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Medicines Regulation in West Africa: Current State and Opportunities

O. Sopein-Mann¹, Z. Ekeocha², S. Byrn³, K. Clase⁴

ABSTRACT

Ndomondo-Sigonda et al. (2017) observed that there is scarcity of information on human resources (personnel devoted to regulation of medicines) in the domain of medicines regulation in the sub-Saharan Africa (SSA). The published information on medicines regulation by the National Medicines Regulatory Authorities (NMRAs) in the Economic Community of West African States (ECOWAS) region are no longer current and consistent with the current realities in the NMRAs. In order to reveal this occurrence, show the trends that exist over the years and make appropriate recommendations, data were collected and compared from 2005, 2010 and 2017 research reports on seven regulatory features of the fifteen Members States of ECOWAS. The results show that there was missing information per regulatory feature and country. There was also an overall increasing trend in the number of NMRAs in the region that showed progress with respect to the measured regulatory features - Autonomy (Authority and Legal form), Marketing Authorization, GMP inspection, Quality Control, Quality Management System, Information Management System and Harmonization and International cooperation. People of Africa have a valuable story to tell as it relates to medicines regulation. This report is written by a West African from the perspective of a West African involved in the study and practice of medicines regulation by the NMRAs in the ECOWAS.

Keywords: medicines, regulation, marketing authorization, Good Manufacturing Practice (GMP), National Medicines Regulatory Authorities (NMRAs); Economic Community of West African States (ECOWAS), West African Health Organization (WAHO), West African Medicines Regulatory Harmonization (WA-MRH)

1. INTRODUCTION

Early History on the Basis of Medicines Regulation

Griffin (2004) narrates the history of the foundation of modern medicines regulation, which started with Mythriddatum and the related product Theriac as the universal panacea in the second century BC and first century AD, respectively. These two products were thought to be effective for all illnesses, but if they did not work as expected, bad quality ingredients and poor manufacturing were blamed. This, then, called for the need to ensure quality of the ingredients, establish standard formulation for these products and ensure competence of the manufacturers.

For this reason, Mythriddatum and Theriac were produced in the public space as it was generally accepted that failure was due to the probable misdemeanor of the manufacturers (pharmacists) (Griffin, 2004). However, in 1745, doubts arose regarding their efficacy and safety due to possible interactions among the ingredients used. By 1746, the products were removed from London Pharmacopoeia; and in 1799, a decree was enacted to convene a group of elite physicians who examined all products before they were released to the public.

From 1540, one of the earliest laws on drug control was established, which permitted the inspection of the premises and wares of the apothecaries; and to bring upon them appropriate sanctions if found guilty of

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non-compliance (Griffin, (2004). The statute specifically permitted the appointment of inspectors, inspection of the apothecaries' stores, destruction of defective and corrupt wares and drugs not suitable for human consumption and charging of higher fees when inspections were excused or refused.

In order to control the quality and standard of mythridatum and theriac, an official and obligatory document was produced called pharmacopoeia, derived from two Greek words, *pharmakon* (drugs) and *poiia* (making). The first pharmacopoeia in Europe was published for the apothecaries in Florence in 1498 and, subsequently, in other cities such as Barcelona in 1535, Nuremberg in 1546 and London (*pharmacopoeia Londinensis*) in 1618 (Griffin, 2004).

The Pharmacopoeia helped establish the standard formulation of mythridatum and theriac which made inspection easier and lifted the limit of the manufacture of the products by one apothecary. During the London plague of 1650, three apothecaries were approved to manufacture mythridatum and theriac in London (Griffin, 2004).

The Food and Drug Legislation came into existence in 1872 and eradicated all of the existing laws and statutes which had allowed the *Censors of the College of Physicians* and *Wardens of the Worshipful Society of Apothecaries* to carry out their activities to serve as the basis of modern day medicines regulation (Griffin, 2004). Mythridatum and Theriac were the motivation for medicines regulation, being the first medicines to be challenged on the bases of efficacy and drug interaction (Griffin, 2004).

Griffin (2004) also stated that the *Medical and Physical Journal*, in 1799, proposed that no product should be advertised and sold to the public without the examination, analysis and declaration of quality by the college of physicians. This is 170 years before the Medicines Act of 1968 in the United States of America.

Rago and Santoso (2008), cited that the history of regulation of medicines dated as far back as 1540 and the history of pharmacopeia in Europe can be traced to the 16th century. However, the accelerated evolution of regulation of medicines came about by some unfortunate events, such as the poisoning by diethylene glycol, where hundreds lost their lives after taking the contaminated mixture and the thalidomide disaster in Europe, where thousands of babies were born deformed, (Rago & Santoso, 2008). After the Thalidomide disaster, several directives (65/65/EEC), laws, regulations and administrative actions arose. Acts in Europe and in the United States of America on regulation of medicines, requirements on current Good Manufacturing Practices (CGMP) and official registration of drug establishments in the USA also came into existence (Rago & Santoso, 2008).

1930 - United States Food and Drug Administration (USFDA) The history of medicines regulation in the United States of America is similar to the UK and Europe. An event in 1906 led to a law which prohibited misbranded and adulterated foods, drinks and drugs in interstate commerce. The law was enforced by the Bureau of Chemistry in the Department of Agriculture, which later became the Food and Drug Administration in 1930. In 1938 the Federal Food, Drug and Cosmetic (FD&C) Act created new provisions for manufacturers to demonstrate that a drug was safe before it could be marketed (USFDA, n.d.). The laws of the United States of America were improved, as occasions demanded. The latest law came in 2003, when an authority under the Pediatric Research Equity Act was granted to the FDA to require sponsors to conduct clinical research for new drugs in pediatric drug applications (USFDA, n.d.).

Ten years after the Council Directive 65/65/EEC in Europe, the idea of harmonization was introduced. The Mutual Recognition Procedure began in 1975 and the Central Procedure, in 1987, to ensure a common market for medicines in Europe (Rago & Santoso, 2008).

Simultaneously, harmonization was expanding beyond Europe. Collaboration started during a discussion among officials from Japan, the European Union and the United States of America during the International Conference of Drug Regulatory Authorities (ICDRA), organized by the World Health Organization (WHO) in 1989. These discussions established the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) in Paris in 1990 (Rago & Santoso, 2008), where dossiers of new and innovative medicines would be evaluated to ensure quick access to the people who needed them most.

Since it is mostly generic medicines that flood many low- and medium-income countries (LMIC), the World Health Organization (WHO) played a supportive role in national, regional, inter-regional and international harmonization to ensure a fast-reaching, international consensus on quality, safety and efficacy standards in order to accelerate entry into the market of quality new and generic medicines.

2003 – The Establishment of the UK Medicines and Healthcare Products Regulatory Agency (MHRA)

According to Breckenridge (2004), the Medicines and Healthcare Products Regulatory Agency (MHRA) was established in the United Kingdom by the merger of the Medicines Control Agency (MCA), which was in

charge of the medicines regulation, and the Medical Devices Agency (MDA), which regulated and controlled the Medical Devices. This merger forced the UK to join the League of Nations with the USA and Europe, where both medicines and medical devices are housed under one organization. The functions of the two erstwhile Agencies (MCA and MDA), became the scientific and organizational reasons behind the formation of MHRA in the UK as well as highlighted the possible challenges it would face.

Some of the organizational challenges, faced by the MHRA, mentioned by Breckenridge (2004), were premised on the co-location of the two agencies, as they were located in different sites. Co-location was necessary to unify an organization, to ensure compatibility of the Information Technology (IT) systems of the two organizations and to address the cultural and scientific challenges of bringing together large and small organizations with different backgrounds. Additional challenges were the need for MHRA to ensure a proactive and effective communication with both stakeholders (patients, healthcare professionals, industries and government) and staff. There was the need to work more closely with other newly established agencies in the UK, whose responsibilities considerably overlap with MHRA. As new countries joined the EU, the need grew for MHRA to provide support for the then London-based EMEA. The EMEA helped new countries build their regulatory medicines and medical devices capacities. It also worked with the EU to ensure that a uniform standard of approval existed across Europe for the new Notified Bodies in the EU that approved medical devices for UK market (Breckenridge, 2004).

The scientific challenges MHRA faced at that time were: tissue engineering and its regulation, which require the combination of human-derived cells; mechanical support and molecular signaling processes (pharmacology and medical devices) for the treatment of individual patients; pharmacogenetics in medicines. In addition, MHRA faced the challenge of increased pressure to have a high percentage of adverse reaction reports in its database, while carrying out exhaustive and effective Post Market Surveillance (PMS) in order to ensure patient safety. The MCA had been criticized for not having exhaustive listings of adverse reactions. MHRA now strives to capture quality rather than quantity of adverse reaction reports.

