If yes, please state which questions were missing in the space after this list of questions.

.....

6. Did you find any questions that should be excluded?

Yes ☐ No☐

If yes, please state the questions that should be excluded in the space after this list of questions.....

7. Did you find the questionnaire useful to reflect on both your agency experience as well that of WA-MRH?

Yes☐ No☐

Name.....Title..... Date.....

Figure 8.2. The Process, Effectiveness and Efficiency Rating (PEER) questionnaire.

CONFIDENTIAL

WA-MRH JOINT ASSESSMENT PROCEDURE

PROCESS EFFECTIVENESS & EFFICIENCY RATING (PEER)

Pic taken from http://www.referenceforbusiness.com/management/De-Ef/Effectiveness-and-Efficiency.html

PEER QUESTIONNAIRE

November 2021

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Figure 8.2. (continued).

INTRODUCTION

The launch of the West Africa Medicines Regulatory Harmonization Project (WA-MRH) in July 2017 was to improve the availability of quality, safe and effective medicines and vaccines in the ECOWAS region.

At least seven (7) National Medicines Regulatory Agencies (NMRAs) have participated in joint assessments of submitted applications for registration of medicines and taken the outcome as a basis for the regulatory decisions in the 15 NMRAs in the ECOWAS region.

In recent years, there has been a drive within regulatory agencies to re-engineer their processes for improved efficiency and effectiveness and this often begins with a baseline evaluation of the current process to identify strengths and weaknesses. *Effectiveness* can be defined as 'doing the right things' often measured by the value derived by customers/stakeholders from an organisation's processes or services while *Efficiency* can be defined as 'doing things right' which saves the organization time and resources.

Study Participants

The PEER Questionnaire is being sent to 7 National Medicines Regulatory Authorities in the ECOWAS region namely, Pharmacy Board of Sierra Leone (PBSL), National Pharmaceutical Regulatory Agency-Burkina Faso, Ministry of Public Health- Republic of Cote d'Ivoire, Ministry of Health and Social Welfare-Republic of Senegal, National Agency for Food and Drug Administration and Control (NAFDAC)-The Federal Republic of Nigeria, Food and Drugs Authority (Ghana-FDA) and the Directorate of Pharmacy, Medicine and Laboratories- Togo

AIM

The aim of this study is to evaluate the effectiveness and efficiency of the current operating model of the WA-MRH initiative including the challenges it faces as well as identifying opportunities for improvement.

STUDY OBJECTIVES

1. Obtaining the views of the individual medicines' regulatory authorities of the WA-MRH initiative about the performance of the programme to date.
2. Identifying the challenges experienced by individual authorities throughout the life cycle of the WA-MRH initiative.
3. Determining the strengths and weaknesses of the initiative
4. Identifying the ways of improving the performance of the work sharing programme.
5. Envisaging the strategy for moving forward

2

Figure 8.2. (continued).

CONFIDENTIALITY

Thank you for agreeing to participate in this survey. **Your responses will be treated in strictest confidence and no identifiers of countries or respondents will be shared with any third party or made public**. External reports or presentations of the data will be kept confidential.

The questionnaire is divided into five short sections and will take 20 minutes to complete. Thank you for taking time to complete it. We value your input!

A. DEMOGRAPHICS

1. Please state the name of your country _____
2. Please provide your responses to the following questions by writing your answer in the space provided or ticking the relevant box.
   a. Age: _____years
   b. Sex: ☐ Male ☐ Female
   c. Number of years of regulatory experience: _____years
3. What is the total number of staff in your agency? _____
4. What is the number of reviewers of marketing authorization applications? _____
5. How many reviewers participate in the WA-MRH joint assessments? _____
   _____
6. Does your agency have a separate record of applications received for assessment under WA-MRH? ☐ Yes ☐ No

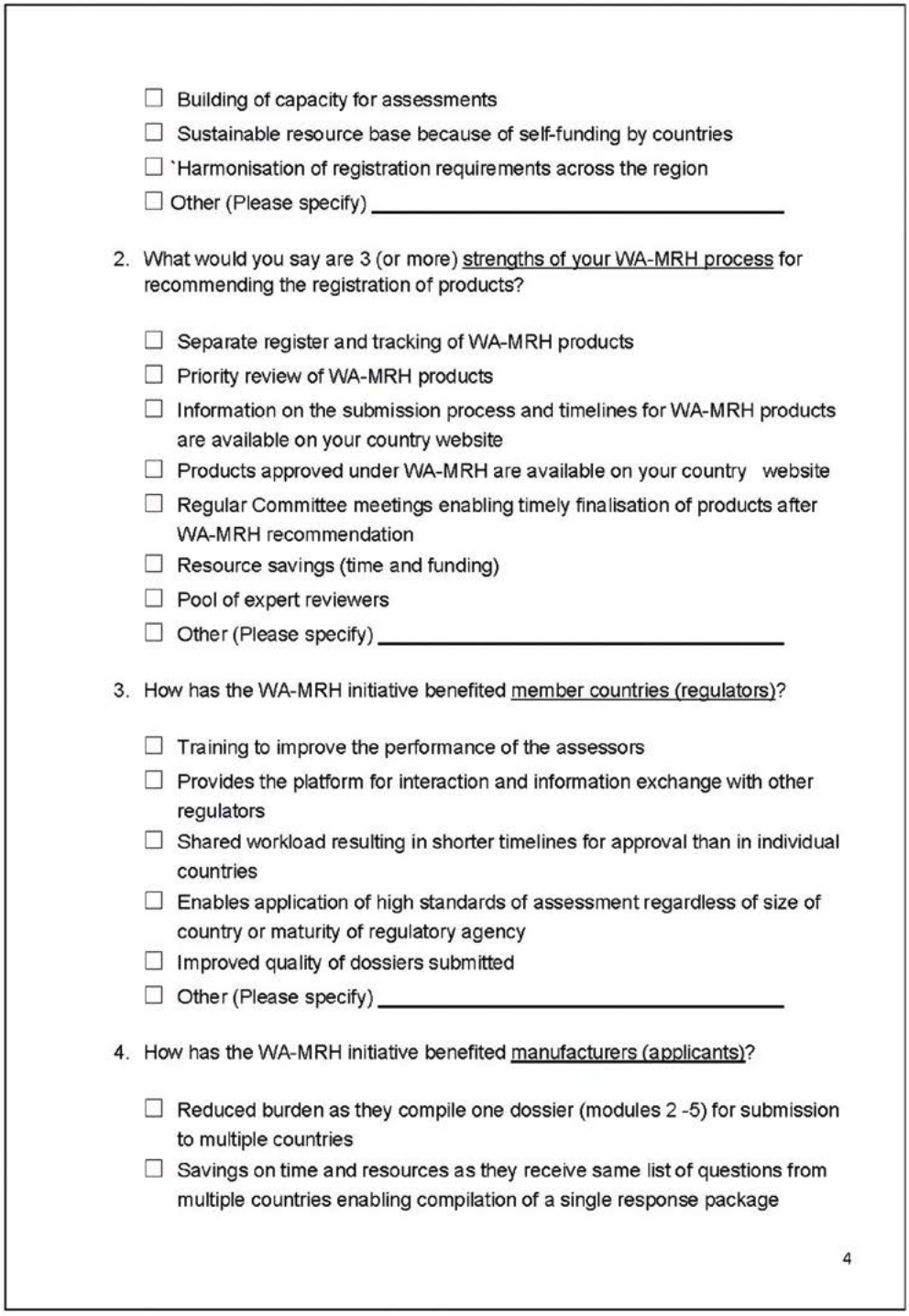
B. VIEWS ON THE BENEFITS OF THE WA-MRH INITIATIVE

Select your answers by ticking the relevant box(es)

1. In your view, what are 3 (or more) benefits of the WA-MRH initiative to date?
   ☐ Leadership commitment/Governance structure
   ☐ Clear Operating Model
   ☐ Shorter timelines for approval
   ☐ Information sharing among regulators

3

Figure 8.2. (continued).



☐ Building of capacity for assessments
☐ Sustainable resource base because of self-funding by countries
☐ `Harmonisation of registration requirements across the region
☐ Other (Please specify) _____

2. What would you say are 3 (or more) strengths of your WA-MRH process for recommending the registration of products?

☐ Separate register and tracking of WA-MRH products
☐ Priority review of WA-MRH products
☐ Information on the submission process and timelines for WA-MRH products are available on your country website
☐ Products approved under WA-MRH are available on your country website
☐ Regular Committee meetings enabling timely finalisation of products after WA-MRH recommendation
☐ Resource savings (time and funding)
☐ Pool of expert reviewers
☐ Other (Please specify) _____

3. How has the WA-MRH initiative benefited member countries (regulators)?

☐ Training to improve the performance of the assessors
☐ Provides the platform for interaction and information exchange with other regulators
☐ Shared workload resulting in shorter timelines for approval than in individual countries
☐ Enables application of high standards of assessment regardless of size of country or maturity of regulatory agency
☐ Improved quality of dossiers submitted
☐ Other (Please specify) _____

4. How has the WA-MRH initiative benefited manufacturers (applicants)?

☐ Reduced burden as they compile one dossier (modules 2 -5) for submission to multiple countries
☐ Savings on time and resources as they receive same list of questions from multiple countries enabling compilation of a single response package

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Figure 8.2. (continued).

☐ Shorter timelines for approval compared to that for the individual countries
☐ Access to various markets at the same time
☐ Other (Please specify) _____

5. How has the WA-MRH initiative benefited patients in your country or in the ECOWAS region?

☐ Quicker access to quality assured medicines
☐ Reduced prices of medicines
☐ Increased availability of medicines
☐ Other (Please specify) _____

C. VIEWS ON CHALLENGES OF THE WA-MRH INITIATIVE

Select your answers by ticking the relevant box(es)

1. In your view, what are 3 (or more) challenges of the WA-MRH initiative?

☐ Lack of detailed information on the process for applicants
☐ Low or decreasing number of applications for assessment
☐ Unequal workload among Partner States
☐ Dependence on the countries' process for communication with applicants and expert Committees
☐ Lack of centralised submission and tracking
☐ Lack of jurisdiction power
☐ Other (please specify) Poor IT infrastructure to support dossier submissions and the assessment process

2. In your view, what are 3 (or more) challenges that you face at country level in assessing/finalising WA-MRH products?

☐ Inadequate human resources
☐ Poor record keeping and tracking of WA-MRH products
☐ Lack of priority review for WA-MRH products
☐ WA-MRH work not recognized as part of agency work to be done during working hours
☐ Unpredictable schedule of Committee meetings

5

Figure 8.2. (continued).

- ☐ Lack of buy-in from expert Committee(s)
- ☐ Failure by manufacturers to follow the requirement to submit the exact same dossier to all countries of interest
- ☐ Failure by manufacturers to adhere to deadlines for response to questions
- ☐ Other (Please specify) Lack of a calendar of WA-MRH activities that factors in NRA activities with an aim to avoid any conflicts

3. What are the challenges faced by manufacturers submitting applications to the WA-MRH initiative?

- ☐ Differences in time to implementation of WA-MRH recommendations by Partner States.
- ☐ Lack of clarity about the process for submission and follow up in each Partner State
- ☐ Lack of information on country websites and the WA-MRH website about the process, milestones, timelines, pending and approved products
- ☐ WA-MRH process is more stringent than some country processes
- ☐ Differing labeling requirements in participating countries
- ☐ Other (Please specify) _____

D. IMPROVING THE PERFORMANCE (EFFECTIVENESS AND EFFICIENCY) OF THE WORK SHARING PROGRAMME

Select your answers by ticking the relevant box(es)

Effectiveness can be defined as 'doing the right thing' often measured by the value derived by customers/stakeholders from an organisation's processes or services while *Efficiency* can be defined as 'doing things right' which saves the organization time and resources.

1. What are 3 or more ways to improve the effectiveness of the WA-MRH initiative in your view?

- ☐ Decision-making transparency e.g. publishing Public Assessment Reports
- ☐ Make publicly available any information that might help applicants in managing their submissions - templates of documents, lists of Q&A, timelines and milestones, disclosure of internal SOPs, etc.
- ☐ Consistency in application of guidelines and decisions
- ☐ Use of risk-based approaches e.g. reliance pathways

6

Figure 8.2. (continued).

- ☐ Engagement and interaction with stakeholders
- ☐ Publishing of pending products
- ☐ Publishing of approved products
- ☐ Minimise the need for country specific documents
- ☐ Other (Please specify) _____

2. What are 3 or more ways to improve the efficiency of the WA-MRH initiative in your view?

- ☐ Specific and clear requirements made easily available to applicants
- ☐ Compliance with target timelines by measuring and monitoring each milestone in the review process
- ☐ Use of robust IT systems
- ☐ Transparency on metrics and statistics e.g. % completed within timeline
- ☐ Improved central tracking of WA-MRH products
- ☐ Improved resources e.g., number of assessors
- ☐ Centralised system for submission of applications and communication with applicants
- ☐ Other (please specify) Expanding the Expert Committee's to include more resources available in the region

E: ENVISAGING THE STRATEGY FOR MOVING FORWARD

1. Rate the following proposals to improve the current WA-MRH operating model from 1 – 3, number 1 representing what you think would be **most effective** in improving efficiency and number 3 the **least effective**. *Enter the appropriate number in the space provided before each proposal.*

- ☐ To continue with the current operating model unchanged
- ☐ To continue with the current operating model and establish WA-MRH integrated information management system to manage and process applications.
- ☐ To continue with the current operating model but provide full information on the process including timelines and milestones as well as approved products on every participating country's website and on the WA-MRH website.

7

Figure 8.2. (continued).

☐ The establishment of a regional administrative body to centrally receive and track WA-MRH applications which would be responsible for allocating work, apportioning the applicable fees to countries, tracking of applications and communication with applicants.

2. In your view, would the establishment of an ECOWAS regional medicines agency, if legally possible, be the best strategy for improved performance going forward? ☐ Yes ☐ No

   Please explain why?

3. In conclusion, what other strategies not previously highlighted can you think of that would strengthen the WA-MRH initiative going forward?

Please feel free to use the comment box below to elaborate on any of your answers or to highlight questions and answers that you believe should have been included in this questionnaire.

Name of person completing the questionnaire:

Title (position):
Date: _____

Thank you for your time and help

8

RESULTS

For clarity, the results are presented in five parts: Part I- Demographics and administrative resources; Part II- Benefits of the WA-MRH initiative; Part III- Challenges of the WA-MRH initiative; Part IV- Improving the performance of the work-sharing initiative; and Part V- Strategies for moving forward.

Part I. Demographics, Technical and Administrative Resources

The age of the respondents ranged from 42 to 50 years and two of the seven respondents were female. The number of years of regulatory experience ranged from 7 to 21 years. Table 7.1 summarises the technical and administrative resources available in each of the participating NMRAs.

Part II. Benefits of the WA-MRH initiative

The benefits of the initiative identified by the NMRAs were the harmonisation of registration requirements across the region, information sharing among regulators and building of capacity for assessments. Leadership commitment and governance structure were selected by half of the respondents as being beneficial, while shorter timelines for approval and a clear operating model were also selected by some of the respondents. It is important to note that the benefit of harmonisation of registration requirements in the region was echoed by all the respondents; signifying that all the NMRAs are in agreement with regard to achieving the main goal of this initiative.

Table 7.1. Technical and administrative resources of NMRAs

	Country						
Assessors	**Burkina Faso**	**Cote d'Ivoire**	**Ghana**	**Nigeria**	**Senegal**	**Sierra Leone**	**Togo**
Number of assessors	27	14	32	12	30	8	30
Number of assessors involved in WA-MRH	8	2	5	5	5	1	2
Keeps separate record of WA-MRH application	No	No	Yes	Yes	Yes	Yes	No

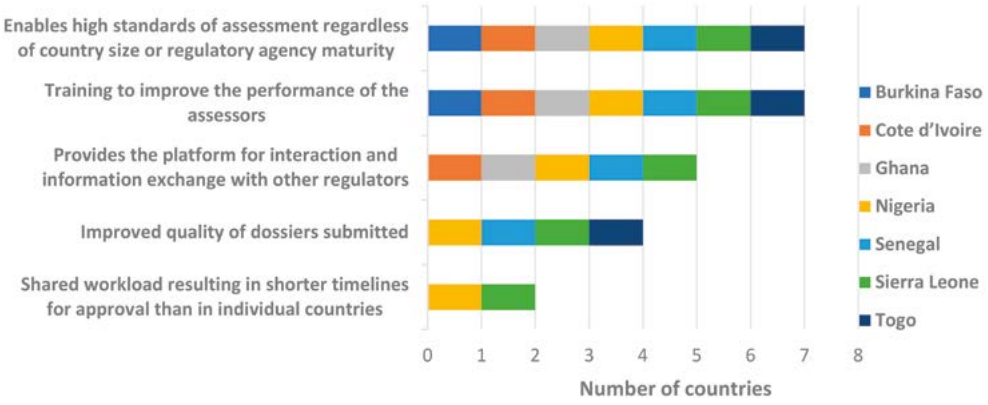
Strengths of the WA-MRH process for recommending the registration of products

The respondents stated that the strengths of the WA-MRH process for recommending the registration of products included regular committee meetings enabling timely finalisation of products after a WA-MRH recommendation, resource savings in time and funding, priority review of WA-MRH products, as well as having a pool of expert reviewers. According to the WA-MRH process, four (one meeting in each quarter) joint assessment meetings are held in each year. Applicants/manufacturers have 60 days to respond to queries arising from the assessment meeting after the first joint assessment and 30 days after the second joint assessment. It is worth noting that the pool of expert reviewers includes those from the NMRAs in Ghana and Nigeria; both having achieved WHO-GBT maturity level- 3 status and therefore considered adequately resourced with regard to regulatory capacity.