2005 - Medicines Regulation in Africa

The first plan 'Mother plan' for medicines regulation in Africa was developed in 2005 during the 1st African Medicines Regulatory Authorities Conference (AMRAC) that was held in Addis Ababa, Ethiopia and was documented as a WHO/AFRO's final report of the medicines regulation cross-sectional view in Africa in

2005. It became the Strategic Plan from 2006-2010, which identified the existing problems of regulation of medicines in 2005 in Africa. It also suggested the strategic approach/interventions and activities needed to be implemented in order to facilitate the required growth of medicines regulation in Africa.

The regulatory landscape was characterized by the following, among others: ineffective licensing system, weak product registration, poor inspection practices, inadequate access to quality control laboratories, inadequate market control, non-existence of pharmacovigilance and control of promotion, lack of clinical trials oversight, inadequate communication and information exchange system, lack of transparency and accountability and conflict of interest. According to the final report, of the 46 sub-Saharan African countries, 7% of the National Medicines Regulatory Authorities (NMRA) had moderately developed medicine regulatory capacity, 63% had minimal capacities, while 30% did not have an NMRA in place. These problems were not improving much despite the efforts of WHO, or other international organizations and donor communities, because of the absence of government support, lack of adequate number of trained and qualified staff, high staff turn-over due to low salaries and lack of incentives, inadequate and unsustainable funding of the NMRAs and weak infrastructure (World Health Organisation, 2005).

In order to solve the problems, the 1st African Medicines Regulatory Authorities Conference (AMRAC) convened representatives from the National Medicines Agencies, regional blocks in the sub-Sahara Africa and members of harmonization initiatives such as ICH, CEAC and SADC. After extensive presentation of the situation and group discussion, the group documented the strength, probable weakness and recommendations, which led to a five-year plan towards improving the scenario. Some of the weaknesses highlighted during the meeting were:

- weak Medicines Regulatory Authorities (MRAs) with limited human and financial resources;
- parallel and overlapping harmonization initiatives;
- lack of structures to coordinate harmonization initiatives, e.g. secretariat;
- inadequate exchange of information and experiences;
- lack of a common understanding of the true meaning and vision/goals of harmonization;
- lack of political commitment;

- lack of commitment from MRAs;
- lack of sustainable funding.

The recommended steps to carry out harmonization were:

- build trust and commitment among technical people towards harmonization;
- secure political commitment and support;
- carry out situation analysis and identify gaps;
- define the vision and goals of harmonization;
- set up administrative structures/secretariat;
- develop common strategies;
- develop common technical requirements, standard, guidelines, procedures;
- update legislations;
- exchange information.

2008: A Call for More Effective Regulatory System in Nigeria, West Africa

Akuse et al. (2012) reported the unfortunate incident which occurred in Nigeria between October and November 2008, where children suffered Acute Kidney Injury (AKI), and eventually died, due to ingestion of a particular type of “teething mixture” containing paracetamol and diphenhydramine that was contaminated with Diethylene Glycol (DEG). Similar incidents occurred in Nigeria in 1999 and in other countries, such as Bangladesh, India, Haiti, Panama, South Africa and the United States of America.

Akuse et al. (2012) carried out a multicenter study where information from hospital records was obtained to review the clinicopathological features of all children with AKI over a six-month period. The study focused on discovering other means of promptly diagnosing and differentiating children who had Acute Kidney Injury (AKI) due to ingestion of Diethylene Glycol (DEG) from those who did not in a resource-constrained environment such as Nigeria.

The results of the study showed that differentiating AKI caused by ingestion of DEG was difficult, and that obtaining detailed drug intake history and improved facilities for hemodialysis for infants, among others, would assist such differentiation. The authors affirmed that prevention of future occurrences would require improved manufacturing practices, effective field drug testing and international monitoring of raw materials imported for pharmaceutical manufacturing, which are

all necessary for effective regulatory systems and structures.

2009-2010, the World Health Organization

The World Health Organization (WHO) carried out a rapid assessment in 2009-2010 which provided insights into the state of medicines regulation in sub-Saharan Africa. The assessment was done on 26 countries: eleven in the East Africa, eight in West Africa, two from South Africa and five countries from Central Africa (WHO, 2010).

The study measured nine core regulatory functions of National Medicines Regulatory Authorities against the background of each countries geographical, socio-economic and pharmaceutical indicators (WHO, 2010). The nine functions that were assessed were the structure and implementation of regulatory function, marketing authorization, licensing activities, import control, inspections, quality control, market surveillance and control of clinical trials.

In each of these core regulatory functions, several sub components were examined. For example, under the assessment of the Marketing Authorization, the following components were assessed in order to identify the gaps:

- the existence of the legal basis to authorize medicines for the market;
- existence of guidance for applicants;
- standard operating procedures (SOPs) for assessment;
- existence of advisory committee;
- existence of external assessors;
- full time assessors;
- Secure filing space;
- computerized system;
- existence of list of approved products including Summary of Products Characteristics (SmPC);
- recognition of stringent regulatory authorities' decisions (WHO, 2010).

According to the report (WHO, 2010), 55% of the eleven countries studies in Eastern Africa had existing legal basis, 27% had inadequate legal basis, and the remaining 9% did not have a legal basis to carry out marketing authorization of medicines. Only 9% had detailed guidance for applicants with respect to information on format and content of submission requirements. 36% had no SOP for assessment of medicines dossiers, 9% had written SOPs, while the remaining countries had SOPs that were either not adequate or very limited.

Regarding the existence of the Advisory Committee for Marketing Authorization, 27% of the East African countries had an operational advisory committee, where 45% had an advisory committee that was either non-operational or non-existent. Advisory committees of the remaining countries were either just a technical committee without the correct expertise and did not have the capacity to review the medicines dossiers. With respect to the existence of external assessors, 45% had no external assessors, 18% had external assessors, while 27% either had no external assessors due to lack of funding, or they were limited in capacity.

As per the existence of full-time assessors, 82% of the countries had an insufficient number. With respect to secure filing space, it was inadequate in 91% of the countries. With respect to existence of a computerized system, 36% had none, 55% had either the WHO Model System for Computer-assisted Drug Registration (SIAMED) in combination with other databases or stand-alone databases, while 9% had not established a regulatory system. Regarding the list of approved products, including SmPC, 91% of the countries had this list in their systems, but were not updated, published and did not include the SmPC. 9% of the countries were marked 'not applicable' because their regulatory system did not exist. 45% of the countries did not recognize decisions of stringent regulatory NRAs. 9% recognized the decisions of US-FDA, WHO PQ and EU, while 18% either required or reviewed the Certificate of Pharmaceutical Product (CPP).

The report (WHO, 2010) also had information on how the eight countries in West Africa fared:

- 50% had adequate legal basis to carry out marketing authorization.
- 100% had inadequate guidance for the applicants.
- 100% had inadequate SOPs for assessment.
- 75% had an Advisory Committee.
- 88% of the countries had external assessors.
- All of the countries had insufficient full-time assessors.
- All of them also had inadequate secure filing space.
- 88% had SIAMED and/or internally networked database or standalone Excel sheets.
- 75% had a list of approved products, but were not published or updated.
- None had the SmPC attached to the list of approved products.

- 63% of the countries did not have a system of recognition of the decision of stringent regulatory authorities.
- 13% requested the CPP.

In Southern Africa, where only two countries were assessed, both had adequate legal basis, one had adequate guidance for applicants, the other had no SOP for assessment. Both countries had Expert Committee or the Advisory Committee, both of the countries had adequate qualified external assessors but the full-time assessors were insufficient. Only one of the countries had secured filing space and a standalone database instead of the required computerized system of filing. In regards to the list of approved products with SPC, both had a list either outdated or without the SPC and both of the countries either recognized the decision of stringent regulatory authorities or requested decisions from other NMRAs.

In Central Africa, five countries were assessed. 60% of the countries had adequate legal basis to carry out Marketing Authorization; 20% had outdated and undetailed guidance for the applicant, 20% had no guidance. 60% had no SOPs for assessment, 20% had validated SOPs, while 20% had inadequate SOPs, with only administrative documents. In 80% of the countries, an advisory committee existed either unofficially or not specific to Market Authorization. 60% had no external assessors and 80% had insufficient full-time assessors. None of the five had an adequately secured filing space and only 40% had the computerized system called SIAMED. The remaining countries had none or other types, which are not optimal. Regarding the list of approved products, which included the SPC, only 20% had the list but did not include the SPC. In respect to the countries that recognize decisions of stringent regulatory authorities, only 40% requested the CPP.

2014, World Health Assembly 67.20

On May 24, 2014, the sixty-seventh World Health Assembly (WHA 67.20), Agenda 15.6, which was on Regulatory System Strengthening for medical products, related with the 2005 Mother Plan on medicines regulation. The highlights and recommendations of the resolution were geared towards the various roles that WHO/AFRO and WHO international could play to fulfill the elements of the plan, which only they could fulfill. The resolution highlighted certain points which accentuated the stance of the World Health Organization to play a pivotal role in support of the establishment and sustainability of an effective regulatory system in developing countries to ensure quality, safe and efficacious medical products that will strengthen

the health systems and outcomes (WHO, 2015).

The resolution linked effective regulation to implementation of universal health coverage, achievement of the Millennium Development Goals 4, reduction of child Mortality, goal 5, Improvement of maternal health) and goal 6, Combating HIV/AIDS, malaria and other diseases. These goals are now Sustainable Development Goal (SDG) 3 (WHO, 2015) (UNDP, n.d.). The resolution also linked effective regulation to the impact of compromised quality, safety and efficacy of medical products on treatment failure, drug resistance, death and reduction of public trust on the health system. The role of WHO's prequalification to procurement, contributions of the investment of good proportion of national budgets, and global initiatives on quality, safe and efficacious medicines were mentioned (WHO, 2015).

Concluding the World Health Assembly (WHA) 67.20 Resolution, the recommendations to Members State, WHO and other stakeholders were in favour of the fulfilment of the 2005 Strategic Plan. Some of the recommendations included:

- assessment of regulatory capacity of the NMRAs using WHO benchmarking tools;
- collaboration of the national NMRAs to form regional blocs that will move towards regulatory convergence and transparency in decision-making;
- development of strong legal basis and political direction to support regulatory systems;
- pooling together of resources, regulatory experts, adopting/adapting already developed technical guidelines and guidance;
- strengthening of regulatory system as a component of expansion of local and regional production of quality, safe and efficacious medicines (WHO, 2015).

2018 Report of IGAD – Inter-Governmental Authority on Development

The Inter-Governmental Authority on Development (IGAD) is one of the Regional Economic Blocs (REC) in Africa, situated in the horn of Africa comprising Djibouti, Ethiopia, Eritrea, Kenya, Somalia, Sudan, South Sudan and Uganda (Adan & Toroitich, 2018). With respect to the Strategic Plan of the AMRAC in 2005, IGAD seems to have made progress in some areas of medicines regulation, but due to challenges highlighted by Adan and Toroitich (2018), there is still much to be done. Some achievements that were mentioned include but not limited to:

- IGAD Member States working together to establish regional cross-border health policies and sector specific strategies on RMNCHN, MRH, TB and HIV;
- MRH Workplan for 2019,
- established Technical Working Groups on Medicines, Pharmacovigilance and Information Management System (IMS),
- prepared draft technical documents on IGAD dossier submission,
- IGAD Marketing Authorization, procedure of Joint Assessment of medicines dossier in IGAD's region and Quality Guidelines.

From the report of Adan and Toroitich (2018), as in other RECs in Africa, the level of medicines regulation in IGAD seemed to be characterized with varied regulatory capacity in the Member States, where medicines regulation was still domiciled in a department under the Ministry of Health (non-autonomous NMRAs). WHO Collaborative Registration Procedure (CRP) was functional in some countries in the region. Junior assessors were trained on medicines dossier assessment. According to Adan and Toroitich (2018), IGAD was not able to implement their MRH activities due to challenges which included inadequate technical and human resources funds. Adan and Toroitich (2018) solicited for equal strengthening and handling of the RECs in Africa in order to fulfill the vision of the AMRH program and AMA.

Industry Perspective of East African Community (EAC) MRH in 2019

After 2005, the SSA countries started earnestly implementing the recommendations from the AMRAC and, by 2009, the African Medicines Regulatory Harmonization (AMRH) agreed to develop regional platforms with harmonized regulatory procedures for the registration of medicines. EAC region started first in 2012 and six years later, by 2018, a study by Storehagen et al. (2019) was conducted to evaluate the industrial perceptions of medicines regulatory harmonization in the East African Community (EAC).

The pharmaceutical industry, though favourably disposed to the medicines regulatory harmonization, still had their reservations regarding the harmonization initiative because of the length of time it took to receive the actual marketing authorization. The challenges included getting all EAC countries to recognize EAC approvals, unexpectedly higher quality standards compared to national procedures, smaller, less attractive markets not appealing from a corporate perspective and the absence of free trade of pharmaceuticals in the EAC region despite the existing EAC Free Trade

Agreement, which officially launched the free movement of goods and services in 2010.

The Storehagen study was a semi-structured interview with document reviews. The main target group for the interviews was pharmaceutical companies (18 companies, including 64% of the total companies who had experienced the EAC joint product assessment procedure, and two EAC-based national medicines regulatory authorities). Although harmonization had been thought to be one of the solutions to modern regulation, the study showed that harmonization must be handled appropriately with all factors correctly mixed before success can be achieved. The method used in the study was effectively able to assess the EAC harmonization. Results showed that improvements were required in order for the current EAC processes to meet the vision of harmonization. Harmonization will result in quicker access to the harmonized markets for quality-assured medicines (Storehagen et al., 2019).

WHO Regulatory Support

The World Health Organization (WHO) offers support with respect to medicines regulation using three approaches:

- development of international norms, standards and guidelines;
- offering of guidance and technical assistance;
- training and collaboration with NMRAs, development organizations, and other UN agencies.

Specifically, WHO assesses the NMRAs, provides guidelines, guidance and manuals, provides training opportunities on model computerized registration system (SIAMED), model web-site, WHO prequalification of medicines moving in international commerce, international cooperation and harmonization and during International Conference of Drug Regulatory Authorities (World Health Organization, 2019).

WHO recognizes the sovereignty of countries' NMRAs to regulate and control. According to WHO (2019), expectation of NMRAs structure and functions:

Solid legal basis, realistic objectives, appropriate organizational structure, adequate number of qualified staff, sustainable financing, access to up-to-date evidence based technical literature, equipment and information, capacity to exert effective market control. MRAs must be accountable to both

the government and the public and their decision-making processes should be transparent. Monitoring and evaluation mechanisms should be built into the regulatory system to assess attainment of established objectives (p. 1).

All of the regulatory support provided by WHO is to ensure effective regulation. Effective regulation involves the following among others: ensuring quality, safety and efficacy of medicines, good manufacturing practice, distribution, storage of medicines, ensuring rational use of medicines by patients and prescribers, enforcement, detection of illegal manufacturing, adequate sanction, fair promotion and advertisement that is geared towards allowing rational use of medicines and observing Good Regulatory Practice (World Health Organization, 2019).

EAC-MRH

The East Africa Community Medicines Regulatory Harmonization (EAC-MRH) Project is the first regional bloc MRH of the African Medicines Regulatory Harmonization Program and Global Medicines Regulatory Harmonization Initiative sponsored by technical and financial partners – AUDA-NEPAD, WHO, World Bank and the BMGF (BCG, 2017). The EAC Secretariat, together with the NMRAs of the Partner State of EAC, took this initiative in order to ensure availability of quality, safe and efficacious medicines.

Some of the successes recorded at the end of five years of EAC MRH Project were the development of harmonized requirements – guidelines, guidance, manuals and SOPs. The Joint Assessment procedure approved nine medicines out of 45 applications that were filed. The median months for obtaining Marketing Authorization was reduced to eight months from 14. Some of the things that were not achieved within the five years included harmonization of the IMS, meeting of the procedure timelines for the Joint Assessment and Good Manufacturing Practice (GMP) (BCG, 2017). After its assessment, the EAC MRH received recommendations for another five years (2018-2022), in which in short term, it would be required to continue the MRH for another 6 months, medium term, prove the sustainability and value addition of the MRH for 18 months and in the long term, establish a semi-autonomous East Africa Healthcare Products Agency – EAHCPA and mutual agreement among the NMRAs before the end of 36 months (BCG, 2017).