Benefits of the WA-MRH initiative to NMRAs

The NMRAs reported that the WA-MRH work-sharing initiative has enabled applications of high standards of assessment regardless of the size of the country or maturity of regulatory agency, the training to improve the performance of the assessors, provided the platform for interaction and information exchange with other regulators, improved quality of dossiers submitted as well as a shared workload resulting in shorter timelines for approval than in individual countries (Figure 8.3). It is of value to note that the NMRAs identified with, though to varying extent, all the benefits of the initiatives at this time.

Figure 7.3. WA-MRH benefits to member countries.



Benefits of the WA-MRH initiative to manufacturers (applicants)

The benefits of the WA-MRH initiative for manufacturers (applicants) included access to various ECOWAS markets at the same time, a reduced burden as they compile one dossier (modules 2-5) for submission to multiple countries, the savings in time and resources as they receive the same list of questions from multiple countries, enabling compilation of a single response package as well as shorter timelines for approval compared with that for the individual countries (Figure 7.4). It is well noted that it is the view of the NMRAs that the manufacturers have experienced, though to varying extent, all the benefits of the initiative at this time.

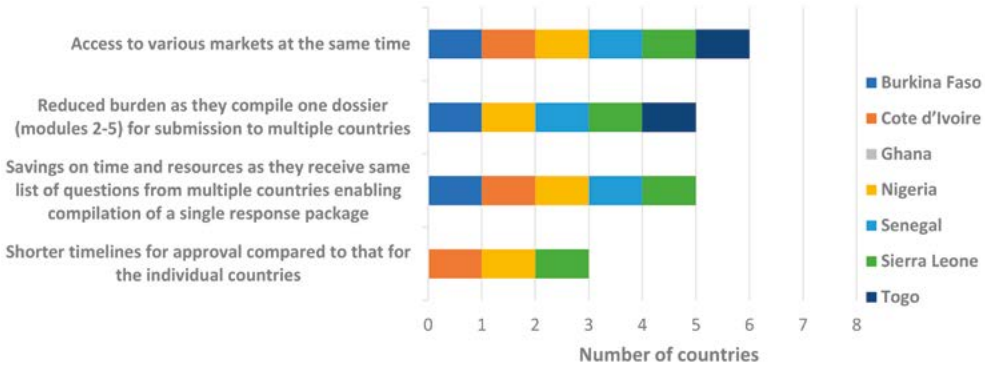
Benefits of the WA-MRH initiative to patients at the country or regional level

The NMRAs reported quicker access to quality assured medicines and increased availability of medicines as the benefits of the WA-MRH work-sharing initiative for patients at either the country or regional level. These two benefits give a good indication that the WA-MRH initiative is presently moving in the right direction by making available quality, safe and efficacious medicines both at the country and regional levels.

Part lll. Challenges of the WA-MRH initiative

The challenges the WA-MRH initiative identified by the NMRAs included the low or decreasing number of applications for assessment, a lack of centralised submission and tracking, a lack of detailed information on the process for applicants, a lack of jurisdiction power, unequal workload among the agencies and the dependence on the countries' process for communication with applicants and Expert Committees. Poor IT infrastructure to support dossier submissions and the assessment process was

Figure 7.4. WA-MRH benefits to manufacturers (applicants).



also presented as another challenge of the WA-MRH initiative (Figure 7.5). In summary, the NMRAs acknowledged that the WA-MRH initiative faces a number of challenges at this time.

Challenges faced at the country level in assessing/finalising WA-MRH products

The views of the respondents regarding the challenges faced at the country level in assessing/finalising WA-MRH products included inadequate human resources, a failure by manufacturers to adhere to deadlines for response to questions, the unpredictable schedule of Committee meetings, the WA-MRH initiative not being recognised as part of the agency work to be carried out during working hours, the failure by manufacturers to follow the requirement to submit the exact same dossier to all countries of interest and a lack of priority review for WA-MRH products. In addition, other challenges faced at the country level in assessing/finalising WA-MRH products included the lack of a WA-MRH calendar of activities to help avoid conflicts and the lack of compatibility of the time limits for the joint assessment procedure with the national procedures (Figure 7.6). It is noted that though the NMRAs are also faced with some challenges regarding the initiative, record keeping and tracking is not a challenge since more than half of the NMRAs keep a separate record of WA-MRH applications (Table 7.1).

Challenges faced by manufacturers submitting applications to the WA-MRH initiative

The challenges identified by the NMRAs were that the WA-MRH process is more stringent than some country processes, the differing labelling requirements in

Figure 7.5. Challenges of the WA-MRH initiative

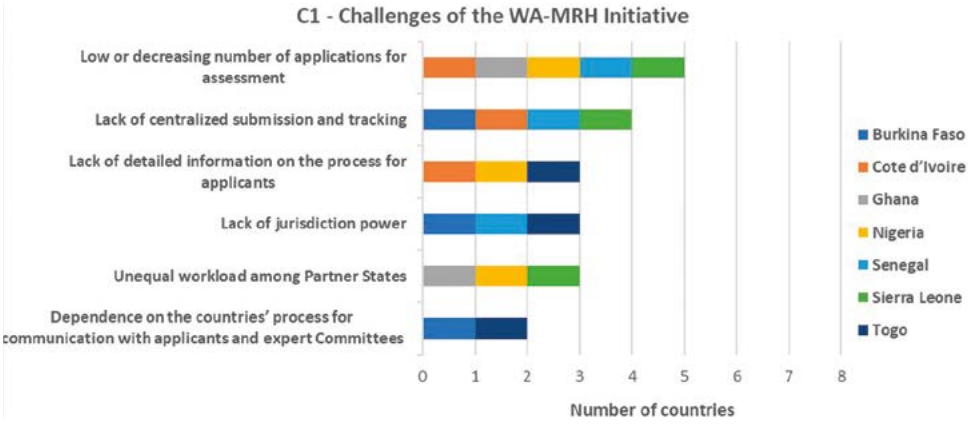
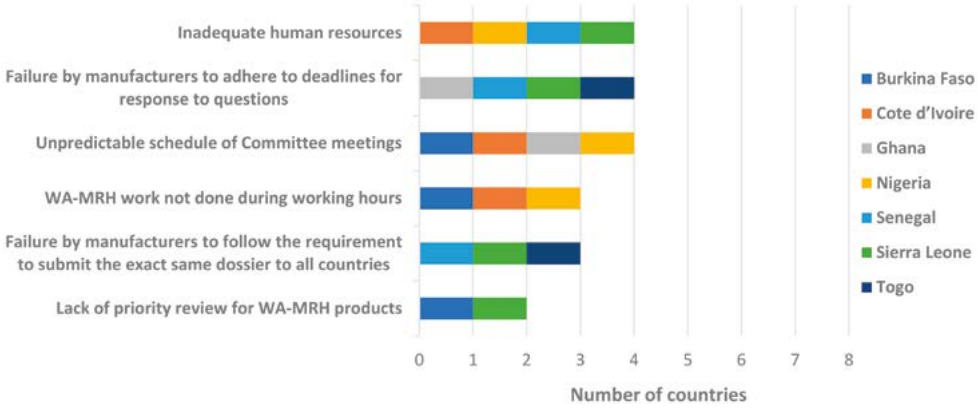


Figure 7.6. Challenges faced at country level in assessing/finalizing WA-MRH products.



participating countries, the lack of clarity about the process for submission and follow-up in each country as well as

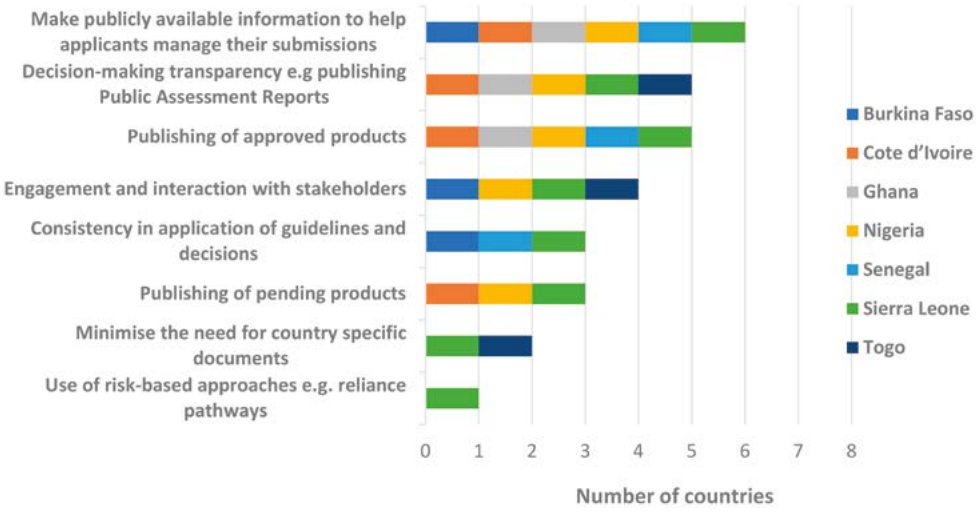
the lack of information on country and the WA-MRH websites about the process, milestones and timelines, as well as pending and approved products. It is noted at this time that the manufacturers submitting applications are also faced with a number of challenges.

Part lV. Improving the performance (effectiveness and efficiency) of the work-sharing programme

Ways to improve the effectiveness of the WA-MRH initiative

The NMRAs identified ideas for improving effectiveness including making any information publicly available that might help applicants in managing their submissions, such as templates of documents, lists of questions and answers, timelines and milestones, disclosure of internal SOPs, decision-making transparency such as publishing Public Assessment Reports, publishing lists of approved products, engagement and interaction with stakeholders, consistency in application of guidelines and decisions, publishing of pending products, minimising the need for country-specific documents and the use of risk-based approaches such as reliance pathways (Figure 7.7). The NMRAs acknowledged that there are multiple options to be considered to improve the effectiveness of the WA-MRH initiative.

Figure 7.7. Ways to improve effectiveness of the WA-MRH initiative.



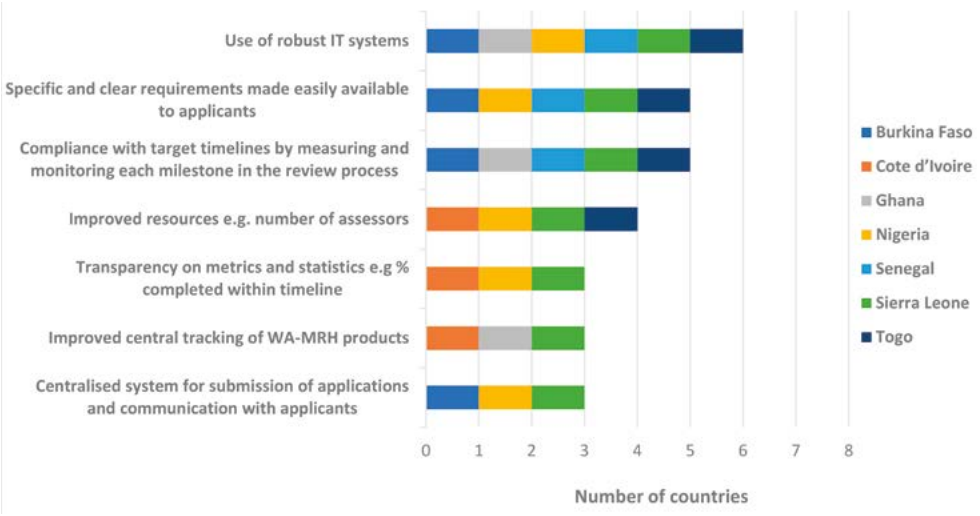
Ways to improve the efficiency of the WA-MRH initiative

Ways to improve the efficiency of the WA-MRH initiative were suggested by the NMRAs, which included the use of robust IT systems, specific and clear requirements made easily available to applicants, compliance with target timelines by measuring and monitoring each milestone in the review process, improved resources; for example, number of assessors, transparency on metrics and statistics; for example, percentage of reviews completed within prescribed timelines, improved central tracking of WA-MRH products and a centralised system for submission of applications and communication with applicants. Expanding the Expert Committees to include more resources available in the region was also presented as an additional way to improve the efficiency of the WA-MRH initiative (Figure 7.8). Similarly, the NMRAs acknowledged that there are multiple options to consider improving the efficiency of the WA-MRH initiative.

Part V. Strategies for moving forward

Finally, possible strategies considered most effective in improving efficiency were to continue with the current operating model but provide full information on the process including timelines and milestones as well as approved products on every participating country's website as well as on the WA-MRH website. Also, the establishment of a regional administrative body to centrally receive and track WA-MRH applications, which would be responsible for allocating work, apportioning the applicable fees to countries, and tracking of applications and communication with applicants. The following suggestions were made:

Figure 7.8. Ways to improve efficiency of the WA-MRH initiative.



"We need to establish communication channels with regulatory agencies in the EU, US as well as the WHO to facilitate reliance-based registrations. This will help reduce the time expended in reviews especially for the active pharmaceutical ingredient which may have been previously accepted in these regions."

"Also, in the medium to long term, there is a need to encourage the inclusion of regulatory sciences in higher institutions in the ECOWAS region. There is still a significant gap in knowledge as it concerns regulatory requirements amongst most manufacturers in the ECOWAS region and this is evidenced by poorly organized product dossiers submitted for registration in most countries."

DISCUSSION

The WA-MRH initiative has been very important, with the most outstanding benefit being the harmonisation of registration requirements within the sub-region. This is of great value to both NMRAs and manufacturers, as it allows the standardisation of the criteria for submission of applications by manufacturers and the assessment by the NMRAs. Whilst the "enthusiasm and commitment of ECOWAS, NMRAs and the pharmaceutical industry toward the implementation of a harmonized medicine regulatory system" for the sub- region have been noted (Kamwanja et al, 2011), it has also been observed that similarly to the status of the ZaZiBoNa initiative, the important benefit of shorter timelines for approval has not been achieved at this time. A solution for this shortcoming should therefore be given a high priority. Lessons can be taken

from the EAC-MRH initiative which has achieved the important benefit of shorter timelines for approval since this was not an outcome for the ZaZiBoNa initiative. (Sithole et al, 2022a; Ngum et al, 2022a). This will enhance the reported benefit of the WA-MRH initiative to patients at the country and regional levels of having quicker access to quality assured medicines.

It is of interest to note that each of the NMRAs involved in the joint assessment procedure enable from 7% to 42% of assessors available to support the WA-MRH initiative, with assessors from Ghana and Nigeria contributing 36% of the total pool of assessors for this initiative. Since some countries are not adequately resourced to be able to contribute their requisite share of assessors to support this initiative, it is appropriate that the relatively better-resourced NMRAs continue to make available more of their assessors for the initiative. It is hoped that as other NMRAs are strengthened, this will result in a positive effect in the WA-MRH initiative, including shorter timelines.

Data available at the end of this study (June 2022) showed that the review and decision for seven applications to the WA-MRH initiative have been completed. Being the most recently implemented joint assessment procedure on the African continent, the WA-MRH initiative is in its early days in comparison to the ZaZiBoNa and EAC-MRH initiatives. Since only a few applications have been finalised and there is a decreasing number of applications for assessment, a further study should be conducted, possibly by engaging the manufacturers to learn about their challenges and encourage their active participation so that more medicines become readily available to patients in the ECOWAS region through this initiative. Valuable lessons and experiences can be drawn from the WHO Prequalification of medicines programme, which has been remarkably successful with expanding its portfolio to reach other unmet needs in an effort to cover a wide range of medicines required for public health (WHO, 2022e).

It is important to note that other challenges of the WA-MRH initiative such as lack of centralised submission and tracking and a poor IT infrastructure to support dossier submissions and the assessment process can be considered as common with the other MRH initiatives in Africa as these challenges were also reported by Sithole and colleagues and also by Ngum and colleagues (Sithole et al, 2002a; Ngum et al 2022a). In addition to providing a robust IT infrastructure to track dossier assessments, the competence of assessors should be adequate to perform to international standards and the fast-tracking of applications should be entertained only when public

health rather than the manufacturers' wishes requires such prioritisation (Hill and Johnson, 2004).