SADC – ZAZIBONA

The ZaZiBoNa, meaning Zambia, Zimbabwe, Botswana and Namibia, in the Southern African Development Community (SADC) region was initiated in 2013 to jointly assess medicine dossiers submitted in these countries. The ZaZiBoNa approach reduced the median timeline from dossier submissions to national Marketing Authorization to eight months, through Collaborative Registration Procedure (CRP) (Ndomondo-Sigonda et al., 2017). At its 12th Session reported in the NEPAD newsletter, six out of 13 dossiers assessed were recommended for approval (NEPAD, 2016).

ECOWAS

The Economic Community of West African States (ECOWAS) is the regional body of the fifteen countries in West Africa (Benin, Burkina Faso, Cabo Verde, Cote d'Ivoire, Ghana, Guinea, Guinea Bissau, Liberia, Mali, Niger, Nigeria, Senegal, Sierra Leone, the Gambia and Togo) (ECOWAS, n.d.) to promote economic integration. It was established on May 25, 1978 by a treaty, termed – Lagos Treaty (ECOWAS, n.d.). The integrated economic activities, as envisaged, revolved around, but were not limited to industry, transport, telecommunications, energy, agriculture, natural resources, commerce, monetary and financial issues, and social as well as cultural matters (ECOWAS, n.d.). Among the specialized Agencies of ECOWAS was the West African Health Organization (WAHO).

WAHO

WAHO was created by the Protocol A/P2/7/87 on July 9, 1987 and signed in Abuja, Nigeria by the Heads of State and government to ensure coordination of regional health interventions within the ECOWAS region (WAHO, n.d.-a, n.d.-b; West African Health Organization, n.d.). Aligning with the desire of the ECOWAS Government to move from being a 'Community of State' to a 'Community of the People' by 2020, WAHO made every effort to produce high impact and cost-effective health interventions that would be felt by members of ECOWAS community and international community as proactive regional health integration instrument (IWAHO, n.d.). According to West African Health Organization, the new Thematic Areas that they were focusing on in the time of recurring epidemics and scarcity of resources included:

1. maternal, child & adolescent health quality standards & centres of excellence
2. pharmaceuticals (medicines & vaccines)
3. prevention & control of communicable and non-communicable diseases)

4. health Information

WAHO also ensured capacity building, youth development, strengthened networks and sustainability during the implementation of any of the thematic areas (WAHO, n.d.).

The big picture of pharmaceuticals (medicines, vaccines and other health products), their manufacture, regulation and key related activities for 2014-2019 were described in the ECOWAS Regional Pharmaceutical Plan (ERPP). This was the consolidated approach (Ossei-Yeboah-Agyeman, 2017) that had been accepted by the international community, Assembly of Health Ministers, Heads of State and Government of ECOWAS Member State (Ossei-Yeboah-Agyeman, 2017).

ECOWAS Regional Pharmaceutical Plan ERPP 2016-2020

The ERPP (ECOWAS, 2014) had eight objectives (Ossei-Yeboah-Agyeman, 2017), which were the following:

- i. strengthen the National Medicines Regulatory Authorities (NMRAs) regulatory capacity and quality infrastructure in the ECOWAS region to achieve International Certification and designation as Regional Centers of Excellence by the year 2018;
- ii. strengthen local production of pharmaceuticals in the region;
- iii. improve and strengthen the governance of the pharmaceutical systems;
- iv. promote and support competitive and efficient regional pharmaceutical manufacturing to ensure the supply of essential medicines produced in the region; support provision to pharmaceutical manufacturing in order to achieve international certification;
- v. reduce incidence of Substandard and Falsified (SF) medical products in the ECOWAS region by 75%;
- vi. establish of a regional medicines regulatory Agency;
- vii. facilitate of the incorporation of ECOWAS policies on TRIPs flexibilities into national laws;
- viii. formulation and implementation of policies that will promote innovation, research and development into pharmaceuticals and medicinal products within the ECOWAS region as

well as establish a competitive grant in the ECOWAS region (WAHO, 2014).

NMRAs in ECOWAS

There were National Medicines Regulatory Authorities (NMRAs) in each of the 15 Member States of ECOWAS. They were, however, different in functionality and system due to their economic and political heritages. Prior to coming together under the West African Medicines Regulatory Harmonization initiative, the eight French countries had regulatory systems similar to that of France, the five English countries had a different system to that and two Portuguese speaking countries had a different system. These were all at different levels of development in terms of autonomy, governance, system and structure.

However, in 2014, with the support of the technical and financial partners such as the New Partnership for Africa's Development (NEPAD), World Health Organization, World Bank, Bill and Melinda Gates Foundation, the two main regional bodies in West Africa (*Union Economie Monetaire Ouest African [UEMOA]* and West African Health Organization under the leadership of the ECOWAS), came together to integrate their medicines regulation harmonization systems and made it more efficient because they agreed to establish the West African Medicines Regulatory Harmonization (WA-MRH) Project. Also established were a Steering Committee comprising the heads of the 15 NMRAs, to provide direction and the Experts Working Groups which were to provide technical assistance and help develop technical documents in the seven major regulatory domains (Ossei-Yeboah-Agyeman, 2017; World Bank, 2012).

Regulatory Functions of the NMRAs in ECOWAS from data obtained from 2005, 2010 and 2017 reports

i. Authority and Legal Forms of the NMRAs

Ndomondo-Sigonda et al. (2017) reported 53 out of 54 countries in the sub-Saharan Africa had NMRAs or administrative entities that carried out some form of regulatory functions. Some were semi-autonomous, meaning they have some levels of independence from the Ministry of Health (MoH) in carrying out their regulatory functions; while others are Departments in the Ministries of Health. The mandate of some NMRAs covered medicines, food, medical devices or cosmetics, while others were medicines and medical devices only. The funding of the NMRAs varied – some were fully funded by the government and therefore, required to remit all revenue generated to the single government treasury; others were permitted by the government to retain some percentage of revenue

generated for day-to-day running of the organization (Ndomondo-Sigonda et al., 2017).

In most of those NMRAs that were departments in the Ministry of Health, the core regulatory functions expected of an NMRA were usually carried out by different departments in or out of the Ministry of Health. In West Africa, there were examples of the semi-autonomous and non-autonomous NMRAs, with core regulatory functions being carried out by several departments of the Ministry of Health. However, throughout the years, there was greater awareness among the government of ECOWAS Members State to grant autonomy or semi-autonomous status to their NMRAs and the increasing number of NMRAs were gradually moving towards becoming an Agency (WAHO, 2018).

ii. Marketing Authorization

The process of registration of medicines (Marketing Authorization) was considered one of the core regulatory functions of NMRAs (Ndomondo-Sigonda et al., 2017; WHO, 2010). WHO's report presented the results of the assessments of regulatory systems of 26 sub-Saharan African countries (24 belonging to the WHO AFRO region of which eight NMRAs were of the West Africa region, six French speaking and two were English speaking) over the last eight years, to identify regulatory gaps and suggest priority activities to strengthen regulatory capacity (WHO, 2010). The report recognized that NMRAs must meet six major requirements in order to be able to assess applications for marketing authorization. They are:

- i. legal basis, giving the NMRA the power to grant, renew, vary, suspend and withdraw of marketing authorization;
- ii. guidelines for applicants regarding the details of technical requirements for medicines dossier to be assessed;
- iii. standardized operating procedures to assess submission, communicate and publish outcomes;
- iv. adequate expert assessors;
- v. secure storage, retrieval and exchange of data with other regulatory departments;
- vi. Mechanisms to consider the decisions of stringent NMRAs (WHO, 2010).

The scenario in West Africa gradually started to resemble the proposed structure by the WHO, especially with the support of technical and financial partners who sponsored the West African Medicines Harmonization Project. The project was officially launched in November 2017 and contributed to the

development of both regional and national capacities in the domain of medicines dossier evaluation and registration (WA-MRH-WAHO, 2017).

iii. Good Manufacturing Practice (GMP)

Good Manufacturing Practice inspection is conducted in pharmaceutical facilities to ensure that manufacturing activities carried out in such facilities were according to recognized international standards (WHO, 2010). The WHO's report of 2010 demonstrated a system to carry out inspections existed in most NMRAs that were assessed. However, this activity was not carried out by the NMRAs in some countries. Sometimes the inspection was done in conjunction with another government institution (WHO, 2010).

All member states in West Africa participated in the WA-MRH Project. The Experts Working Group on GMP established in the WA-MRH Project, developed guidelines, guidance and SOPs in accordance to WHO international GMP Guidelines. There was ongoing joint inspection, which included training among the experts and other Members State. The EAC-MRH has a similar group as the WA-MRH which developed harmonized guidelines on GMP inspection (Ndomondo-Sigonda et al., 2017).