For the WA-MRH to be successful, other mechanisms should be considered, such as making any information that might help applicants in managing their submissions publicly available (templates of documents and lists of questions and answers), and providing decision-making transparency through such means as publishing Public Assessment Reports as well as lists of approved products. The need for these mechanisms, which were also reported by Sithole and colleagues and again by Ngum and colleagues (Sithole et al, 2002a; Ngum et al, 2022a) confirm the simIlarity of issues associated with these initiatives being implemented across the different subregions in Africa. A study of the challenges affecting some of the harmonisation initiatives being implemented in other parts of the world would also be of value (Mendez and Trejo, 2020).

It is timely to note that medicine harmonisation initiatives and effective collaborative mechanisms amongst NMRAs can promote efficient utilisation of limited human, technical and financial resources to perform regulatory activities to improve patients' access to medicines in West Africa as well as other parts of the continent (Azatyan, 2013; AUDA-NEPAD, 2022; Mukanga, 2018).

Finally, the majority of the NMRAs regarded the establishment of a regional administrative body, if legally possible, as the best strategy to improve performance going forward. Reasons to support this included:

- Promote mutual recognition of decisions by other NMRAs and will also reduce the time limit for granting marketing authorisations
- "Have staff dedicated exclusively to the agency"
- "Relieve some regulatory burden from participating countries"
- "If properly established, without conflicts with national sovereignty, the ECOWAS regional medicines agency will improve the quality of medicines available in the region. and also facilitate the centralised registration of products to improve access to medicines and help coordinate pharmacovigilance activities and control substandard products in the region"
- "Enable accountability and transparency"
- "Make it possible to save material, technical and financial resources, preventing bottlenecks in the approval process at the NMRA level. However, it will also be necessary to maintain operational and efficient NMRAs to guarantee the quality, safety and effectiveness of the medicines that do not fall within the framework of the centralised procedure"

There was, however, a suggestion that firstly, the current system should be strengthened, since the creation of a regional agency may not be required in view of the establishment of the African Medicines Agency.

This study identified the strengths and challenges of the WA-MRH initiative as experienced by the NMRA as well as the many options available to improve its effectiveness and efficiency. The key recommendations which have been proposed, if implemented, should further strengthen this initiative to enable it to fulfil its core mandate which is to "Improve the availability of quality, safe and effective medicines and vaccines in the ECOWAS region".

RECOMMENDATIONS

The key recommendations to strengthen the WA-MRH initiative going forward are as follows:

- **Digitalization of regulatory processes**: Availability of a robust IT system would facilitate a centralised system for submission of applications and communication with applicants.
- **Promotion of regulatory reliance mechanisms:** These mechanisms will reduce or eliminate duplication in dossier assessments and ultimately lead to shorter approval timelines at the regional level.
- **Bridging the gap in academia by providing current knowledge in regulatory science:** Academic institutions should be encouraged to provide relevant and current courses to support pharmaceutical regulation in the region.
- **Training of more assessors to increase human resource capacity in the region, especially in lesser- matured regulatory authorities**: This would go a long way to positively impact the effectiveness and efficiency of this initiative.

The scope of this study was limited to the process and operating model of the WA-MRH initiative. In addition, there were only seven applications assessed by the initiative during the three years of its operation and a small number of the member countries were involved in such assessment. However, this early evaluation of the effectiveness and efficiency of the initiative is instrumental in identifying the achievements and the challenges moving forward, as more of the seven member countries become engaged in the assessment of applications. Going forward, it would be helpful to obtain quantitative data to support these views. Such data would include actual metrics of the time taken to register the medicines in NMRAs following a recommendation from WA-MRH.

CHAPTER 08

THE WEST AFRICAN MEDICINE REGULATORY HARMONIZATION INITIATIVE: THE VIEWS OF THE SPONSORING PHARMACEUTICAL COMPANIES

SUMMARY

This study examined the challenges being encountered and identified strategies that would strengthen the ECOWAS-MRH initiative moving forward. The Process Effectiveness and Efficiency Rating (PEER) questionnaire was used to collect data from manufacturers who have submitted applications to the joint assessment procedure and had identified recommendations for improving the performance of the ECOWAS-MRH initiative.

Ten pharmaceutical manufacturers (one innovator, four foreign generic and five local generic) took part in the study. They all reported that harmonization of registration requirements across the region had resulted in a reduced application burden and this was considered as a major benefit. This resulted in shorter timelines for approvals when compared to the individualized response to each country. Another benefit of a harmonised registration process is the simultaneous accessibility of their medicines in various markets.

The key challenges to this initiative included a lack of centralized submission and tracking, differences in regulatory performance of the NMRAs, a lack of detailed information on the joint assessment procedure for applicants and a low motivation to use the ECOWAS-MRH route with a preference for other regulatory pathways in the ECOWAS member states.

By identifying the strengths and strategies for improving the ECOWAS-MRH initiative to achieve its objectives, this study identified three approaches to increase the effectiveness of this initiative. Firstly, the implementation of risk-based approaches such as reliance pathways, secondly, establishment of a robust IT system as well as building capacity of assessors to facilitate processing and monitoring the milestones for applications and finally, initiating a priority review of ECOWAS-MRH products which is key to the regulatory assessment process.

INTRODUCTION

It is the responsibility of every country to establish an effective and efficient medicine regulatory system to ensure the patients' timely access to quality, safe and efficacious medicines (WHO, 2014b). Vogel (2002) noted that "...until recently, drug regulation was virtually synonymous with national sovereignty". Globally, regulation of medicines is comparatively stringent when compared to the regulation of other consumables. To achieve an effective and efficient medicine regulatory system, there are multiple stakeholders involved. Notable stakeholders are the manufacturers of medicines and vaccines (Roth et al., 2018).

The active engagement and co-operation of manufacturers with regulators in the medicine regulatory system is vital to the success of a national health system. Currently there are multiple national jurisdictions that manufacturers have to contend with in order to obtain the requisite raw or starting materials, intermediate or semi-finished products, and where applicable, packaging materials from one country into another so as to manufacture a finished pharmaceutical product or vaccine. Furthermore, there are multinational pharmaceutical companies who conduct activities such as contract manufacturing across several countries worldwide which underlines the complex nature of the manufacturing of medicines and vaccines. The ideal regulatory environment that will benefit manufacturers will be one that many of such countries subscribe to under an umbrella of harmonization. There is evidence to show that pharmaceutical manufacturers have a selective-bias with regard to regulatory systems that provide transparency, accountability and predictability (Vogel 2002; Lakkis,2010, Preston et al, 2012; Sillo et al, 2020).

Considering the above, there are presently various regulatory mechanisms available such as the well-established centralised authorization procedure of the European Union. In this procedure manufacturers apply for a single centralised marketing authorisation for a product, which is valid throughout the European Union member states as well as Iceland, Liechtenstein and Norway (European Medicines Agency, 2022). Similarly, there are Medicine Regulatory Harmonization (MRH) initiatives which meet expectations of stakeholders and encourage manufacturers to submit marketing authorization applications in other regions of the world such as the WHO (WHO, 2008; Lakkis, 2010; Ncube et al, 2021)

Currently various diseases such as malaria and tuberculosis are predominantly in Africa, with the World Health Organization stating that in 2017, 92% of the 219 million cases of malaria reported worldwide were from Africa (WHO, 2022f). Therefore, after all these

years of using well-established medicines (generics), it is worth recommending that to obtain better patient outcomes, new medicines and vaccines should be developed by manufacturers primarily in Africa for use by the African population. At this point the African challenge of assessing applications for marketing authorization for new chemical entities and vaccines becomes evident (WHO, 2008). Moran and colleagues (2011), have published a number of mechanisms that could be explored; notable among these is to establish an ideal drug regulatory system in Africa and enhance the regulatory capacity of assessors to make it possible for them to assess to a high standard and in a timely manner the quality, safety and efficacy data of new medicines to be used in Africa (Moran M et al, 2011; Roth L et al, 2018).This suggestion is now being taken forward with the establishment of the African Medicines Agency.

Medicine regulatory harmonization appears to be an effective mechanism for deploying technical, human and financial resources efficiently for the benefit of the population. According to the World Health Organization, manufacturers who participate in the WHO prequalification programme enjoy various benefits such as 'increased sales or market access, improved image or brand, reduced manufacturing costs and increased capacity/skills. By extrapolation, manufacturers who participate in similar harmonization initiatives like the ECOWAS-MRH can also experience their share of these benefits by having access to patients in all the 15 member states of ECOWAS, making this a win-win situation for both the manufacturers and patients (WHO, 2022g).

About a decade ago, Narsai and colleagues reported that there was inadequate information in the literature detailing the views of pharmaceutical manufacturers about the regulatory systems in Africa (Narsai et al, 2012). The situation has now seen some improvements following studies which were published in 2022 by Sithole and colleagues with reference to the ZaZiBona initiative (Sithole et al, 2022b) and also by Ngum and colleagues with reference to the East African community's initiative (Ngum et al, 2022a). More studies should therefore be conducted and published so that much-needed data becomes available to all stakeholders at this time. Additionally, opportunities that can be explored to have a better alignment between industry and regulators should be pursued and "the fact should not be forgotten that access to medicines on time for everyone is a human right rather than a luxury" (Oge, 2020).

As a result of completing an earlier study aimed at assessing the effectiveness and efficiency of the current operating model of the ECOWAS-MRH initiative by the NMRAs in the member countries (Owusu-Asante et al., 2022), this present study aimed to assess

the effectiveness and efficiency of the ECOWAS-MRH initiative by the pharmaceutical industry to obtain a holistic view of the current status of the initiative.

STUDY OBJECTIVES

The objectives of this study were to

1. Obtain the views of the pharmaceutical manufacturers or their local representatives of the ECOWAS-MRH initiative about the performance of the programme to date
2. Identify the challenges experienced by the manufacturers throughout the life cycle of the ECOWAS-MRH initiative
3. Determine the strengths and weaknesses of the initiative
4. Identify the ways of improving the performance of the work sharing programme
5. Envisage the strategy for moving forward.

METHODS

Study Participants

All ten pharmaceutical manufacturers who have submitted marketing authorization applications for assessment of medicines at the regional level since the beginning of the ECOWAS-MRH initiative participated in the study. The study participants were classified as Innovator, Generics (foreign) -manufacturer outside ECOWAS and Generics (local)- manufacturer within ECOWAS.

Data Collection

Data for the study was obtained through completion of the Process Effectiveness and Efficiency Rating (PEER) questionnaire (Ngum et al., 2022a; Sithole et al., 2022b) by applicants between October 2022 and January 2023.

The questionnaire consisted of five sections namely; demographics, the benefits and challenges of the ECOWAS-MRH initiative, improving the performance (effectiveness and efficiency) of the work sharing programme and envisaging the strategy for moving forward.

Semi-structured interviews with a checklist were conducted with each manufacturer to validate and elaborate their responses in the PEER questionnaire. This also provided the study participants with an opportunity to discuss any difficulty they faced in responding to some of the sections of the questionnaire. In addition, this post-completion of the questionnaire was designed for the manufacturers

through a dialogue to reflect both their experience of the initiative and that of the ECOWAS-MRH.

EVALUATION OF THE PEER QUESTIONNAIRE

1. Did you find the questions clear and straightforward to respond?

Yes ☐ No ☐

2. Did you find the response options relevant to the heading of each section (A to E)?

Yes ☐ No ☐

3. Did you find the questions relevant to the aims and objectives of the study?

Yes ☐ No ☐

4. Did you find the questions relevant to you and the ECOWAS-MRH work sharing initiative?

Yes ☐ No ☐

5. Did you find any relevant questions missing?

Yes ☐ No ☐

If yes, please state which questions were missing in the space after this list of questions.

.....

6. Did you find any questions that should be excluded?

Yes ☐ No ☐

If yes, please state the questions that should be excluded in the space after this list of questions.....

7. Did you find the questionnaire useful to reflect on both your experience as well that of ECOWAS-MRH initiative?

Yes ☐ No ☐

Name..... Applicant.....

Date.....

RESULTS

For clarity, the results of the study are presented in five parts: Part I - Demographics; Part II - Benefits of the ECOWAS-MRH initiative; Part III - Challenges of the ECOWAS-MRH initiative; Part IV - Improving the performance (Effectiveness and Efficiency) of the work sharing programme; and Part V - Envisaging the strategy for moving forward.

Part I. Demographics

The respondents were mostly regulatory affairs managers with varying years of regulatory experience ranging from 3 to 30 years. In this study there was one (10%) innovator pharmaceutical manufacturer, four (40%) generic (foreign) manufacturers and five (50%) local generic (local) manufacturers. A summary of the manufacturers and their product categories is provided in Table 9.1.

Eight out of the 20 submissions have been issued with recommendation letters. The remaining submissions have either been deferred or are still in the screening phase for various reasons.

Both the innovator and foreign generics are available in almost all the ECOWAS member states with the exception of Guinea Bissau. However local generics are mostly available in Nigeria and Ghana (Figure 8.2).

Half of manufacturers keep a separate record of applications submitted for assessment under the ECOWAS-MRH initiative to facilitate tracking and adherence to deadlines.

Currently, the benefits of the ECOWAS-MRH initiative identified by most of the manufacturers were the harmonisation of registration requirements across the region (80%), information sharing among regulators (50%) and capacity building (40%) for assessments. However, the benefits of leadership commitment/ governance structure (30%) and shorter timelines for approval (30%) were identified by a few of the respondents (Figure 8.3).

Part II. Benefits of the ECOWAS-MRH Initiative

Strengths of the ECOWAS-MRH process for recommending the registration of products

The strengths of the ECOWAS-MRH process for recommending the registration of products were identified as priority review of ECOWAS-MRH products, regular committee meetings enabling timely finalisation of products after ECOWAS-MRH

Figure 9.1. The Process, Effectiveness and Efficiency Rating (PEER-IND) questionnaire.

CONFIDENTIAL

ECOWAS COLLABORATIVE MEDICINES REGISTRATION INITIATIVE

PROCESS EFFECTIVENESS & EFFICIENCY RATING (PEER-IND)

Pic taken from http://www.reference-for-business.com/management/De-Ba/Effectiveness-and-Efficiency.html

PEER-IND QUESTIONNAIRE

October, 2022

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Figure 9.1. (continued).

INTRODUCTION

The ECOWAS collaborative medicines registration initiative was established in 2017. Since its inception, there has not been a formal and structured evaluation of this work sharing programme and for its future direction.,

A recent study has been carried out among the seven active members of the ECOWAS-MRH work sharing initiative using a similar questionnaire to the one being sent to the applicants, so that the benefit is gained from both key stakeholders.

In recent years, there has been a drive within regulatory agencies to re-engineer their processes for improved efficiency and effectiveness and this often begins with a baseline evaluation of the current process to identify strengths and weaknesses. *Effectiveness* can be defined as 'doing the right thing' often measured by the value derived by customers/stakeholders from an organisation's processes or services while *Efficiency* can be defined as 'doing things right' which saves the organization time and resources.

Study Participants

The PEER Questionnaire is being sent to applicants and/or local agents who have submitted marketing authorisation applications for assessment under the ECOWAS-MRH initiative.

AIM

The aim of this study is to evaluate the effectiveness and efficiency of the current operating model of the ECOWAS-MRH initiative including the challenges it faces as well as identifying opportunities for improvement.

STUDY OBJECTIVES

1. Obtaining the views of the applicants and/or local agents of the ECOWAS-MRH initiative about the performance of the programme to date.
2. Identifying the challenges experienced by individual applicants and/or local agents throughout the life cycle of the ECOWAS-MRH initiative.
3. Determining the strengths and weaknesses of the initiative
4. Identifying the ways of improving the performance of the work sharing programme.
5. Envisaging the strategy for moving forward

2

Figure 9.1. (continued).

CONFIDENTIALITY

Thank you for agreeing to participate in this survey. **Your responses will be treated in strictest confidence and no identifiers of companies or respondents will be shared with any third party or made public.** External reports or presentations of the data will include only blinded results together with appropriate analytical interpretations.

The questionnaire is divided into five short sections and will take 20 minutes to complete. Thank you for taking time to complete it. We value your input!

A. DEMOGRAPHICS

1. Please state the name of your company _____

2. Please provide your responses to the following questions by writing your answer in the space provided or ticking the relevant box.

   a. Age: _____years

   b. Sex: ☐ Male ☐ Female

   c. Number of years of regulatory affairs experience: _____years

3. State the ECOWAS countries in which your company markets products

☐	Benin	☐	Mali
☐	Burkina Faso	☐	Niger
☐	Cape Verde	☐	Nigeria
☐	Ivory Coast	☐	Ghana
☐	The Gambia	☐	Senegal
☐	Guinea Bissau	☐	Sierra Leone
☐	Guinea	☐	Togo
☐	Liberia		

4. Do you have a separate record of applications submitted for assessment under ECOWAS-MRH initiative to facilitate tracking and adherence to deadlines?
   ☐ Yes ☐ No

5. For local agents, state the applicants that you represent that have submitted applications to ECOWAS-MRH initiative

_____

3

Figure 9.1. (continued).

B. VIEWS ON THE BENEFITS OF THE ECOWAS-MRH INITIATIVE
Select your answers by ticking the relevant box(es)

1. In your view, what are **3 (or more)** benefits of the ECOWAS-MRH initiative to date?

- ☐ Leadership commitment/Governance structure
- ☐ Clear Operating Model
- ☐ Shorter timelines for approval
- ☐ Information sharing among regulators
- ☐ Building of capacity for assessments
- ☐ Sustainable resource base because of self-funding by countries
- ☐ `Harmonisation of registration requirements across the region
- ☐ Other (Please specify) _____

2. What would you say are **3 (or more)** strengths of the process for ECOWAS-MRH products in any of the countries?

- ☐ Separate register and tracking of ECOWAS-MRH products
- ☐ Priority review of ECOWAS-MRH products
- ☐ Information on the submission process and timelines for ECOWAS-MRH products are available on country websites
- ☐ Products approved under ECOWAS-MRH are available on the country website
- ☐ Regular Committee meetings enabling timely finalisation of products after ECOWAS-MRH recommendation
- ☐ Other (Please specify) _____

3. How has the ECOWAS-MRH initiative benefited you as applicants?

- ☐ Reduced burden as aplicants compile one dossier (modules 2 -5) for submission to multiple countries
- ☐ Savings on time and resources as applicants receive the same list of questions from multiple countries enabling compilation of a single response package
- ☐ Shorter timelines for approval compared to that for the individual countries

4

Figure 9.1. (continued).

☐ Access to various markets at the same time
☐ Other (Please specify) _____

4. How has the ECOWAS-MRH initiative benefited patients in the individual countries or in the ECOWAS region?

☐ Quicker access to quality assured medicines
☐ Reduced prices of medicines
☐ Increased availability of medicines
☐ Other (Please specify) _____

C. VIEWS ON CHALLENGES OF THE ECOWAS-MRH INITIATIVE
Select your answers by ticking the relevant box(es)

1. In your view, what are 3 (or more) challenges of the ECOWAS-MRH initiative?

☐ Lack of detailed information on the process for applicants
☐ Differences in regulatory performance of the countries
☐ Dependence on the countries' process for communication with applicants
☐ Lack of centralised submission and tracking
☐ Lack of ability to mandate central registration
☐ Other (please specify) _____

2. What are the **challenges** faced by **applicants** submitting applications to the ECOWAS-MRH initiative?

☐ Differences in time to implementation of ECOWAS-MRH recommendations by member countries.
☐ Lack of clarity about the process for submission and follow up in each country
☐ Lack of information on country websites and the ECOWAS-MRH website about the process, milestones, timelines for pending and approved products
☐ ECOWAS-MRH process is more stringent than individual country processes for reviews and GMP audits
☐ Differing labeling requirements in participating countries
☐ Failure by countries to adhere to promised timelines

5

Figure 9.1. (continued).

- ☐ Risk of losing access to all member states once a product is rejected by ECOWAS-MRH (i.e can no longer pursue registration in individual countries)
- ☐ Low motivation and appeal to use the ECOWAS-MRH route as there are few success stories available or publicized
- ☐ Low motivation to use the ECOWAS-MRH route as other review routes are now being used by individual countries e.g reliance on SRA approvals or other ECOWAS countries are faster
- ☐ Other (Please specify) _____

3. In your view, what do you believe are the challenges faced by agencies in reviewing the ECOWAS-MRH applications?_____

_____

_____

_____

_____

_____

_____

_____

_____

D. IMPROVING THE PERFORMANCE (EFFECTIVENESS AND EFFICIENCY) OF THE WORK SHARING PROGRAMME

Select your answers by ticking the relevant box(es)

Effectiveness can be defined as 'doing the right thing' often measured by the value derived by customers/stakeholders from an organisation's processes or services while *Efficiency* can be defined as 'doing things right' which saves the organization time and resources.

1. What are **3 or more ways** to improve the effectiveness of the ECOWAS-MRH initiative in your view?

- ☐ Decision-making transparency e.g., publishing Public Assessment Reports
- ☐ Make publicly available any information that might help applicants in managing their submissions - templates of documents, lists of Q&A, timelines and milestones, disclosure of internal SOPs, etc.
- ☐ Consistency in application of guidelines and decisions
- ☐ Use of risk-based approaches e.g., reliance pathways
- ☐ Engagement and interaction with stakeholders
- ☐ Publishing of pending products

6

Figure 9.1. (continued).

☐ Publishing of approved products
☐ Minimising the need for country specific documents
☐ Other (Please specify) _____

2. What are **3 or more ways** to improve the <u>efficiency</u> of the ECOWAS-MRH initiative in your view?

☐ Specific and clear requirements made easily available to applicants
☐ Compliance with target timelines by measuring and monitoring each milestone in the review process
☐ Use of robust IT systems
☐ Transparency on metrics and statistics e.g., % completed within a timeline
☐ Improved central tracking of ECOWAS-MRH products
☐ Improved resources e.g., number of assessors
☐ Centralised system for submission of applications and communication with applicants
☐ Other (please specify) _____

E: ENVISAGING THE STRATEGY FOR MOVING FORWARD

1. Rate the following proposals to improve the current ECOWAS-MRH operating model from 1 – 3, number 1 representing what you think would be **most effective** in improving efficiency and number 3 the **least effective**.
Enter the appropriate number in the space provided before each proposal.

☐ To continue with the current operating model unchanged.

☐ To continue with the current operating model, but provide full information on the process including timelines and milestones as well as approved products on every participating country's website and on the ECOWAS-MRH website.

☐ The establishment of a regional administrative body to centrally receive and track ECOWAS-MRH applications which would be responsible for allocating work, apportioning the applicable fees to countries, tracking of applications and communication with applicants.

7

Figure 9.1. (continued).

2. In your view, would the establishment of an ECOWAS regional medicines agency, if legally possible, be the best strategy for improved performance going forward? ☐ Yes ☐ No

   Please explain why?_____

3. In conclusion, what other strategies not previously highlighted can you think of that would strengthen the ECOWAS-MRH initiative going forward?

Please feel free to use the comment box below to elaborate on any of your answers or to highlight questions and answers that you believe should have been included in this questionnaire.

Name of person completing the questionnaire: _____

Title (position): _____

Date: _____

Thank you for your time and help

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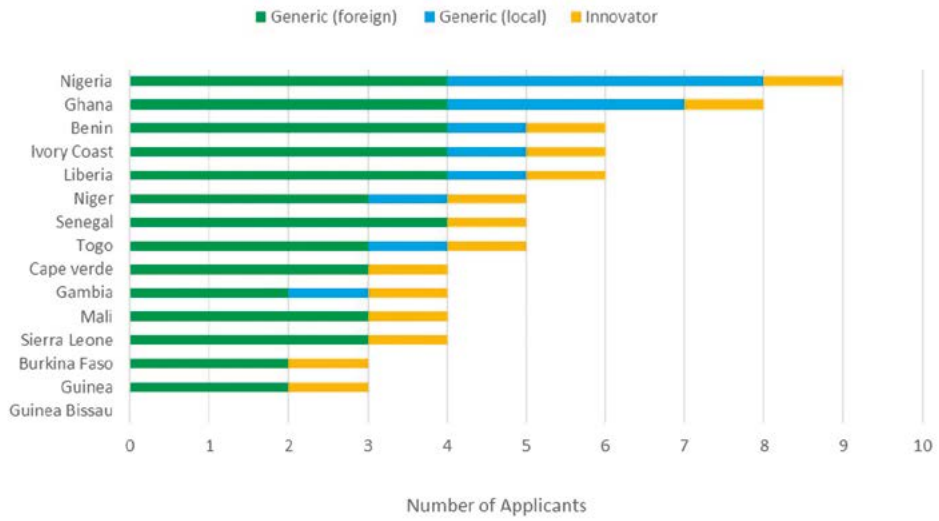
Table 8.1. Pharmaceutical companies participating in study

Name of manufacturer	Innovator	Foreign Generics	Local Generics	Number of submissions	Therapeutic category	Status
Drugfield Pharmaceuticals Ltd			√	1	Disinfectant & antiseptic	Approved
Cipla Quality Chemical Industries Ltd		√		4	Antiretroviral (4)	Approved (3) Deferred (1)
Pfizer Specialties Ltd	√			1	Biological product	Approved
Mission Pharma A/S, Denmark		√		1	Reproductive health product	Approved
Novartis Pharma AG		√		1	Biological product	Approved
Emzor Pharmaceutical Industries Ltd			√	5	Antidiarrhoeal Antimalarial (2) Disinfectant& antiseptic Reproductive health product	Approved (1) Deferred (1) Screened (3)
Juhel Nigeria Ltd			√	1	Antifungal	Deferred
May & Baker			√	3	Antibacterial Antimalarial Antiretroviral	Screened (3)
M& G Pharmaceuticals Ltd			√	2	Antidiarrhoeal (2)	Screened (2)
Laurus Laboratories Ltd		√		1	Antiretroviral	Screened (1)

Figure 8.2. Availability of products in ECOWAS countries.



recommendation, separate register and tracking of ECOWAS-MRH products and products approved under ECOWAS-MRH made available on each country's website. Medicines and vaccines eligible for the ECOWAS-MRH joint assessment are those included in the WHO's Essential Medicine list, HIV/AIDS, malaria, tuberculosis, reproductive health, neglected tropical diseases, antibiotics, for public health emergencies, registered by stringent regulatory authorities, prequalified by WHO, registered under Swissmedic procedure for scientific advice and Marketing Authorisation for Global Health Products (MAGHP), granted a scientific opinion in line with the European Medicines Agency's Article 58 of Regulation (EC) No 726/2004, life-saving commodities by the UN Commission on life saving medicines for women and children and other priority medicinal products as determined by WAHO. Upon completion of the ECOWAS-MRH joint assessment for such eligible medicines and vaccines, these are then granted marketing authorization via the national registration system in the relevant country (WA-MRH, 2021; European Medicines Agency, 2023). Priority review of such applications therefore facilitates quicker access to these medicines and vaccines by patients in the ECOWAS region.

Benefits of the ECOWAS-MRH initiative to applicants

The benefits of the ECOWAS-MRH initiative identified by applicants (manufacturers) included: a reduced burden as applicants compile one dossier (modules 2-5) for submission to multiple countries and savings in time and resources as applicants receive the same list of questions from multiple countries enabling the compilation

of a single response package, shorter timelines for approval compared to that for the individual countries and access to various markets at the same time. A better understanding of the requirements in the countries was stated as an additional benefit of the ECOWAS-MRH initiative to manufacturers (Figure 8.4).

Benefits of the ECOWAS-MRH initiative to patients at the country or regional level

Increased availability of medicines and quicker access to quality assured medicines were reported as benefits of the ECOWAS-MRH initiative for patients in the country or in the ECOWAS region by the manufacturers.

Figure 8.3. Benefits of the ECOWAS-MRH initiative.

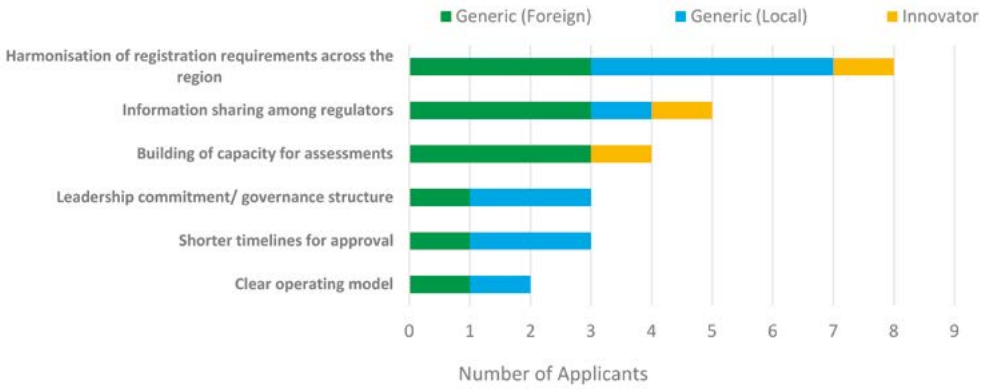
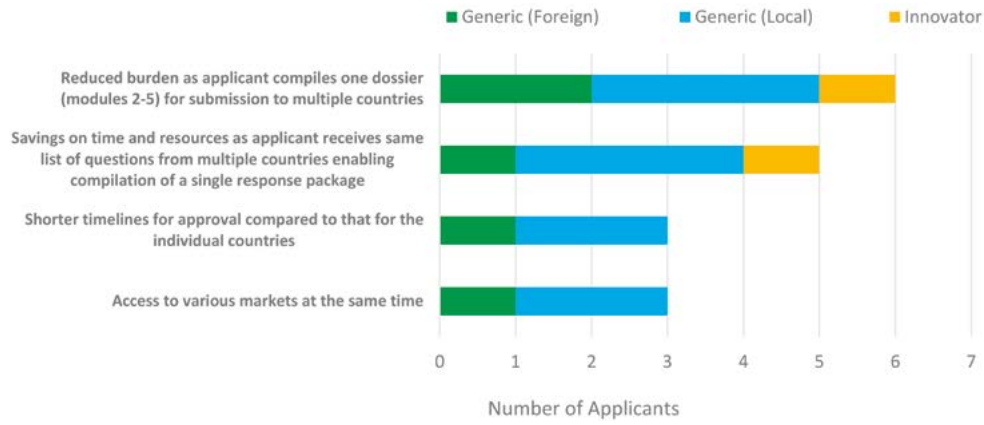


Figure 8.4. Benefits of the ECOWAS-MRH initiative to applicants.



Part lll. Challenges of the ECOWAS-MRH Initiative

The lack of ability to mandate central registration differences in the regulatory performance of the countries and dependence on the countries' process for communication with applicants, lack of a centralised submission and tracking as well as detailed information on the process for applicants were identified as challenges of the ECOWAS-MRH initiative.

It is worth noting that in addition to the above, other challenges remain, namely, lack of processes in the NMRAs on how to move from regional approval to local approval in the ECOWAS countries, no clear process to follow to get approval, and lack of NMRA's responsiveness in communicating updates of application status. (Figure 8.5).

Challenges faced by applicants submitting applications to the ECOWAS-MRH initiative

Additional challenges identified by applicants (Figure 8.6) included: low motivation and appeal to use the ECOWAS-MRH route as there are few success stories available or publicized, lack of clarity about the process for submission and follow up in each country, differing labelling requirements in participating countries and low motivation to use the ECOWAS-MRH route as other review routes are now being used by individual countries e.g., reliance on SRA approvals or other ECOWAS countries are faster, failure by countries to adhere to promised timelines, risk of losing access to all member states once a product is rejected by ECOWAS-MRH (i.e., can no longer pursue registration in individual countries), lack of information on country websites and the ECOWAS-MRH website about the process, milestones, timelines, pending and approved products, ECOWAS-MRH process is more stringent than some country processes and

Figure 8.5. Challenges of the ECOWAS-MRH initiative.

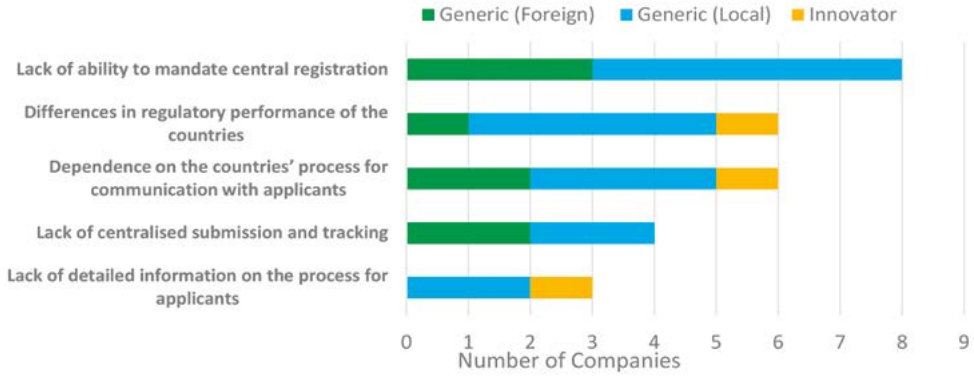
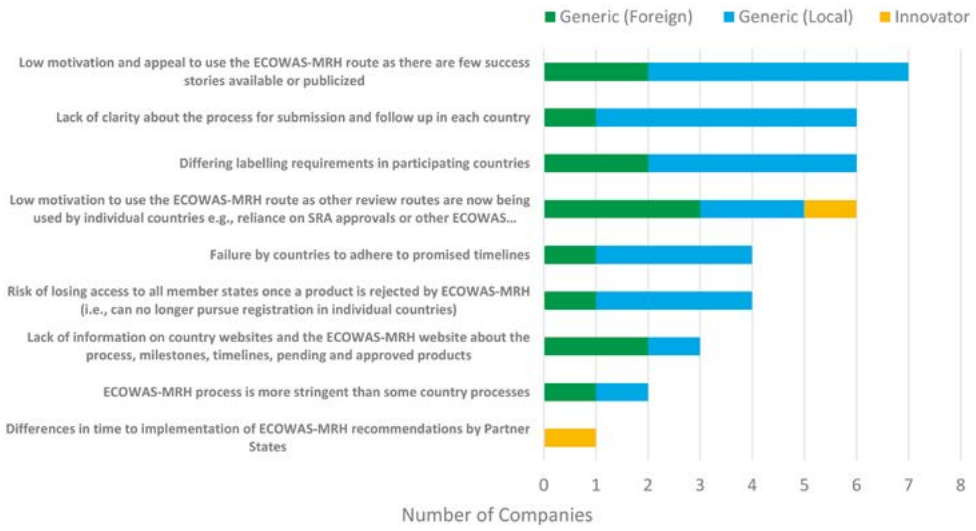


Figure 8.6. Challenges faced by applicants submitting applications to the ECOWAS-MRH initiative.



differences in time to implementation of ECOWAS-MRH recommendations by Partner States were identified as challenges faced by manufacturers submitting applications to the ECOWAS-MRH initiative.