The West African Health Organization (WAHO) working with the United Nations Industrial Development Organization (UNIDO), assessed manufacturing facilities and trained both NMRAs inspectors and manufacturers in Members State of ECOWAS. GMP roadmaps were developed for the region and nations with or without manufacturing sites. They also developed Corrective Action and Preventive Action (CAPA) for all manufacturers that were assessed (Ekeigwe, 2019).

iv. Quality Control of Medicines

The United States Pharmacopoeia (USP) worked in collaboration with AUDA-NEPAD, WAHO and other Regional blocs to establish the Network of Official Medicines Control Laboratories (NOMCOL) for laboratories within Africa and its regional blocs. WAHO, in conjunction with USP, carried out an assessment of the laboratories in West Africa and proposed recommendations that would strengthen the capacity of the laboratories in the region with respect to purchase and maintenance of laboratory equipment, training of human resource and purchase of reference standards to help with testing.

v. Quality Management Systems (QMS)

The WHO report of the rapid assessment of 26 NMRAs in sub-Saharan Africa revealed that as of 2010, none of the NMRAs had established a robust and comprehensive Quality Management System to support their regulatory functions (WHO, 2010).

According to the 2017 report of Ndomondo-Sigonda et al., the East African Community Medicines Regulatory, harmonization was able to develop harmonized guidelines on Quality Management System (QMS). The QMS of NMRAs in West Africa were assessed between 2015 and 2017 and, based on observed gaps, developed the roadmaps to be followed by each Member State to arrive at attaining ISO 9001:2015 and Pharmaceutical Inspection Cooperation Scheme (PICS) (Ossei-Yeboah-Agyeman, 2018; WAHO, 2018).

vi. Information Management System

The Information Management Systems (IMS) in the NMRAs in West Africa were upgraded since the WA-MRH Project. Harmonized guidelines and SOPs were developed. A handful of NMRAs in the West African region had functional websites where regulatory information such as registration status of medicines, licensed manufacturing sites and information were shared with relevant stakeholders. The development of some of these websites were sponsored by the WA-MRH project.

vii. Harmonization and International Cooperation

All NMRAs in West Africa were participating in the West Africa Medicines Regulatory Harmonization Project (WA-MRH), which is discussed below:

WA-MRH Project

The West African Medicines Regulatory Harmonization Project (WA-MRH) launched in November 2017 with the aim to ensure availability of quality medicines through harmonization of regulatory systems that will be effective and transparent. The WA-MRH Project had an initial focus on four domains of medicines regulation, namely: medicines evaluation and registration, Good Manufacturing Practice (GMP) Inspection, Quality Management System (QMS) and Information Management System (IMS). These focus areas were sponsored in the past, for two years, by the technical and financial partners of the umbrella program and initiative – AMRH and GMRHI (WHO, AUDA-NEPAD, World Bank, Bill and Melinda Gates Foundation, Swissmedic).

Table 1 Summary of timelines, occurrences accomplishments of each time period stated above and their significance.

	Occurrences / details of each time period	Accomplishments of each time period	Significance
Early History	a. Beginning of Regulatory Inspections and Enforcement in London.	the history of the foundation of modern medicines regulation	Beginning of medicines regulation.
	b. The Beginning of the Pharmacopoeia in Florence, Europe.	Helped establish the standard formulations of medicines and thereby lifted the limit of the manufacturers of medicines.	Standard formulations of medicines became possible, several manufacturers for one medicines became possible and regulatory inspection was established.
1540-1865	Further Development to Medicines Regulation in Europe	The accelerated evolution of regulation of medicines in Europe.	Commencement of medicines regulation in Europe.
Modern	a. United States Food and Drug Administration (USFDA) 1930-1938.	The formation of the Food and Drug Administration from Bureau of Chemistry in the Department of Agriculture; The creation of new provisions in federal Food, Drug and Cosmetic (FD&C) Act for manufacturers to demonstrate that a drug was safe before it could be marketed.	Commencement of medicines regulation in the United States of America.
	b. 1975 – Commencement of Harmonization in Europe	The idea of harmonization was introduced. The Mutual Recognition Procedure began and the Central Procedure to ensure a common market for medicines in Europe; Collaboration started among Japan, the European Union and the United States of America to yield International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) where dossiers of new and innovative medicines would be evaluated to ensure quick access to the people who needed them most.	The commencement of the Common Technical Document (CTD) used in the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH).
	c. 2003 – The Establishment of the UK Medicines and Healthcare Products Regulatory Agency (MHRA)	Establishment of the Medicines and Healthcare Products Regulatory Agency (MHRA) in the United Kingdom (UK).	The UK joined the League of Nations - USA and in Europe, where both medicines and medical devices are housed under one organization.
	d. 2005 - Medicines Regulation in Africa	Documentation of the strengths, weaknesses, opportunities and recommendations of medicines regulation in Africa and development of a five-year strategic plan for improvement.	Setting of the first set of strategies and roadmap for development of medicines regulation in Africa.

	<p>e. 2014, World Health Assembly 67.20</p>	<p>Assessment of regulatory capacity of the NMRAs using WHO Global Benchmarking Tools (WHO-GBT);</p> <p>Collaboration of the national NMRAs to form regional blocs that will move towards collaboration, regulatory convergence, and transparency in decision-making;</p> <p>Development of strong legal basis and political direction to support the regulatory systems;</p> <p>Pooling together of resources, regulatory experts, not re-inventing the wheels but adopting / adapting already developed technical guidelines and guidance;</p> <p>Strengthening of regulatory system as a component of expansion of local and regional production of quality, safe and efficacious medicines (WHO, 2015).</p>	<p>A call of the WHO to Regulatory System Strengthening for medical products.</p> <p>Highlighted the pivotal role of the World Health Organization to support of the establishment and sustainability of an effective regulatory system in developing countries.</p>
	<p>f. ECOWAS Regional Pharmaceutical Plan ERPP 2016-2020.</p>	<p>The consolidated approach for development of medicines regulation in the West Africa accepted by the ECOWAS Assembly of Health Ministers, Heads of State and Government and international community.</p> <ul style="list-style-type: none"> ix. Strengthen NMRAs regulatory capacity and quality infrastructure in the ECOWAS region to achieve International Certification and designation as Regional Centers of Excellence; x. strengthen local production of pharmaceuticals in the region; xi. improve and strengthen the governance of the pharmaceutical systems; xii. promote and support competitive and efficient regional pharmaceutical manufacturing to ensure the supply of essential medicines produced in the region; 	<p>The involvement of 15 Members States in West African Medicines Regulatory Harmonization (WAMRH) Project with the support to with the support of technical and financial partners;</p> <p>The ECOWAS harmonized Common Technical Document (CTD); Etc.</p>

		<ul style="list-style-type: none">xiii. reduce incidence of Sub-standard and Falsified (SF) medical products in the ECOWAS region by 75%;xiv. establish of a regional medicines regulatory Agency;xv. facilitate the incorporation of ECOWAS policies on TRIPs flexibilities into national laws;xvi. Formulation and implementation of policies that will promote innovation, research and development of pharmaceuticals and medicinal products within the ECOWAS region as well as establish a competitive grant in the ECOWAS region.	
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Justification

The literature revealed that there was a scarcity of information on human resources in the arena of medicines regulation in sub-Saharan Africa (SSA) (Ndomondo-Sigonda et al., 2017). This scarcity of information was also found in all the domains of medicines regulation in sub-Saharan Africa.

The information on medicines regulation were not easily found. The published information on medicines regulation in ECOWAS region was no longer current. Additionally, the available information was no longer consistent with the current realities in the NMRAs. Much has changed, but the published information on medicines regulation in Africa are still those that were presented in 2005, 2010 and 2017. There was also a need to know the trend, how the region fared since the 2005 meeting of the heads of African medicines regulatory authorities.

Objective

This research paper had three main objectives:

1. It aimed to put together a story of medicines regulation in Africa.
2. It compared the data found in 2005, 2010 and 2017 research papers and reports and attempted to discover any trend (increasing or decreasing) in the state of medicines regulation in West Africa.
3. The results of the comparison revealed the existence of any gaps, proposed solution(s) or available opportunities that were within and outside the region to address those gaps.

2. METHODS

Documentation review

A literature map was prepared to provide the framework and scope that guided the search and review of relevant literature.

The search of the literature was carried out according to the literature map, which is in a hierarchical structure, from top to bottom, using the dates, starting at the earliest time when events occurred in medicines regulation to the latest time, leading to the bottom with

the proposed study. The selected literature was summarized, building bridges between related topics in Medicines Regulation and identifying central issues of previous scholarly work written on medicines regulation across the globe, in Africa and more specifically, West Africa.

Choice of Reference Research Paper and Report

During the literature search and review, some reports and research papers stood out because they had information on the assessment that was done on medicines regulatory systems and structure in sub-Saharan Africa and their outcomes at specific times in the past. There was one 2005 report of the First African Medicines Regulatory Authorities Conference, which had information on the state of the regulatory systems and structure in Africa as of 2005, which proposed a strategic plan (2006-2010) with recommendations and next steps going forward. This, then, became a reference to measure subsequent medicines regulatory plans and activities in the continent.

Another important document that was used was the report of the rapid assessment of 26 NMRAs in sub-Saharan Africa that was carried out by the World Health Organization (WHO) between 2006-2010. This became another point of reference to compare what was found in 2005 to what WHO reported in their 2010 published report.

A third report, a paper by Ndomondo-Sigonda et al. (2017) compiled the state of medicines regulation in all the NMRAs in the sub-Saharan Africa as of 2016. This report described the trend of medicines regulation since 2005, when the regulatory authorities first met.

The following systems and structure of medicine regulation were the focus of the comparison: authority and legal forms of the NMRAs, existence of Marketing Authorization, conduct of Good Manufacturing Practice inspection, harmonization and international cooperation, existence of Quality Management System, Information Management System and Quality Control Laboratory(s). These seven areas were chosen as the focus because their existence in a medicines regulatory system gave an idea of the maturity of the NMRA. During the courses of this study, several other reports and papers were consulted in order to obtain specific information on these seven focus areas; some of which were the reports of countries under the WA-MRH Project, Project Papers of World Bank funded Projects, reports of WA-MRH and SWEDD Projects and reports of other activities as were deemed fit. Certain information on Quality Management Systems of

the NMRAs were obtained from reports of assessments and surveys.

Choice of Countries and Collation of Data in the Research

The countries that were chosen for a closer look from the 2005, 2010 and 2017 reports were the fifteen Members States of ECOWAS. The data obtained from the Strategic Plan 2006-2010 were mined from the report of the First African Medicines Regulatory Conference and were regarded as the 2005 data. The data from the report of the assessment of regulatory systems of twenty-six countries that the WHO assessed were mined from the report and were taken as the 2010 data. The data on medicines regulatory report of Ndomondo-Sigonda (2017) were mined and used as the 2017 data. The data that were obtained from the 2005 Strategic Plan were used as the baseline to compare the data obtained from the reports of 2010 and 2017.

Analysis of the report obtained

The data obtained from the 2005, 2010 and 2017 reports were analyzed. In order to quantify the information obtained from the reports, all responses that had a "Yes" or positive inclinations were assigned "1," while the "No" or negative inclination responses were awarded a "0." In any situation where a response was "Yes/No," "0.5" was assigned. The countries in which the reports had no information on the regulatory feature were assigned nothing.

The sum of these numbers obtained by the 15 countries per regulatory feature were taken and percentages calculated. The information from the 2005 report was used as the reference for this study. 6.67% derived from one over fifteen was assigned as the least percentage of the chosen regulatory features for all the 15 ECOWAS countries. A zero (0) could not be assigned to that year even though, the report did not have information on specific countries' NMRAs, it was the year that the regulatory problems were identified, captured in a report and solutions were proposed in form of a strategic plan.

Advantages of the research work

This study highlights the trends that are in medicines regulatory systems of the 15 NMRAs in ECOWAS region from the data gathered from 2005, 2010 and 2017. The trend that was revealed by this study will demonstrate to stakeholders (manufacturers, donor partners, researchers, policy makers, WAHO management) whether medicines regulated by the NMRAs in the region were progressing. This research

also concluded on how the NMRAs have matured according to pre-determined expectations. In future work, this study with its methodology could be used to understudy the remaining core regulatory areas in the NMRAs to allow for discovery and filling of existing gaps.

3. RESULTS AND DISCUSSION

The results obtained from the comparisons of 2005, 2010 and 2017 data revealed the following major points:

- None of the papers had information on all the Members State of ECOWAS as demonstrated by Tables 1, A3-A9.
- The three papers used for comparison did not measure the same parameter/indicators. One paper measured some set of indicators and left out one or more, while the other papers measured other indicators, hence empty spaces in Tables 3-9.
- Information on core regulatory features that was not provided in the paper was unavailable on the websites of NMRAs, various reports, national government websites, WHO websites and African Union website.
- Another reason why some of the Members States in ECOWAS were omitted or not measured could have been due to the sampling size per regional blocs and/or inclusion – exclusion criteria.
- The comparison of the data obtained in 2005, 2010 and 2017 showed an increasing trend in the number of NMRAS that became autonomous over the years – 2005 (6.67%); 2010 (13.33%) and 2017 (26.67%). This demonstrated that the governments of countries in ECOWAS were becoming more aware of the need to grant some form of independence to their NMRAs in order to have unhindered/unrestricted judgement of medicines with respect to quality, safety and efficacy.
- Concerning Marketing Authorization, the 2010 and 2017 reports had varying information. There are some countries that the 2010 report said they have NMRAs that grant Marketing Authorization (MA), which the 2017 report said were unavailable.
- This led to the fluctuating trend that is observed by the following percentage when the 2005, 2010 and 2017 were compared – 2005 (6.67%), 2010 (53.33%) and 2017 (33.33%).

- The variation observed in the information derived from the countries and NMRAs' data may have resulted from the difference in the methodology used to derive the 2005 and 2010 data.
- The 2010 report explained that countries were visited in order to obtain or confirm the information, while the methodology used in the 2017 was a search of information on the NMRAs' and countries' websites and reports.
- Regarding conduct of Good Manufacturing Practice (GMP) by the NMRAs or another body/institution in the countries, there was an increasing trend in the number of NMRAs conducting GMP inspection, 2005 (6.67%), 2010 (20%) and 2017 (40%).
- The 2010 report specified that regulatory inspection was being done in some countries, by another entirely different government institution; or the responsibility for regulatory inspection was shared with such institution.
- The 2017 report did not specify whether the regulatory GMP inspection was done solely by the NMRAs or was shared with other governmental institutions.
- The comparison of the 2005, 2007 and 2010 reports, regarding Quality Control of Medicines, showed an increasing trend in the number of countries that were testing medicines for declaration of quality – 2005 (6.67%); 2010 (20%) and 2017 (53.33%).
- The Quality Management System (QMS) showed an increasing trend (Appendix VI) in the number of NMRAs with QMS, 2005 (6.67%); 2010 (10%) and 2017 (26.67%) despite that the report of 2017 had “unavailable” as information for most of the NMRAs.
- Information Management System (IMS) was a regulatory feature not captured in the 2017 report, but was captured by 2010 report. There is an increasing trend (Appendix VII) observed – 2005 (6.67%) and 2010 (20%).
- The aspect of Harmonization and International Cooperation was not reported in one of the reports (2010). However, a steep increase was observed between the two reports that reported this regulatory feature. There was an increase in the number of countries/NMRAs involved in harmonization and international cooperation over the years – 2005 (6.67%) and 2017 (86.67%).
- Overall, from the results obtained by comparing the data from the 2005, 2010 and 2017 reports, it can be said that there was increase in the number of the NMRAs that have progressed in the seven regulatory features that were measured in this paper.
- Literature showed the beginning of medicines regulation as early as 200 BC – 100 AD. The beginning of the UK's Medicines and Healthcare Products Regulatory Agency (MHRA) in 2003 was found and the report of the First African Medicines Regulatory Conference that took place in Addis Ababa in 2005, where the Mother-Plan (a Strategic Plan 2005-2010) for Medicines Regulation in Africa was formed was discovered.

Table 2 Summary of Regulatory Features of the MRAs in ECOWAS derived from the 2005, 2017 and 2019 Reports.

S/N°	Some Features of a Medicines Regulatory Authority	2005	2010	2017
	Authority and Legal Form of the NMRAs	6.67	13.33	26.67
	Marketing Authorization	6.67	53.33	33.33
	Good Manufacturing practice Inspection	6.67	20	40
	Quality Control Laboratories	6.67	20	53.33
	Quality Management System	6.67	10	26.67
	Information Management System	6.67	20	-
	Harmonization and International Cooperation	6.67	-	86.67

Figure 1 Percentage information captured on some core regulatory features of the NMRAs in ECOWAS in the 2005, 2010, 2017 Reports.