8

Challenges faced by agencies in reviewing the ECOWAS-MRH applications

Comments by manufacturers to the challenges faced by the NMRAs in reviewing the ECOWAS-MRH applications were related to personnel, resources as well as the application and review process as follows:

- Lack of enough personnel
- Lack of proper knowledge of the review process
- Unharmonised system of review
- Lack of information on country websites and the ECOWAS-MRH website about the process, milestones, timelines for pending and approved products
- Each member country has different requirements for Module 1 and applicants have to meet all countries requirements.
- There are no clear processes to follow once approval has been received from the ECOWAS MRH procedure.
- Bringing together regulators from all the member countries in a timely manner to review the dossiers/applications.
- Delay in response time between applicants and reviewers

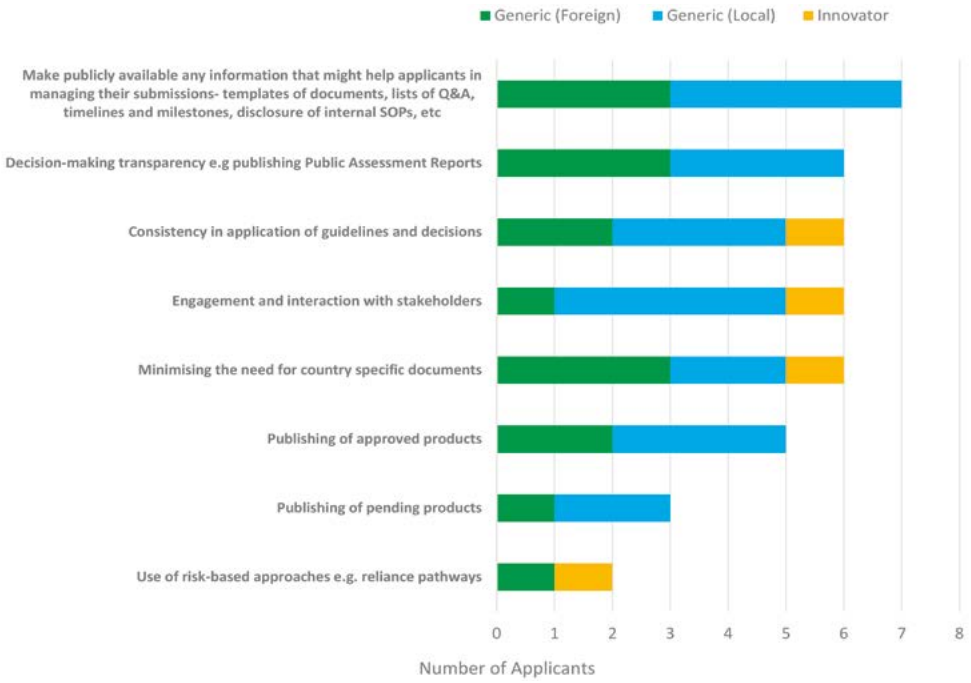
Part lV. Improving the Performance (Effectiveness and Efficiency) of the Work Sharing Programme

Suggestions from manufacturers to improve the effectiveness of the ECOWAS-MRH initiative (Figure 8.7) were to make publicly available any information that might help applicants in managing their submissions, templates of documents, lists of Q&A, timelines and milestones, disclosure of internal SOPs; decision/making transparency, example, publishing Public Assessment Reports; consistency in application of guidelines and decisions, engagement and interaction with stakeholders; minimizing the need for country specific documents; publishing of pending and approved products;-and the use of risk-based approaches such as reliance pathways.

Ways to improve the efficiency of the ECOWAS-MRH initiative

The manufacturer's suggested the following ways to improve the efficiency of the ECOWAS-MRH initiative; improved central tracking of ECOWAS-MRH products , specific and clear requirements made easily available to applicants, use of robust IT systems, centralised system for submission of applications and communication with applicants, compliance with target timelines by measuring and monitoring each milestone in the review process and transparency on metrics and statistics, example,

Figure 8.7. Ways to improve the effectiveness of the ECOWAS-MRH initiative.



percentage completed within timelines and improved resources, example, number of assessors (Figure 8.8).

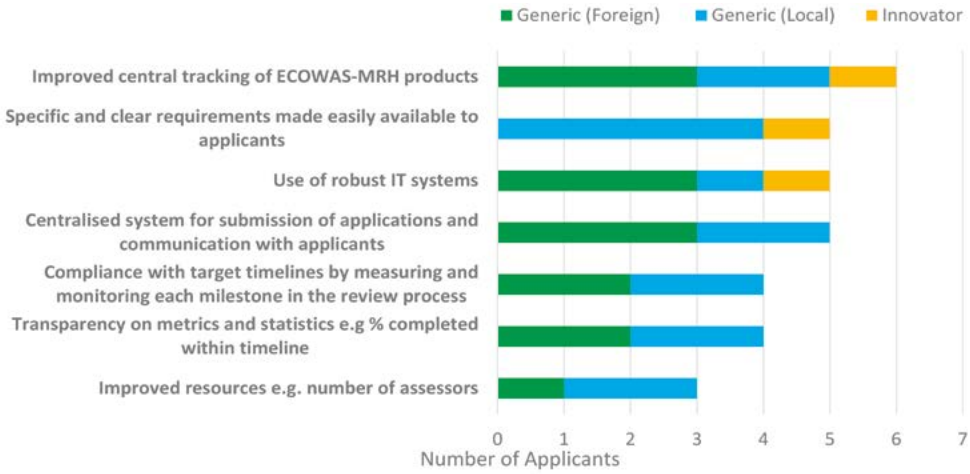
Part V. Strategy for Moving Forward

The most effective strategies proposed by the manufacturers to improve efficiency of the ECOWAS-MRH initiative were the establishment of a regional administrative body to centrally receive and track ECOWAS-MRH applications which would be responsible for allocating work, apportioning the applicable fees to countries, tracking of applications and communication with applicants. On the other hand, the least effective to improve efficiency of the ECOWAS-MRH initiative was to continue with the current operation of the model without any changes. Seventy percent of the respondents agreed that the establishment of an ECOWAS regional medicines agency, if legally possible, will be the best strategy for improved performance going forward.

The respondents finally provided strategies that could be considered in strengthening the ECOWAS-MRH initiative going forward as follows:

- Implement one-time payment process by ECOWAS and waive payment of separate statutory registration fees to individual agencies.
- Harmonize labelling across all ECOWAS countries, so there is no individual country-specific labelling apart from labels approved by ECOWAS.
- Standardized and harmonized Module-1 requirement across the ECOWAS countries should ~~to~~ be followed to expedite the registration process.

Figure 8.8. Ways to improve the efficiency of the ECOWAS-MRH initiative.



- Harmonization of Module 1 requirements e.g., one CPP for any of the member countries or for countries where commercialization is being planned should suffice for the registration and not necessarily submitting 15 CPPs if there are no plans by the applicants to commercialize in all member countries.
- ECOWAS approval should allow individual applicants to market their product in different countries which would benefit quicker access of medicines.
- ECOWAS should initiate an online portal application system to ease the application submissions, tracking and faster evaluation.
- Ensure effective follow ups, process and prompt communication to applicants is carried out.
- Ensure a link to the application process is available on all country NMRA websites.
- Create a clear path for products emanating in the process for applicants to follow in ECOWAS.
- Include a significant reduction in country GMP fees for sites already evaluated through the process.
- Discourage a situation where a new set of GMP fees have to be paid to each NMRA as this will greatly impact the ability to progress the application in each ECOWAS country.
- Concentrate the ECOWAS-MRH initiative solely on the quality and efficacy of the products as decisions bordering on products' commercial presentation should be left to individual countries for effective cost management.
- Improve communication of the multiple benefits of the ECOWAS-MRH initiative as it is presently poorly communicated among participating companies.
- Strengthen the regulatory function and inspection.
- Respond quickly to submitted documents, especially dossiers from applicants.

DISCUSSION

This study obtained the views of the pharmaceutical manufacturers about the performance of the programme to date, identified the challenges experienced by the manufacturers throughout the life cycle of the ECOWAS-MRH initiative, determined the strengths and weaknesses of the initiative, identified the ways of improving the performance of the work sharing programme and envisaging the strategy for moving forward which has been very successful. The manufacturers expressed their views on all aspects of the ECOWAS-MRH initiative and offered very valuable suggestions for its improvement.

The important benefit of harmonisation of registration requirements across the region was identified by almost all the manufacturers at this time. It is noted that in a similar study of the ECOWAS-MRH initiative by the authors (Owusu-Asante et al, 2022), the benefit of harmonisation of registration requirements across the region was also highlighted by the NMRAs. Since the views of the manufacturers and NMRAs are the same at this time regarding this benefit, and furthermore regarding their views on the benefits of the initiative to patients, it is expected that both stakeholders would cooperate and work together to facilitate registration of medicines and vaccines within the ECOWAS member states which would ultimately result in patients having timely access to these products. The medicines regulatory harmonization initiative in East Africa (EAC-MRH) aims to improve the registration timelines without compromising the quality of dossiers submitted for marketing authorization. The joint assessment procedure which is patronised by the national medicines regulatory authorities (NMRAs) in the East African region and pharmaceutical manufacturers in other parts of the world is a classic example of this harmonization initiative (AllAfrica.com, 2012, Dansie, et al, 2019; Giaquinto et al, 2020).

The strength of the ECOWAS-MRH initiative to prioritise the review of ECOWAS-MRH products for subsequent registration in the member states, which was also noted by the manufacturers can also be maximized in order to help make such medicines and vaccines available for public health use in a timely manner. With the manufacturers having clearly identified all the benefits they derive from the ECOWAS-MRH initiative (Figure 8.4) resulting in savings in time and resources and access to various markets at the same time, this should be enough justification to ensure that the ECOWAS-MRH initiative is supported to achieve its mandate.

Some of the challenges of the ECOWAS-MRH initiative namely, lack of centralised submission and tracking which were identified by the manufacturers in the study have also been identified by the NMRAs in the previous study (Owusu-Asante et al, 2022). Similar to the studies conducted with regard to the EAC-MRH and ZaZiBoNa (Sithole et al, 2022b; Ngum et al, 2022a), these challenges were also reported with regard to the respective regional MRH initiatives. In addition, the manufacturers in this study identified other challenges which were specific to the ECOWAS-MRH initiative such as differences in regulatory performance of the countries and dependence on the countries' process for communication with applicants, and lack of detailed information on the process for applicants.

The challenges faced by manufacturers submitting applications to the ECOWAS-MRH initiative such as low motivation to use the ECOWAS-MRH route and preference for other regulatory pathways in the ECOWAS member states is reflected in the low number of manufacturers who have accessed the ECOWAS-MRH initiative to date (Blanc, 2020). Other challenges such as lack of information on country websites and the ECOWAS-MRH website about the process, milestones, timelines, pending and approved products have also been reported by the NMRAs (Owusu-Asante et al, 2022) and should therefore be addressed for the joint-benefit of the NMRAs and manufacturers.

To improve the effectiveness of the ECOWAS-MRH initiative, suggested by the manufacturers was previously provided by the NMRAs, such as making publicly available any information that might help applicants in managing their submissions-templates of documents, lists of questions and answers, timelines and milestones, decision-making transparency aids e.g publishing Public Assessment Reports, consistency in application of guidelines and decisions, engagement and interaction with stakeholders, minimizing the need for country specific documents and publishing of pending and approved products. Use of risk-based approaches for example, reliance pathways were also provided as other ways that could be explored to improve the effectiveness of the ECOWAS-MRH initiative. The WHO Prequalification Programme's success stories should be examined and piloted in the ECOWAS region (WHO, 2022g).

The suggestions presented by the manufacturers to improve the efficiency of the ECOWAS-MRH initiative, were also previously provided by the NMRAs, such as implementing robust IT systems and building capacity of assessors to facilitate processing and monitoring milestones of applications should also be explored. Similar to the NMRAs, the manufacturers' viewed the establishment of a regional administrative body, an ECOWAS regional medicines agency, if legally possible, to manage the ECOWAS-MRH initiative as the most progressive way forward.

The views of the NMRAs from the previous study ((Owusu-Asante et al, 2022) have been endorsed by the manufacturers and therefore should be noted. Five of the ten manufacturers who participated in the study were based in the ECOWAS region. Local manufacturers in the region should be technically and financially supported in order to encourage them to benefit from the ECOWAS initiative.

This study identified the benefits and challenges of the ECOWAS-MRH initiative as experienced by the manufacturers as well as strategies available to improve its effectiveness and efficiency. The key recommendations which have been proposed, if implemented, should further strengthen this initiative to enable it to fulfil its mandate in the ECOWAS region.

RECOMMENDATIONS

The key recommendations for improving the ECOWAS-MRH initiative are:

- **Incentives to manufacturers in ECOWAS -** through fast-track processing of applications and reducing GMP inspection fees to encourage more submissions from manufacturers to the ECOWAS-MRH initiative.
- **Engaging with the WHO Prequalification Programme** - to create a facilitated regulatory pathway for medicines and vaccines which have been issued with recommendation letters following successful completion of the ECOWAS-MRH joint assessment procedure.
- **Eligibility for international procurement agencies** - to source such medicines and vaccines with recommendation letters for public health use in situations where there are no prequalified alternatives.
- **Training of manufacturers** - to develop their skills, knowledge, and competence.
- **Convening Stakeholders' meetings** - on a biannual basis to engage with manufacturers and update them on the requirements to ensure compliance with regulations.

CHAPTER 09

A NEW IMPROVED REGULATORY REVIEW MODEL FOR THE ECOWAS REGIONAL INITIATIVE: ALIGNING TO THE FUTURE ROLE OF THE AMA

SUMMARY

- Since the beginning of the ECOWAS joint assessment procedure in 2019, twenty-six product applications have been submitted to the procedure, out of this number twelve product representing 46% of the total product applications have been approved at the regional level.
- The studies presented in this chapter aimed to evaluate the regulatory review process of the ECOWAS-MRH initiative and that of the participating countries and applicants with the goal of improving the process and enhancing patients' access to medicines within the ECOWAS and beyond.
- Data were collected from 2021 to 2023 using the literature review method and the questionnaire technique (OpERA, PEER, PEER-IND).
- The benefits/ successes of the initiative to the NMRAs and the pharmaceutical industry have been presented. Lastly the challenges experienced by individual authorities and pharmaceutical industry throughout the life cycle of the ECOWAS-MRH initiative, ways of improving the performance of the work-sharing programme and the strategy envisaged for moving forward have all been identified.
- A proposed improved model for the NMRAs in ECOWAS, including improvements to the current operating model of the ECOWAS-MRH initiative has been recommended.

INTRODUCTION

The Economic Community of West African States (ECOWAS) is a regional economic community in Africa, consisting of fifteen member states all of which are located in West Africa. The member states are Benin, Burkina Faso, Cape Verde, Cote d'Ivoire, Gambia, Ghana, Guinea, Guinea Bissau, Liberia, Mali, Niger, Nigeria, Senegal, Sierra Leone and Togo. As of April 2025, the population of ECOWAS was estimated to be about four hundred and sixty-four million persons (Conway et al, 2020; Worldometer, 2025).

To enhance timely access to quality, safe and efficacious medicines by the patients in West Africa, the West African Health Organization in collaboration with the fifteen national medicines regulatory authorities (NMRAs) in West Africa established the economic community of west African states -medicines regulatory harmonization (ECOWAS-MRH) initiative 'under the framework of the African Medicines Regulatory Harmonization (AMRH)' in 2017 (ECOWAS, 2021). With regard to this initiative, some selected NMRAs jointly assess applications for marketing authorisations for the sub-region (ECOWAS, 2021; Owusu-Asante et al, 2022).

Specific products which are jointly assessed in the ECOWAS-MRH initiative include; antimalarials, antiretrovirals, essential medicines as listed by the WHO, medicines for tuberculosis, reproductive health, neglected tropical diseases, medicines for public health emergencies, prequalified products by the WHO, approved products by stringent regulatory authorities and biological products including vaccines. These products, upon successful completion of the joint assessment, can then be processed within 60days through an NMRA's registration procedure for a marketing authorisation to be issued. An NMRA is identified to act as coordinator for a period of two years to handle submissions and liaises between WAHO and applicants. Submissions to the joint assessment procedure are to be processed between approximately 120 and 226 calendar days (ECOWAS, 2021; ; Owusu-Asante et al, 2022).

Assessment of the Regulatory Review Process of the ECOWAS-MRH initiative

Since the beginning of the ECOWAS joint assessment procedure in 2019, twenty-six (26) product applications have been submitted to the procedure, out of this number twelve (12) products representing 46% of the total product applications have been approved at the regional level (Table 10.1).

Table 9.1. Status of approvals by the ECOWAS-MRH initiative

Status of approvals by the ECOWAS-MRH initiative from 2019- 2024	
Year	**No of products approved**
2019	1
2020	0
2021	3
2022	7
2023	0
2024	1

At the start of this research, it was noted that there was little literature on the ECOWAS-MRH initiative, possibly due to the fact that because the ECOWAS-MRH initiative was relatively the newest among the other initiatives in Africa. Furthermore, it was clearly evident that the NMRAs that are active in the ECOWAS-MRH initiative had been established prior to the setting up of the initiative. This research, therefore aimed to evaluate the regulatory review process of the ECOWAS-MRH initiative and that of the participating countries with the goal of improving the process and enhancing patients' access to medicines within the ECOWAS and beyond. It was considered logical that in this research the regulatory systems of individual selected countries that are active in the ECOWAS-MRH initiative are initially assessed and then this could be followed with the assessment of the ECOWAS-MRH initiative.

9

METHODS

Based on the results from other studies and experience gained throughout the work it was concluded that in order to make a comprehensive assessment of the current state of the regulatory process in the ECOWAS-MRH regional initiative and subsequently propose improvement to the current system, it would be imperative to focus on the assessment of individual member countries of the regional initiative as well as that by the sponsors. Therefore, two studies were conducted in 2022 to determine the effectiveness and efficiency of the regional ECOWAS-MRH Initiative.

Study 1: All seven active NMRAs of the ECOWAS-MRH initiative namely, National Pharmaceutical Regulatory Agency-Burkina Faso, Ministry of Public Health- Republic of Cote d'Ivoire, Food and Drugs Authority (Ghana-FDA), National Agency for Food and Drug Administration and Control (NAFDAC) -The Federal Republic of Nigeria, Ministry of Health and Social Welfare-Republic of Senegal, Pharmacy Board of Sierra Leone (PBSL) and the Directorate of Pharmacy, Medicine and Laboratories - Togo,

participated in the study between January and June 2022. The Process Effectiveness and Efficiency Rating (PEER) questionnaire, previously developed and validated by Ngum and colleagues to evaluate the performance of the East African Community joint assessment procedure (Ngum, 2022), was used to collect the study data. The PEER questionnaire consists of five parts as follows: authority resources, benefits of the ECOWAS-MRH initiative, challenges of the ECOWAS-MRH initiative, improving the performance (effectiveness and efficiency) of the work-sharing programme and strategy for moving forward (Chapter 7).

Study 2: All ten pharmaceutical manufacturers who have submitted marketing authorization applications for assessment of medicines at the regional level since the beginning of the ECOWAS-MRH initiative participated in the study. The study participants were classified as Innovator, Generics (foreign) -manufacturer outside ECOWAS and Generics (local)- manufacturer within ECOWAS. Data for the study was obtained through completion of the Process Effectiveness and Efficiency Rating (PEER) questionnaire (Ngum et al., 2022; Sithole et al., 2022) by applicants between October 2022 and January 2023.

The questionnaire consisted of five sections namely; demographics, the benefits and challenges of the ECOWAS-MRH initiative, improving the performance (effectiveness and efficiency) of the work sharing programme and envisaging the strategy for moving forward (Chapter 8).

RESULTS AND DISCUSSION

Following the successful assessment of the effectiveness and efficiency of the ZaZiBoNa and EAC-MRH initiatives (Sithole et al, 2022a; Sithole et al, 2022b; Ngum et al, 2022a; Ngum et al, 2022b). and the launch of the African Medicines Agency, it was timely that the ECOWAS-MRH initiative was assessed and hence the implementation of two corresponding studies (Owusu-Asante et al,2022; Owusu-Asante et al,2023). The studies aimed to assess the effectiveness and efficiency of the West African Medicines Regulatory Harmonization Initiative by the member countries and the pharmaceutical industry respectively.

The objectives of these studies were to obtain the views of the individual active NMRAs of the ECOWAS-MRH initiative and the pharmaceutical industries that have submitted applications to the initiative about the performance of the programme to date, determine the benefits/ successes of the initiative to the NMRAs and the pharmaceutical industry, identify the challenges experienced by individual

authorities and pharmaceutical industry throughout the life cycle of the ECOWAS-MRH initiative, identify the ways of improving the performance of the work-sharing programme and envisage the strategy for moving forward (Owusu-Asante et al,2022; Owusu-Asante et al,2023).

Successes of the ECOWAS-MRH Initiative

The NMRAs reported that the ECOWAS-MRH work-sharing initiative has enabled applications of high standards of assessment regardless of the size of the country or maturity of regulatory agency. The training to improve the performance of the assessors provided the platform for interaction and information exchange with other regulators. There has been improvement in the quality of dossiers submitted and also sharing of the workload has resulted in shorter timelines for approval than in individual countries (Owusu-Asante et al,2022; Owusu-Asante et al,2023). The benefits of the ECOWAS-MRH initiative for manufacturers (applicants) included access to various ECOWAS markets at the same time, a reduced burden as they compiled one dossier (modules 2-5) for submission to multiple countries. The savings in time and resources as they received the same list of questions from multiple countries, enabled compilation of a single response package as well as shorter timelines for approval compared with that for the individual countries. The NMRAs and the manufacturers reported quicker access to quality assured medicines and increased availability of medicines as the benefits of the work-sharing initiative for patients at either the country or regional level. These benefits give a good indication that the ECOWAS-MRH initiative is presently moving in the right direction by making available quality, safe and efficacious medicines both at the country and regional levels (Owusu-Asante et al,2022; Owusu-Asante et al,2023).

Challenges of the ECOWAS-MRH Initiative

The challenges of the ECOWAS-MRH initiative which were identified by the NMRAs included the low or decreasing number of applications for assessment, lack of centralised submission and tracking, lack of detailed information on the process for applicants, lack of jurisdictional power, unequal workload among the agencies and dependence on the countries' processes for communication with applicants and expert committees. Poor IT infrastructure to support dossier submissions and the assessment process was also presented as another challenge of the ECOWAS-MRH initiative (Owusu-Asante et al,2022; Owusu-Asante et al,2023). The views of the regulators regarding the challenges faced at the country level in assessing/finalising ECOWAS-MRH products included inadequate human resources, failure by manufacturers to adhere to deadlines for response to questions, unpredictable

schedule of committee meetings, the ECOWAS-MRH initiative's work not being recognised as part of the agency workload to be carried out during working hours, failure by manufacturers to follow the requirement to submit the exact same dossier to all countries of interest and lack of priority review for ECOWAS-MRH products (Owusu-Asante et al,2022; Owusu-Asante et al,2023). In addition, other challenges faced at the country level in assessing/finalising ECOWAS-MRH products included lack of an ECOWAS-MRH calendar of activities to help avoid conflicts and lack of compatibility of the time limits for the joint assessment procedure with the national procedures. The challenges identified by the NMRAs were that the ECOWAS-MRH process was more stringent than some country processes, the differing labelling requirements in participating countries, the lack of clarity about the process for submission and follow-up in each country as well as the lack of information on country and ECOWAS-MRH websites about the process, milestones and timelines, as well as pending and approved products (Owusu-Asante et al,2022; Owusu-Asante et al,2023).

It is worth noting that in addition to the above, other challenges remain, namely, lack of processes in the NMRAs on how to move from regional approval to local approval in the ECOWAS countries and lack of NMRA's responsiveness in communicating updates of application status (Owusu-Asante et al,2022; Owusu-Asante et al,2023). Additional challenges identified by the manufacturers included low motivation to use the ECOWAS-MRH route as other faster review routes are now being used by individual countries e.g., reliance on SRA approvals and other ECOWAS countries, failure by countries to adhere to promised timelines, risk of losing access to all member states once a product is rejected by ECOWAS-MRH (i.e., can no longer pursue registration in individual countries), lack of information on country websites and the ECOWAS-MRH website about the process, milestones, timelines, pending and approved products (Owusu-Asante et al,2022; Owusu-Asante et al,2023).

In view of the numerous challenges that have been presented above, it is necessary to propose an improved regulatory review system for the ECOWAS-MRH initiative at this time.

PROPOSED IMPROVED REGULATORY REVIEW SYSTEM FOR ECOWAS-MRH INITIATIVE

For the purpose of clarity, the results will be presented in three parts as follows; Part I: A proposed improved model for the NMRAs in ECOWAS; Part II: Proposed improvements to the current operating model of the ECOWAS-MRH initiative and Part III: A proposed new improved model for the ECOWAS-MRH initiative.

Part I: Proposed improved model for the NMRAs in ECOWAS

Following the completion of these studies above to review the regulatory review system for the ECOWAS and the various challenges that have been elucidated, these are some recommendations that are to be addressed at the country level.

Human resource capacity

It is well known that the NMRAs in ECOWAS have inadequate human resources; this is with regard to both number of personnel as well as competence. This has also been highlighted in this research. It should therefore be a top priority for the NMRAs to recruit more competent technical personnel in order to carry out both national and regional assessments in a timely manner.

Good review practices and regulatory timelines

From the study which assessed the good review practices of the active NMRAs (Owusu-Asante et al, 2024), it was noted that comparison of the transparency and communication parameters implemented by the NMRAs showed that there were still some parameters to be implemented by the agencies. On a positive note however, it was found from the study that there could therefore be an opportunity for the exchange of strategies amongst the NMRAs in order for each of the NMRAs to implement all remaining parameters. All agencies should have internal tracking systems to monitor the progress of marketing authorization applications in order to meet their target timelines. To further promote transparency in their regulatory processes, agencies in the region would benefit from implementing additional good review practice measures as well as sharing of assessment reports with applicants and publishing approval times as well as the summary basis of approval to all stakeholders. Following this is the recommendation that all agencies should implement the 10 quality decision-making practices in their NMRAs. It is hoped that as the NMRAs fully implement good review practices in their countries, all stakeholders, most importantly patients will reap the resultant benefit of improved access to medicines (Owusu-Asante et al, 2024).

Processing of regional approvals by NMRAs

The ECOWAS-MRH initiative's work was not being recognised as part of the agency workload to be carried out during working hours. In addition, other challenges faced at the country level in assessing/finalising ECOWAS-MRH products included the lack of an ECOWAS-MRH calendar of activities to help avoid conflicts and the lack of compatibility of the time limits for the joint assessment procedure with the national

procedures. In addition to the above, other challenges remain, namely, lack of processes in the NMRAs on how to move from regional approval to local approval in the ECOWAS countries. There were no clear processes to follow to get approval and lack of NMRA's responsiveness in communicating updates of application status needed to be addressed. It is hereby recommended that all agencies process applications submitted via the ECOWAS-MRH procedure through the verification review pathway in order to expedite their approvals at the country level.

The ECOWAS-MRH process

According to this research, the NMRAs have found that the ECOWAS-MRH process is more stringent than their country processes. This is a disincentive for manufacturers and the ECOWAS-MRH initiative. It is therefore not surprising that both the number of submissions to and approvals from the ECOWAS-MRH initiative are relatively low when compared to the EAC-MRH and ZaZiBoNa initiatives.

It was also reported that there was no clarity about the ECOWAS-MRH process on the 'websites of the NMRAs. The lack of information in a way contributes to the lack of publicity about the ECOWAS joint assessment procedure.

The low motivation and appeal for manufacturers to use the ECOWAS-MRH route as other faster review routes are now being used by individual countries e.g., reliance on SRA approvals or other ECOWAS countries is an issue that needs to be well managed by all stakeholders. The few success stories of the ECOWAS-MRH initiative which are available should be publicized by the NMRAs in order to attract more patronage by all stakeholders.

A mutual recognition procedure, in which products which are already registered by any of the agencies that have maturity level-3 status are subsequently reviewed at the national and regional levels via a priority pathway should be established to significantly reduce duplication in assessments and use resources more efficiently. NMRAs active in the ECOWAS-MRH initiative should have a formal assessment to periodically measure the quality of their decision-making processes in place with regard to processing of applications submitted to the ECOWAS-MRH initiative. This will help to promote continuous improvement in their regulatory processes.

Benefit-risk assessment

Presently benefit risk assessment is not carried out in any of the agencies in ECOWAS, and since it is fundamental to the review of new medicines, it is strongly recommended

that NMRAs in ECOWAS incorporate a structured benefit-risk assessment framework in making their national and regional regulatory decisions (USFDA, 2022).

IT infrastructure

Agencies should develop their websites to include detailed information about the ECOWAS-MRH process, milestones and timelines, as well as pending and approved products as this was reported as a drawback to submitting applications to the regional initiative. NMRAs in ECOWAS should put in all the efforts required to ensure that the regional initiative is a success. Agencies should invest in robust IT systems to help in the efficient tracking of applications.

A proposed improved model for the NMRAs in ECOWAS is presented in Figure 9.1.

Part II: Proposed improvements to the current operating model of the ECOWAS-MRH initiative

While it is yet to be fully understood why more than 50% of the applications to the ECOWAS-MRH have not been approved at the regional level as of this time, the following were reported as challenges of the initiative:

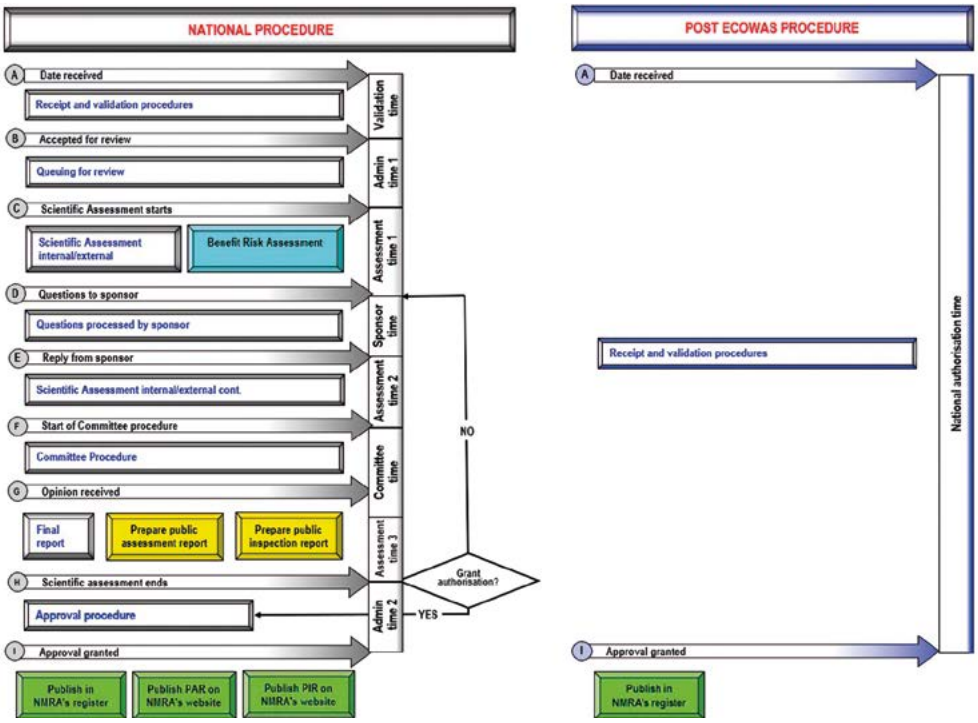
Challenges of the ECOWAS-MRH initiative

According to the study the lack of ability to mandate central registration, differences in the regulatory performance of the countries and dependence on the countries' process for communication with applicants, lack of a centralised submission and tracking as well as detailed information on the process for applicants were identified as challenges of the ECOWAS-MRH initiative.

Additional challenges identified by applicants included risk of losing access to all member states once a product is rejected by the ECOWAS-MRH (i.e., can no longer pursue registration in individual countries), lack of information on the WAHO website about the ECOWAS-MRH process, milestones, timelines, pending and approved products. Furthermore, the ECOWAS-MRH process was found by the active NMRAs in ECOWAS to be more stringent than some country processes and differences in time to implementation of ECOWAS-MRH recommendations by the countries were identified as challenges faced by manufacturers submitting applications to the ECOWAS-MRH initiative.

The following improvements to the current operating model of the ECOWAS-MRH initiative are proposed:

Figure 9.1. Proposed improved model for NMRAs in ECOWAS.



Transparency and Communication

Information that might help applicants in managing their submissions, such as templates of documents, lists of questions and answers, timelines and milestones, decision-making transparency such as publishing Public Assessment Reports should be publicly available on the WAHO website.