The literature post-2005 regarding the regulation of medicines in Africa, the Regional Economic Blocs revealed that the ongoing, vibrant activities on regulatory harmonization in the RECs, development of the African Union Model Law, development of in-country

medicines policies, regulation and legislation, establishment of Regulatory Centres of Excellence (RCOREs), were all recommended activities from the 2005 Mother Plan made by the Heads of the NMRAs and stakeholders. The contributions of various stakeholders of medicines regulation such as WHO, Stringent Regulatory Authorities (SRAs) were in tandem with the Mother-Plan over the years.

Future Study

Future study would consider 2019 data on medicines regulation in Africa/West Africa and compare it with the results of 2005, 2010 and 2017 to trend progress and determine if any had been made. The 2019 data that would be collected would served as baseline data, which would be used to start the assessment of the other core regulatory functions carried out by the NMRAs in ECOWAS going forward.

A copy of the proposed questionnaire is in Appendix 1 of this paper.

Another future focus of this study would to carry out qualitative study which will allow to go into the details of these identified systems and structures in order to measure their strength and quality.

4. CONCLUSION

In conclusion, the comparison of the 2005, 2010 and 2017 reports showed that there was missing information on the regulatory features of countries that were studied. The indicators measured in the different reports compared, were, in some cases, not the same, maybe due to the differences in objective of studies, exclusion and inclusion criteria which are peculiar to studies and the methodology used. Overall, the comparison of the report revealed that there was cumulative progress in the regulatory features measured in Members State of ECOWAS over the years 2005 through 2017.

The essence of the finding of the study is that Africa and its regional blocs', especially West Africa's, medicines regulatory landscape changed. The development of Medicines Regulation has made significant progress. The contributions to improvement in the West Africa region have been gradual but sure.

5. RECOMMENDATIONS FOR NEXT STEPS (OPPORTUNITIES)

The recommendations and next steps that are specific to this research follows:

- Keep updating unifying regional and national indicators on which the Monitoring and Evaluation Officers at the regional and national levels should be trained and re-trained. The Africa Union Development Agency – New Partnership for Africa's Development (AUDA-NEPAD), RECs with the collaboration of WHO, unified the indicators that are now being measured in the regional blocs. The training of West African regional and national Monitoring and Evaluation (M&E) officers on the uniformed AMRH M&E Data Collection Tool (AUDA-NEPAD, 2019b) was conducted in Abidjan, Cote d'Ivoire in 2019 (AUDA-NEPAD, 2019a). The process of development of uniform indicators was completed in 2017, piloted in 2018 in the regional blocs with accompanying training and collection of data in 2019.
- Ensure that each of the NMRAs in West Africa has functional and robust Information Management System (IMS) exemplified by a functional website linked to the government websites. Further, ensure that the regulatory information and the vital signs of regulatory authorities are obvious and available to interested stakeholders.
- The regional, continental institutions, technical and financial development partners (WAHO, AUDA-NEPAD, WHO, World Bank, BMGF) should ensure continued advocacies towards the

governments of ECOWAS Members State for securing adequate authority and autonomous legal status for the NMRAs in the West Africa region.

- Continue to advocate that all regulatory functions are carried out by only the NMRAs. For example, the Good Manufacturing Practice inspections are carried out solely by the NMRAs of the countries and not shared among governmental institutions.
- With respect to the Quality Control laboratories, WAHO and the AUDA-NEPAD should keep up the advocacies to government of countries to finance their National Medicines Control Laboratories (NMQCLs). These NMQCLs are faced with numerous challenges ranging from inadequate equipment, maintenance of them, reference agents and qualitative and quantitative human resources. WAHO, USP and WHO are working in collaboration directly with the NMQCLs to ensure that these needs are met (Ekeigwe, 2019; WAHO-USP, 2019).
- All the NMRAs in ECOWAS are actually participating the West African Medicines Regulatory Harmonization (WA-MRH) Project and have benefited with respect to strengthening capacities in Dossier evaluation, GMP inspection, QMS, IMS (WAHO, 2020; World Bank, 2012).
- The NMRAs are further encouraged to continue to explore the opportunities available in the regional and continental medicines regulatory initiatives (AMRH and WA-MRH) with regards to Information Management System and Harmonization / international cooperation.

This recommendations from this research encouraged all stakeholders to take steps towards complete implementation of the interventions proposed in the 2005 Mother plan and subsequent continental and regional plans. The recommendations also encourage Competent Authorities, responsible bodies, organizations and institutions to cooperate and collaborate, specifically to review the Mother plan, and propose another Strategic Plan (5-10 year) for medicines regulation in Africa.

- The regional and national regulatory authorities should make use of available opportunities in the continent and region to strengthen their regulatory capacities. Some of which are the opportunities available in the proposed Africa Medicines Agency, Africa Medicines Regulatory Harmonization (AMRH) and the regional harmonization initiatives. Others include harmonized guidelines, guidance and procedures for the Joint Assessment (JA) of medicines dossiers procedure, joint inspections, Quality Management System which provide minimum acceptable standards. There is also the Information Management System for

sharing and exchanging of information among Members State (Ndomondo-Sigonda et al., 2017).

Additional opportunities that should be seized are the pool of regional/continental experts, the Regional Centre of Regulatory Excellence (RCOREs) that ensure sustainable training in the regions/continent, Network of Medicines Control Laboratories (NOMCOLs), the alignment of Africa Vaccines Regulatory Forum (AVAREF) with AMRH, WHO Collaborative Registration Procedure.

The results of this work demonstrate value for similar reviews by other regional blocs to demonstrate the progress that their regions have made with respect to the Strategic Plan of 2005, WHO assessment report of 2010 and other published literature. Members State in ECOWAS that are still lagging behind in one regulatory function, structure and system should continue to make efforts, whether with advocacies with their governments through the specialized regional body on health (WAHO) or building of capacities using opportunities of their governments' subventions in order to ensure sustainability or provisions made by regional, continental and international initiatives. There will be a need to establish a list of the expectations for the coming years or to develop another plan for medicines regulation in Africa, teased from African Union Agenda 2063 or other continental, plan that will be monitored and evaluated to demonstrate progress made.

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APPENDIX A

Proposed questionnaire for review towards the 2019-2020 survey

Table A2 A sample of one of the proposed Questionnaires to gather information on the systems and structure for granting Marketing Authorization in the NMRAs in ECOWAS.

Questionnaire

Name of NMRA:

Country:

Date:

Information on the System of Registration of Medicines in NMRA in ECOWAS

Data Collection (2019)			
S/N ^o	Data Collection Requirements (What needs to be measured?)	Response (Yes / Non)	Remarks (Evidence)
	Is NMRA using the Common Technical Documents (CTD) format as the requirement for submission of medicines dossiers for Registration in 2019?		
	Is NMRA doing paper submission of registration applications in 2019?		
	Is NMRA doing paper submission of medicines dossiers in 2019?		
	Is NMRA doing on-line submission of registration applications in 2019? (Evidence: URL)		
	Is NMRA doing on-line submission of medicines dossiers in 2019? (Evidence: URL)		
	Does NMRA has on-line tracking system for applications under-going registration in 2019? (Evidence: URL)		
	Do individuals have to come in person to track the applications under-going registration in 2019?		
	Does your NMRA have Guidelines, Standard Operating Procedure (SOPs) and Guidance for registration of medicines in 2019? (Evidence)		
	Does your NMRA have National Medicines Policy (NMP) in 2019? (Evidence)		
	Does your NMRA have established timelines for registration of medicines in 2019? (Evidence)		
	Does your NMRAs have documented timelines in 2019? (Evidence)		
	Does your NMRA have systematic tracking in 2019? (Evidence)		
	Does your NMRA have electronic notification when registration is completed in 2019?		
	Does your NMRAs post list of registered medicines on on-line (website of NMRA) in 2019? (Evidence: URL).		
	Does your NMRA have a paper publication of registered medicines in 2019?		

Does your NMRA have paper notification when registration of medicines is completed in 2019? (Evidence: Sample of the letter).

Do applicants have to come in person to be informed of the completion of the registration of their products in 2019?

Does your NMRA registers medicines less than 100 days in 2019?

Does your NMRA register medicines between 100 – 200 days in 2019?

Does your NMRA register medicines between 200-365 days in 2019?

How long does it take before Registration Certificates are ready after the approval of the Registration Committee (Median / Average time)?

Does your NMRA have backlogs of Registration Certificates to produce in 2019?

How many registration officers have your NMRAs?

How many of the registration officers have Bachelor of Pharmacy, B.Sc. level in Chemistry and other related sciences?