Transparency on metrics and statistics for example, percentage of reviews completed within prescribed timelines should be available to all stakeholders. Additionally lists of approved and pending products should also be available on the WAHO website.

WAHO should have engagements and interaction with stakeholders and should be consistent in application of relevant guidelines.

Use of risk-based approaches

The ECOWAS-MRH initiative should recognize NMRAs that have achieved maturity level 3 status as reference agencies and accept applications that have been previously approved by such agencies in its reliance review pathways. This will avoid duplicating

assessments of applications and lead to faster approvals at the regional level (Sithole et al, 2024).

Use of robust IT systems

The enormous benefits of investing in a robust IT system to facilitate electronic submissions, monitoring and tracking of applications cannot all be listed here. The IT system would help applicants and WAHO comply with target timelines by measuring and monitoring each milestone in the review process (Ngum et al, 2025).

Best strategy for moving forward

From the relevant studies which have been conducted at this time, it has been noted that to improve the performance of the ECOWAS-MRH initiative, the current system should be strengthened to enable it to fulfil its mandate in the ECOWAS region, since the creation of a regional agency may not be required in view of the establishment of the African Medicines Agency. The current model whereby a lead coordinating NMRAs is tasked for a period of two years, to receive and assign assessors and also communicate with applicants and WAHO could be improved by tasking WAHO with these responsibilities accordingly. This is because for applications that are not processed within the two-year tenure of the coordinating NMRAs, there may be issues/delays when tracking such applications subsequently.

Part III: A proposed new improved model for the ECOWAS-MRH initiative

With regard to the proposed improvements to the current operating model of the ECOWAS-MRH initiative, a proposed new improved model for the ECOWAS-MRH initiative is presented in Figure 9.2.

In this improved model, all applications are submitted to WAHO to handle their assignment for assessment and communications with applicants seamlessly.

A tabular comparison of the current and proposed operating model of the ECOWAS-MRH initiative has been presented in Table 9.2

Considerations to be made for implementation of the centralised model

The WAHO has been proposed by this research to be responsible for the receipt of all submissions throughout each year. It is expected that the institution will be granted a legally binding framework and equipped with a robust IT infrastructure to make it efficient in communicating with all stakeholders. The institution would have to be adequately resourced with technical personnel and supported by competent staff

from the NMRAs in order to carry out its responsibilities. Applications that have been assessed by other maturity level 3 NMRAs should be processed via a reliance pathway in order to avoid duplication of assessments and enable such products to be readily accessible in the ECOWAS region.

Figure 9.2. Proposed new improved model for the ECOWAS-MRH initiative.

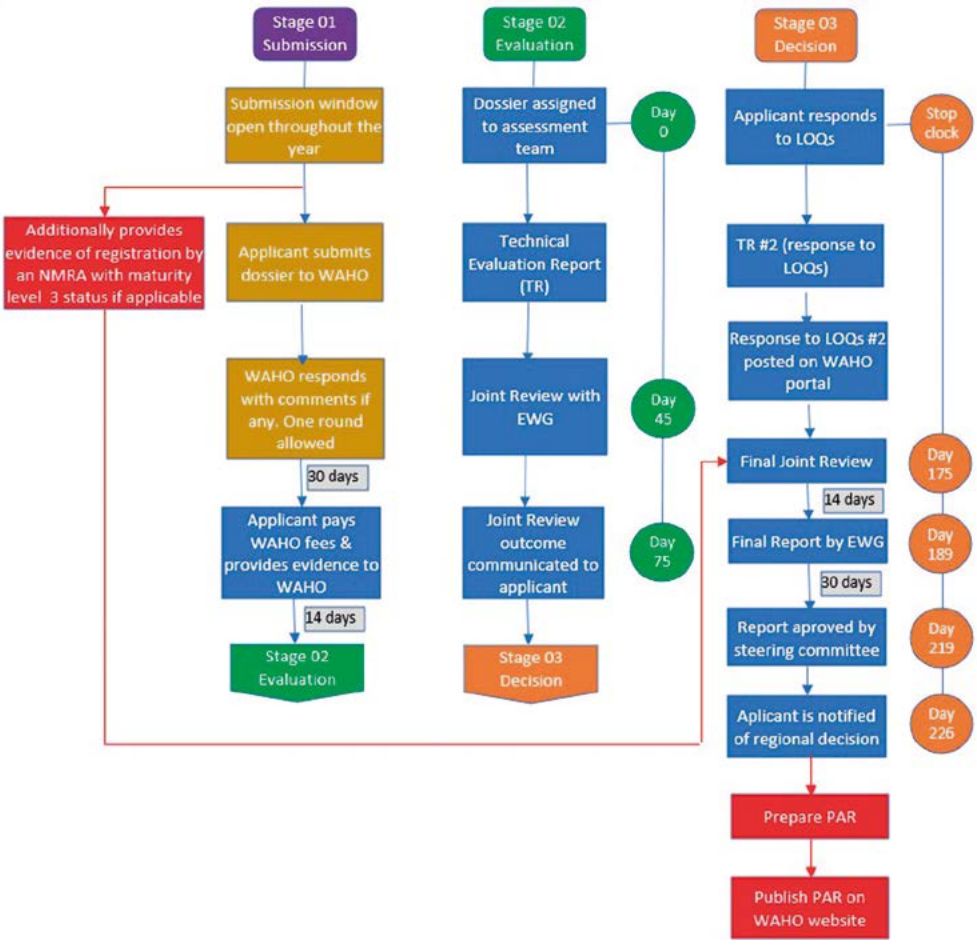


Table 9.2. Comparison of the current and proposed operating models of the ECOWAS-MRH initiative

Criteria	Current ECOWAS-MRH initiative	Proposed ECOWAS-MRH initiative
Legal Framework	None	Legal binding document
Governing Body	Heads of ECOWAS NMRAs (Joint Steering Committee)	Same as for current
Secretariat	WAHO	WAHO
Submission window opening	Opening in February, May, July and	Opening throughout the year
Process	Submission to lead coordinating NMRA	Centralised submission to WAHO
Fees	Regional and national	Same as for current
Expert Committees/ Technical Working Groups	- Medicines Evaluation & Registration - Good Manufacturing Practices - Quality Control - Quality Management Systems - Information Management System - Pharmacovigilance & Clinical Trials - Policy,Legislation & Regulation	Same as for current
Scope of products	- Products on WHO's Essential Medicine List - Programme Medicines (HIV/AIDS, Malaria, Tuberculosis, Reproductive Health, Neglected Tropical Diseases and Antibiotics) - Medicines used in Public Health Emergencies - Products registered by Stringent Regulatory Authorities, prequalified by WHO, registered under Swissmedic MAGHP Procedure or EMA Article 58 12:12(Positive Scientific opinion) - Life Saving Commodities (LSC) by the UN Commission on Life Serving Medicines for Women and Children - Biological products (including Vaccines) - Blood products; Medical Devices on a WAHO specific list to be published in the EOI - Other priority medical products that WAHO will determine from time to time	Current scope of products and Products registered by ML3 NMRAs

CHAPTER 10

CONCLUDING REMARKS

INTRODUCTION

The World Health Organization (WHO) has reported that 'a 2016 study estimated that the overall time required for registration of new or innovative medicines and vaccines in low- and middle-income countries (LMICs) is typically four to seven years after a marketing authorization dossier has been submitted. This compares with one to two years, on average in high income countries (HICs). Reasons for the longer registration times in LMICs include bottle necks caused by multi-stage approval processes, inadequate funding, and different standards and requirements applied by national regulatory authorities (NRAs), all of which impose additional or duplicative work on manufacturers' applications. Furthermore, although they are not well understood by policy-makers, health care workers and even by regulators, national requirements for repeated official batch release testing often are a major obstacle to market access' (WHO, 2019).

The WHO in recognizing its important role in establishing standards for medical products for compliance by manufacturers and regulators in this era of globalization has set out in the 'WHO's 2019-2023 Regulatory Action Plan ways to help build effective and efficient regulatory systems to enable timely access to quality medical products' (WHO,2019d). It is not surprising that the first strategic priority of the Action Plan is to 'strengthen country and regional regulatory systems in line with the drive towards universal health coverage (UHC)' (WHO,2019d). The WHO acknowledges that though there are countries which have limited resources to establish and maintain effective and efficient regulatory systems, possible solutions 'have to be tailored to the diverse needs of countries' (WHO, 2019d). Furthermore 'solutions should also incorporate internationally recognised, sciened -based and harmonized standards, along with increased collaboration among regulators to strengthen regulatory decision-making' (WHO, 2019d).

In 2018, a WHO survey reported that 'only 30% of NRAs had the capacity to effectively and efficiently regulate products on their markets' (WHO,2019d). The challenge of limited capacity to assess applications for marketing authorization for new active substances and also applications for variations in registered products has also been highlighted by the WHO (WHO, 2019d). According to the WHO 'the challenges presented by the increasing complexity and globalization of trade are exacerbated by lack of coordinated regulation, even in the same region' (WHO, 2019d).

In response to the limited resources for optimal regulatory functionality, the WHO has proposed the building of capacity, increased collaboration and implementing reliance

as ideal solutions (WHO,2019d). The WHO has introduced *a framework for evaluating and publicly designating regulatory authorities as WHO Listed Authorities (WLA).* A WLA is defined as 'a regulatory authority or a regional regulatory system which has been documented to comply with all the relevant indicators and requirements specified by WHO for the requested scope of listing based on an established benchmarking (GBT) and a performance evaluation process' (WHO, 2024f). 'Implementation of the WLA framework is intended to promote access and supply of safe, effective and quality medical products. The framework also provides for the optimal use of limited resources by facilitating reliance on the work products and decisions of trusted agencies in the decision-making of regulatory authorities' (WHO, 2024g).

With reference to the WHO global benchmarking tool, there are presently eight NMRAs, in Africa consisting of Ghana, Nigeria and Senegal in the West-African sub region, and Egypt, Rwanda, Senegal, South Africa and Zimbabwe that have stable, well-functioning and integrated regulatory systems and have therefore 'reached Maturity Level 3 (ML3) in WHO's global classification of national regulatory authorities, underscoring their commitment to ensuring safe, effective and high-quality medical products for their populations' (WHO, 2024c). The WHO views each of these ML3-classified NMRAs to be 'eligible for consideration as a WLA' (WHO, 2024g).

It is the view of the WHO that 'strong regulatory authorities perform critical functions like rapid product authorization contributing to better outcomes' (WHO,2024c).

From the WHO 'regulatory control of medical products to protect public health is fully acknowledged. The issue is how to regulate effectively, efficiently and transparently, such that the interests of the health care system are served' (WHO, 2021).

10

Best regulatory practices such as reliance and regulatory harmonization are highlighted currently. Reliance which is defined as 'the act whereby a regulatory authority in one jurisdiction takes into account and give significant weight to assessments by another regulatory authority or trusted institution in reaching its own decision; and the relying authority remains independent, responsible and accountable for the decisions taken' is encouraged among regulatory authorities irrespective of their maturity or geographical location (WHO, 2021). Regulatory harmonization is defined as 'a process whereby the technical guidelines of participating authorities in several countries are made uniform' (WHO, 2021). NMRAs have been advised to institutionalize strategies that promote best regulatory practices such as reliance and harmonization to achieve the optimal regulatory impact (WHO, 2021). With the presence of some ML-3 NMRAs

in West Africa, It should be a good idea to practice reliance with the ML-3 authorities acting as reference agencies.

A significant strategy to build the capacity of NMRAs in Africa has been made by the 'African Medicines Regulation Harmonization (AMRH) programme which was started in 2009 as a response to addressing challenges faced by NMRAs in Africa. These challenges include: weak or non-coherent legislative frameworks, sluggish medicine registration processes and subsequent delayed approval decision, inefficiency and limited technical capacity, among others. This situation translates into poor access to priority essential medicines by patients and is a contributing factor to over-priced medicines' (AUDA-NEPAD, 2025).

According to AUDA-NEPAD 'the AMRH Initiative has so far been implemented in five regional economic communities namely, East African Community (EAC), Southern African Development Community (SADC), the Economic Community of West African Styates (ECOWAS), the Economic Community of Central African States (ECCAS) and, the Intergovernmental Authority for Development (IGAD)' (AUDA-NEPAD, 2025).

Following the successful assessment of the medicines regulatory harmonization initiatives in the EAC and SADC in recent years (Sithole et al, 2020, 2012a, 2021b, 2022a, 2022b, 2024; Ngum et al 2022a, 2022b,2024a, 2024b, 2025) and the launch of the African Medicines Agency, an assessment of the regulatory review systems in the ECOWAS has not been conducted. This research, therefore aimed to evaluate the regulatory review process of the ECOWAS-MRH initiative and that of the participating countries with the goal of improving the process and enhancing patients' access to medicines within the ECOWAS and beyond.

A total of six studies have been conducted with regard to this research as follows; firstly the review processes and practices within the FDA Ghana were assessed (Study 1: Chapter 3), secondly good review practices at the FDA Ghana as it strives to become a WHO listed agency were evaluated (Study 2: Chapter 3), thirdly a comparative study among the African NMRAs that have achieved WHO GBT maturity level 3 status was carried out (Study 3:Chapter 4), fourthly a two-part series study was conducted to provide an insight into the implementation of good review practices and also to compare the review models and regulatory timelines of countries that actively participate in the ECOWAS-MRH initiative (Study 4: Chapter 5 and 6), fifthly an assessment of the effectiveness and efficiency of the ECOWAS-MRH initiative by the active NMRAs was conducted (Study 5: Chapter 7) and finally an assessment of the effectiveness and

efficiency of the ECOWAS-MRH initiative by the pharmaceutical manufacturers who have submitted marketing authorization applications for assessment of medicines at the regional level since the beginning of the ECOWAS-MRH initiative participated in the last study (Study 6: Chapter 8). The data from each study were analysed to facilitate a detailed assessment of the regulatory review process of the ECOWAS-MRH and that of the active NMRAs of the initiative.

RESEARCH OUTCOMES AND CONTRIBUTIONS

There was very limited information on the assessment of the ECOWAS-MRH initiative in the literature at the start of the research. This was possibly due to the relatively young existence of the initiative relative to the other MRH initiatives of the AMRH programme.

From the first study (Chapter 2) it was noted that the FDA Ghana employs the three established regulatory review models for assessing marketing authorisation applications. The extent to which quality, safety and efficacy data are assessed depends on the review model. Currently, there is not an electronic tracking system in place and therefore the obvious challenges associated with a manual system are evident in the data collection processes.

This study has demonstrated that generic medicines (including biosimilars) are processed faster than NASs, mainly because of their relatively simpler clinical requirements. FDA Ghana has also developed adequate technical capacity to assess these generic applications.

Making available public assessment reports for all marketing authorisation applications and pursuing the implementation of an electronic tracking system are some of the recommendations from the study which are being addressed by the FDA Ghana.

From the second study (Chapter 3), It was noted that the study provided a baseline for the FDA Ghana's knowledge, attitudes and practices as well as areas for improvement. As a result of having a baseline it is now possible to work towards achieving an improvement in the regulatory performance of the FDA Ghana as it prepares to become a WHO listed authority.

From the third study (Chapter 4), it was noted that this comparative study showed that similarities among these authorities also translated into their strengths. The study also revealed that the human resource capacity in African NMRAs is inadequate to fully

execute regulatory mandates. Review process map comparisons revealed the important observation that these NMRAs conducted labelling review early in the review process rather than at the end, which would facilitate the preparation of public assessment reports. An important recommendation from the study which has been implemented was that the recently established AMA should engage these maturity level-3 NMRAs to explore ways that the AMA could benefit from their experience and resources, thereby supporting the effectiveness and efficiency of the AMA in achieving its overall goal.

From the fourth study (Chapter 5) it was noted that the comparison of the transparency and communication parameters and continuous improvement initiatives implemented by the NMRAs also showed that there were still some of the parameters to be implemented by the agencies. There could therefore be an opportunity for the exchange of strategies in order for each of the NMRAs to implement all remaining parameters. Comparing the training and education initiatives which have been implemented by the NMRAs showed that Sierra Leone and additionally Ghana could serve as a reference to the other NMRAs accordingly.

This study has therefore shown that resources are available in the ECOWAS region for the NMRAs to rely on as well as to improve their respective good review practices.

Additionally, from the fourth study (Chapter 6), it was noted that the comparative study of the review models and regulatory timelines of countries participating in the ECOWAS-MRH initiative has highlighted both the similarities among the agencies and also the gaps which are to be addressed in order to improve the regulatory systems in these countries. A number of key recommendations for improving review models and regulatory timelines of the countries participating in the ECOWAS-MRH initiatives were made. It was recommended that the ECOWAS-MRH initiative should be recognized as a reference such that Agencies should process applications submitted via the ECOWAS-MRH procedure through the verification review pathway in order to expedite their approvals at the country level.

From the fifth study (Chapter 7) it was noted that the study identified the strengths of the ECOWAS-MRH initiative as well as strategies for improvement and achievement of its objectives. The centralised submission of a dossier and its tracking is key to the regulatory assessment process. This research has demonstrated that amongst other considerations, a robust information technology system, coupled with the necessary human resource capacity would greatly enhance the effectiveness and efficiency of the ECOWAS-MRH initiative.

From the final study (Chapter 8) it was noted that by identifying the strengths and strategies for improving the ECOWAS-MRH initiative to achieve its objectives, the study identified three approaches to increase the effectiveness of this initiative. Firstly, the implementation of risk-based approaches such as reliance pathways, secondly, establishment of a robust IT system as well as building capacity of assessors to facilitate processing and monitoring the milestones for applications and finally, initiating a priority review of ECOWAS-MRH products which is key to the regulatory assessment process.

STUDY LIMITATIONS

The scope of the research was limited to the regulatory review process and timelines. The duration of the key milestones (except for receipt and approval dates) were not assessed. It was not possible to separate agency time from the sponsor/applicant's time. Public assessment reports were not available to review how applications for marketing authorisations including Summary of Product Characteristics and patient information leaflets were handled by each agency.

For chapter 2, the metrics which were collated were only for those applications that have been approved. Metrics on applications which were deferred or not approved were not included.

For chapter 4 some of the data for the EDA were obtained from publicly accessible domain information on the EDA website. The scope of this study was limited to the six NMRAs in Africa that have achieved maturity level 3 status as of June 2024. Subsequent to this Rwanda and Senegal have achieved maturity level 3 status. Going forward it would be helpful to obtain the respective data from these two additional NMRAs.

For chapters 5 and 6, some of the agencies did not provide the metrics of NASs, generics and WHO prequalified generics as requested by the study. The study was limited to only the seven active NMRAs of the ECOWAS-MRH initiative. Going forward it would be helpful to obtain the respective date from the remaining eight NMRAs who also apply the decisions from the ECOWAS-MHR in their various jurisdictions.

For chapters 7 and 8, the scope of these studies was limited to the process and operating model of the ECOWAS-MRH initiative. In addition, there were only seven applications assessed by the initiative during the three years of its operation and a small number of the member countries were involved in such assessment. However, this early evaluation of the effectiveness and efficiency of the initiative is instrumental

in identifying the achievements and the challenges moving forward, as more of the seven member countries become engaged in the assessment of applications. Going forward, it would be helpful to obtain quantitative data to support these views. Such data would include actual metrics of the time taken to register the medicines in NMRAs following a recommendation from ECOWAS-MRH.

FUTURE WORK

Benefit risk assessment

This research covered the regulatory review systems of the NMRAs that are active in the ECOWAS-MRH initiative and also NMRAs in Africa that have achieved WHO GBT maturity level 3 status. Presently benefit risk assessment is not carried out in any of the agencies in ECOWAS, since it is fundamental to the review of new medicines, it should be incorporated into the regulatory review processes. It will therefore be important to conduct a study on the implementation of a benefit-risk assessment framework in the near future.

Implementation of good review practices by other NMRAs

A study of implementation of good review practices regarding knowledge, attitude and practices of the other NMRAs should be conducted using the questionnaire which was deployed for study 2 (Chapter 3).

Quality Decision-making Practices

Presently the agencies in the ECOWAS region do not appear to have implemented quality decision-making practices; due to its importance to efficient and effective NMRAs, this should will be addressed in future research.

Reliance

Implementation of reliance by NMRAs is a 'hot topic' and therefore should be covered in any subsequent studies. This research has recommended that applications that have obtained regional approval and other NMRAs that have achieved maturity level 3 should be considered for processing at the national level via a reliance pathway. It will be of relevance to conduct a study on the implementation of the reliance pathway accordingly.

ECOWAS-MRH Initiative

The current views of both regulators and manufacturers regarding the effectiveness and efficiency of the ECOWAS-MRH initiative should be collated in a future study. This will enable stakeholders have a current detailed view of the initiative.

Assessment of the regulatory performance of African NMRAs who have recently achieved maturity level 3 status

It is important that the regulatory performance of other African NMRAs who were not covered in this research are also similarly assessed using the OpERA questionnaire for other NMRAs to learn from them.

CONCLUSIONS

In the dynamic and exciting current regulatory environment in Africa with the establishment of the African Medicines Agency (AMA), it is hoped that this body of work will contribute to the operationalization of the AMA and ultimately improvement in the availability of affordability of new medicines for the people of the 52 countries in Africa. Furthermore, moving forward, the collaboration and partnership of all stakeholders would be the key to the success of the AMA.

APPENDIX &

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LIST OF ABBREVIATIONS

AMA	African Medicines Agency
APEC	Asia-Pacific Economic Cooperation
BfArM	Federal Institute for Drugs and Medical Devices
BRAIN	Benefit-Risk Assessment in New and Old Drugs
CIRS	Centre for innovation in regulatory science
CPP	Certificate of pharmaceutical product
CTD	Common Technical Document
EAC	East African Community
ECOWAS/WA	Economic Community of West African States
EDA	Egyptian Drug Authority
EDQM	European Directorate for the Quality of Medicines and HealthCare
EMA	European Medicines Agency
FDA Ghana	Food and Drugs Authority, Ghana
FDA/USFDA	United States Food and Drug Administration
GBT	Global Benchmarking Tool (GBT)
GMP	Good manufacturing practice
GRevP	Good review practices
ICH	International Conference on Harmonization of Technical Requirements for the registration of pharmaceuticals for human use
LMICs	Low and middle- income countries
MCAZ	Medicines Control Authority of Zimbabwe
MHRA	Medicines and Healthcare products Regulatory Agency
MLEs	Major line extensions
MRH	Medicines Regulatory Harmonisation
NAFDAC	National Agency for Food and Drug Administration and Control of Nigeria
NASs	New active substances
NMRAs	National Medicines Regulatory Authorities
OpERA	Optimizing efficiencies in regulatory agencies
PBSL	Pharmacy Board of Sierra Leone
PEER	Process, Effectiveness and Efficiency Rating
PhRMA BRAT	Pharmaceutical Research and Manufacturers of America Benefit-Risk Action Team
PrOACT-URL	Problem, Objectives, Alternatives, Consequences, Trade-offs, Uncertainty, Risk Tolerance, Linked decisions
QDMPs	Quality Decision-making Practices
QoDoS	Quality of Decision-Making Orientation Scheme
QMS	Quality management systems

SADC	Southern African Development Community
SAHPRA	South African Health Products Regulatory Authority
SRAs	Stringent regulatory authorities
TMDA	Tanzania Medicines and Medical Devices Authority
UMBRA	Universal/harmonised methodology for benefit-risk assessment
WAHO	West African Health Organization
WHO	World Health Organization
WLA	WHO-listed authorities
ZaZiBoNa	Zambia, Zimbabwe, Botswana and Namibia

ABOUT THE AUTHORS

Dr. Mercy Acquaye Owusu-Asante
B Pharm (Hons), MSc, PhD.

Dr Owusu-Asante is the Head of the Manufacturing Facilities Department (MFD) at the Ghana Food and Drugs Authority (FDA, Ghana). She is also a consultant assessor in the World Health Organization's (WHO) prequalification of Medicines Programme.

Dr. Owusu-Asante received her Bachelor of Pharmacy (Honours) at the Kwame Nkrumah University of Science and Technology in Ghana. Dr. Owusu-Asante was awarded a Master of Science in Pharmaceutical Services and Medicines Control from the University of Bradford, United Kingdom. Dr. Owusu-Asante was awarded a Doctor of Philosophy (Pharmacy) by the University of Hertfordshire, United Kingdom.

Dr Owusu-Asante has over 25 years' experience as a pharmacist at FDA Ghana. In her current role as head of the Manufacturing Facilities Department (MFD), she ensures manufacturers comply with Good Manufacturing Practices (GMP) and undertakes regulatory inspections to confirm compliance. Dr Owusu-Asante issues licenses for the manufacturer of food, drugs, cosmetics, medical devices and household chemical substances to GMP compliant manufacturers.

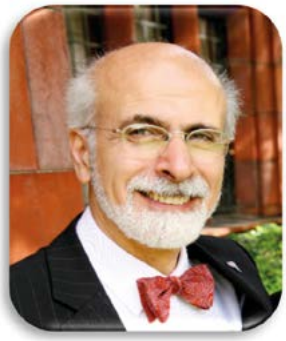
Prior to her current role as Head of the Manufacturing Facilities Department, at FDA, Ghana, Dr Owusu-Asante was the Head of the Drug Evaluation and Registration Department at the Agency. Drawing on over 15 years' expertise from the WHO prequalification of medicines programme, Dr Owusu-Asante successfully lead her team's attainment in 2013 to be the first Agency in the Economic Community of West African States (ECOWAS) to implement submission of medicines dossiers in the common technical document (CTD) format. As part of the CTD format, Dr Owusu-Asante's team also implemented electronic assessments of dossiers at FDA, Ghana. Her success with the implementation of the CTD dossier submission in Ghana, led Dr Owusu-Asante to be a facilitator in the introduction of CTD dossier submissions in Nigeria.

For over 7 years at FDA Ghana, Dr Owusu-Asante served as Head of Technical support Department. In this role, she actively participated in the implementation of the Good Manufacturing Practice Roadmap by the pharmaceutical manufacturers in Ghana.

Dr Owusu-Asante's has conducted studies to evaluate the regulatory review system in the Economic Community of West African States with a view to contributing to the operationalisation of the African Medicines Agency. She has published her research findings in peer-reviewed journals and presented them at international conferences.

Dr. Owusu-Asante has facilitated training workshops for the WHO prequalification of medicines programme.

Dr Owusu-Asante's overarching goal is to ensure Ghana, and the West African region have readily available access to safe, quality, and efficacious medicines to meet the health needs of their citizens. Dr Owusu-Asante aims to collaborate with relevant public health professionals to make accessible medicines for all, a reality, for a healthy West Africa.



Professor Sam Salek
BSc PhD RPh FFPM GFMD FRPS FESCP MCMS

Sam Salek is Professor of Pharmacoepidemiology in the School of Life and Medical Sciences, University of Hertfordshire, UK where he leads the Public Health & Patient Safety research group. He is also the Director of the Institute of Medicine Development, Cardiff, UK, a visiting Professor at the State of Hessen, Germany and Vice-President of the PharmaTrain Federation. Professor Salek is the co-founder and the past chair of the Patient Engagement Special Interest Group of the International Society of Quality of Research, co-chairs the European Hematology Association Scientific Working Group for Quality of Life and Symptoms and chairs the EHA SWG 'Gaucher's Disease Task Force'.

Professor Salek completed his undergraduate degree at the University of Oklahoma in 1978. He later moved to Cardiff where he studied for his PhD, 1985–1989. Since completing his PhD, Professor Salek has held a number of academic posts on both sides of the Atlantic. His major research interests include: pharmaceutical regulatory science to improve patient access to new medicines; benefit-risk assessment of medicines; development, evaluation and application of instruments to assess patient-reported outcomes and health-related quality of life (HRQoL); and pharmacoeconomics/ health economics. Over the past four decades he has received a number of government and industry research grants for projects in the areas of pharmaceutical regulatory science covering jurisdictions such as Middle East, Far East, Africa, India, South and North America.

Professor Salek has developed a few undergraduate, postgraduate diploma and MSc programmes over the past 35 years which they continue to be successful. Of noteworthy: he developed and modernised the 2-year part-time Postgraduate Course in Pharmaceutical Medicine (Dip Pharm Med) and was the Course Director of the same for 30 years; he is the founder of the MSc in International Pharmaeconomic & Health Economics in 2007 and was the Programme Director of the same until 2015; he is the founder of the Integrated Master of Regulatory Science (an undergraduate programme) which received approval from the University of Hertfordshire Validation Board in April 2017 and commenced in September 2018.

Professor Salek is a fellow of the Royal College of Physicians, the Royal Pharmaceutical Society of Great Britain, European Society of Clinical Pharmacy, Global Fellow of

the IFAPP in Medicines Development and member of the Cardiff Medical Society. He is a member of five Editorial boards and has published 19 books and over 650 journal articles and abstracts. He has developed and validated 11 general and disease-specific patient-reported HRQoL measures, a quality decision making tool (QoDoS), a quality outpatient discharge information checklist, whilst also collaborating with the pharmaceutical industry to design HRQoL protocols for clinical trials. Increasingly, Professor Salek is shifting his emphasis towards the practical applications of HRQoL measures in clinical decision-making and policy, quality decision-making and patient engagement in research as partners/collaborators.

Professor Stuart Walker
BSc PhD (Lond) MFPM FRSC FIBiol. FRCPath

Professor Stuart Walker is an Independent Consultant in Pharmaceutical Medicine and Founder of both CMR International & the Centre for Innovation in Regulatory Science. For thirty-five years he held the position of Professor of Pharmaceutical Medicine, School of Pharmacy & Pharmaceutical Sciences, Cardiff University,Wales, but now is Professor of Regulatory Science, University of Hertfordshire, Hatfield, UK. He is also a Fellow of the School of Pharmacy, London University, Academic Regulatory Expert, Center of Regulatory Excellence, Singapore and Honorary Professor, University of Witwatersrand, South Africa. Professor Walker spent ten years at London University, which included lectureships in biochemical pharmacology at St Mary's Hospital Medical School and Clinical Pharmacology at the Cardiothoracic Institute. This was followed by eight years with Glaxo Group Research in the UK where he had international responsibility for several major clinical research programmes.

Current research interests include studies to improve productivity, efficiency and decision-making in global drug development and the regulatory review process. In addition he has been involved in Good Review Practices in the Regulatory Environment in the Developing Markets of the Asia-Pacific Region, Latin America, Africa & the Middle East, including the Benefit Risk Assessment & Quality Decision making Practices as well as public policy issues that relate to these research activities. During his research career, Professor Walker has supervised forty PhD programmes, co-authored over 400 research papers and co-edited more than thirty books in the fields of toxicology, drug discovery, clinical development, regulatory policies, the Benefit/ Risk Assessment of Medicines and more recently Quality Decision-Making Practices.

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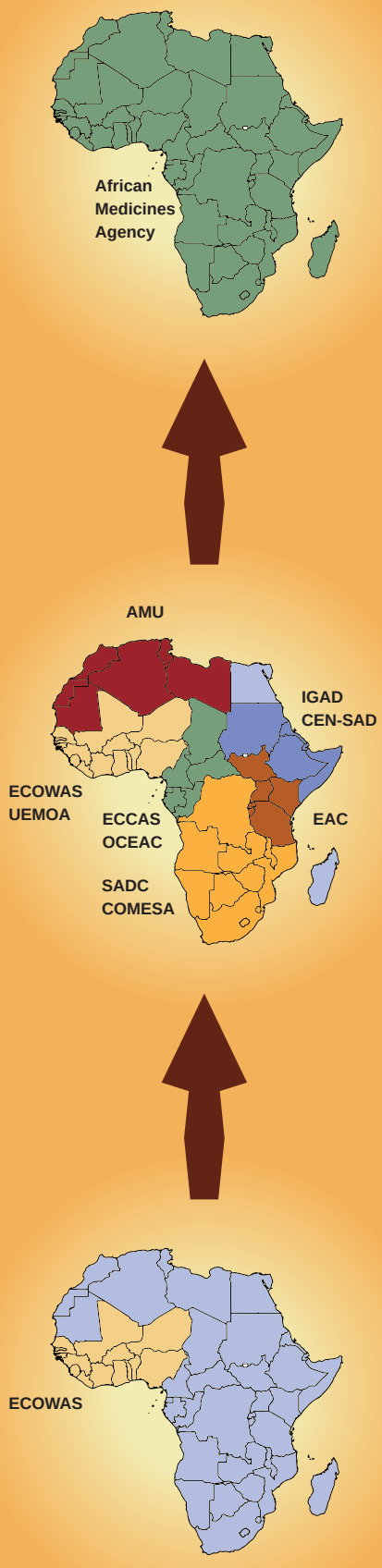
Professor Walker has been a member of a number of academic, professional and industrial committees as well as the editorial boards of several scientific journals. He was given the "Drug Information Association" Outstanding Service Award in 2001 and received a Lifetime Achievement Award from Informa in the same year & the TOPRA lifetime achievement award in 2011. He is frequently involved in the organisation of national and international meetings on key issues that concern the pharmaceutical industry and the Regulatory Review and has lectured extensively throughout Europe, the United States, Japan and the Asia-Pacific Region, Latin America as well as Africa & the Middle East.

The Current Regulatory Environment in Africa and the Future Role of the African Medicines Agency: Contribution of the ECOWAS Region

Mercy Acquaye Owusu-Asante
Sam Salek
Stuart Walker



The African Medicines Agency is a key African institution established by treaty to enhance the regulation of medical products in Africa. One of its key aims is the promotion and strengthening of medicines regulatory harmonisation across Africa. It will do so by coordinating ongoing regulatory harmonisation initiatives, building capacity amongst member states and by sharing best practices.

This book therefore provides timely expert information for consideration and possible adoption during the operationalisation of the AMA. This book is a must-read for all those with an interest in medicines regulation in Africa.

Dr Delese Mimi Darko
Director General
African Medicines Agency