How many of the registration officers have Master's Degree in Pharmaceutical Science or related sciences?

How many of the registration officers have Ph.D. degree in Pharmaceutical Science or other related sciences?

How many of the registration officers that are female?

What is the Age bracket of the registration officers?

What is the average number of years they have worked in the registration Department / Directorate?

What is the average number of years they got employed in the NMRAs?

Is your NMRA at the Maturity level 2 or higher in Registration and Marketing Authorization in 2019?

APPENDIX B:

Tables 3 - 9 comparing the data from 2005, 2010 and 2017 reports

Table A3 Comparison of 2005, 2010 and 2017 data on Authority and Legal Forms of NMRAs in ECOWAS.

1. Authority and Legal Form of NMRAs						
Status at Year Point (Autonomous =1, Not Autonomous = 0)						
2005		2010		Y/N (1/0) U=0	2017	Y/N (1/0) U=0
Country 1		Dept. within MoH		0	Dept. within MoH	0
Country 2		Dept. within MoH		0	Dept. within MoH	0
Country 3		U		0	Autonomous	1
Country 4		Dept. within MoH		0	Dept. within MoH	0
Country 5		Autonomous		1	Autonomous	1
Country 6		U		0	Dept. within MoH	0
Country 7	Problem to be addressed inappropriate legal status of national medicines regulatory authorities to carry out their regulatory functions	U		0	Dept. within MoH	0
Country 8		U		0	Dept. within MoH	0
Country 9		Board under the control of MoH		0	Board under the control of MoH	0
Country 10		Dept within the Min. of Public Health		0	Dept. within the Min. of Public Health	0
Country 11		Autonomous		1	Autonomous	1
Country 12		Parastatal Agency (+Professional Council +Enforcement Agency)		0	Parastatal Agency (+Professional Council +Enforcement Agency)	0
Country 13					Dept. within MoH	0
Country 14					Autonomous	1
Country 15					Dept. within MoH	0
Total		1	Total	2	Total	4
%		6.67	%	13.33	%	26.67

Vacant spaces = U = no available information on that parameter in the literature consulted or the regulatory authority was not in existence or they were not part of the sample size for those studies in the literature.

Table A4 Comparison of data on the existence of Marketing Authorization process in ECOWAS NMRAs in 2005, 2010 and 2017 reports.

2. Marketing Authorization by NMRA

NMRA	2005	$\Sigma U=1$	2010	Y/U (1/0)	2017	Y/U (1/0)
Country 1		U	Yes	1	U	0
Country 2		U	Yes	1	Yes	1
Country 3		U	U	0	U	0
Country 4		U	Yes	1	Yes	1
Country 5		U	Yes	1	Yes	1
Country 6		U	U	0	U	0
Country 7	<u>Problem to be Addressed</u>	U	U	0	U	0
Country 8	1. Inadequate human resource.	U	U	0	U	0
Country 9	2. Inadequate legislation and regulation.	U	Yes	1	U	0
Country 10	3. Inadequate tools - guidelines, SOPs not fully developed.	U	Yes	1	U	0
Country 11	4. Inadequate funding	U	Yes	1	U	0
Country 12		U	Yes	1	Yes	1
Country 13		U	Yes	1	U	0
Country 14		U	U	0	Yes	1
Country 15		U	U	0	U	0
Total		1	Total	8	Total	5
%		6.67	%	53.33	%	33.33

Yes = NMRA grants MA; Vacant spaces = **U** = no available information on that parameter in the literature consulted or the regulatory authority was not in existence or they were not part of the sample size for those studies in the literature.

Table A5 Comparison of NMRAs in ECOWAS conducting GMP Inspection as found in the 2005, 2010 and 2017 reports.

3. Inspection of Manufacturing Sites by NMRA (Desktop review or actual inspection)						
NMRA	2005	$\Sigma U=1$	2010	Y=1 N=U=0 Y/N=0.5 (1/0)	2017	Y/U (1/0)
Country 1		U	No	0	U	U
Country 2		U	Yes/No	0.5	Yes	1
Country 3	<u>Problem to be Addressed</u>	U	U	U	U	U
Country 4	1. Local production firms non-compliant with GMP / MRA not trained in GMP.	U	Yes/No	0.5	Yes	1
Country 5		U	No	0	Yes	1
Country 6		U	U	U	U	U

Country 7	U	U	U	U	U
Country 8	U	U	U	U	U
Country 9	U	Yes/No	0.5	U	U
Country 10	U	Yes/No	0.5	U	U
Country 11	U	Yes	1	Yes	1
Country 12	U	No	0	Yes	1
Country 13	U	U	U	Yes	1
Country 14	U	U	U	U	U
Country 15	U	U	U	U	U
Total	1	Total	3	Total	6
%	6.67	%	20	%	40

Yes = NMRA does the inspection; **No** = Another Institution does the inspection; **Yes/No** = NMRA and another Institution do the Inspection
 Vacant spaces = **U** = no available information on that parameter in the literature consulted or the regulatory authority was not in existence or they were not part of the sample size for those studies in the literature.

Table A6 Comparison of NMRAs in ECOWAS in the 2005, 2010, 2017 reports that conduct Quality Control of Medicines.

4. Quality Control of Medicines						
NMRA	2005	$\sum U=1$	2010	Y/N=U (1/0)	2017	Y/U (1/0)
Country 1		U	No	0	U	0
Country 2		U	No	0	Yes	1
Country 3		U	U	0	U	0
Country 4		U	No	0	Yes	1
Country 5		U	No	0	Yes	1
Country 6		U	U	0	U	0
Country 7	<u>Problems to be Addressed</u> 1. Weak Quality Control (need to re-equip the laboratories; strengthen QC management systems.	U	U	0	U	0
Country 8		U	U	0	Yes	1
Country 9		U	Yes	1	Yes	1
Country 10		U	No	0	U	0
Country 11		U	Yes	1	Yes	1
Country 12		U	No	1	Yes	1
Country 13		U	U	0	Yes	1

Country 14		U	U	0	U	0
Country 15		U	U	0	U	0
Total		1	Total	3	Total	8
%		6.67	%	20	%	53.33

Yes = NMRA does the Quality Control; **No** = Another Institution does the Quality Control or it is not done at all.

Vacant spaces = **U** = no available information on that parameter in the literature consulted or the regulatory authority was not in existence or they were not part of the sample size for those studies in the literature.

Table A7 Comparison of NMRAs in ECOWAS in the 2005, 2010, 2017 reports with Quality Management System.

5. Quality Management System						
NMRA	2005	$\Sigma U=1$	2010	Y/N=U (1/0)	2017	Y/U (1/0)
Country 1		U	U	0	Yes	1
Country 2		U	No	0	Yes	1
Country 3		U	U	0	Yes	1
Country 4		U	U	0	Yes	1
Country 5		U	Being drafted	0.5	U	0
Country 6		U	U	0	U	0
Country 7		U	U	0	U	0
Country 8	<u>Problem to be Addressed</u> No information on Quality Management Systems of Members State of ECOWAS in the 2005 report	U	U	0	U	0
Country 9		U	No	0	U	0
Country 10		U	No	0	U	0
Country 11		U	Being drafted	0.5	U	0
Country 12		U	Yes, for administrative processes	0.5	U	0
Country 13		U	U	0	U	0
Country 14		U	U	0	U	0
Country 15		U	U	0	U	0
Total		1	Total	1.5	Total	4
%		6.67	%	10	%	26.67

Yes = QMS exists; **No** = QMS does not exist; **anything in between** = 0.5.

Vacant spaces = **U** = no available information on that parameter in the literature consulted or the regulatory authority was not in existence or they were not part of the sample size for those studies in the literature.

Table A8 Comparison of NMRA in ECOWAS in the 2005, 2010, 2017 reports with Information Management System.

6. Information Management System (functional Websites: share info. with stakeholders)					
	2005	$\Sigma U=1$	2010	2017	$\Sigma U=1$
Country 1		U	0		U
Country 2		U	No	0	U
Country 3		U	U	0	U
Country 4		U	No	0	U
Country 5		U	Yes	1	U
Country 6		U	U	0	U
Country 7		U	U	0	U
Country 8	Problem to be Addressed 1. Weak Information Management System and lack of access to independent information	U	U	0	U
Country 9		U	U	0	U
Country 10		U	No	0	U
Country 11		U	Yes	1	U
Country 12		U	Yes	1	U
Country 13		U	U	0	U
Country 14		U	U	0	U
Country 15		U	U	0	U
	Total	1	Total	3	Total
	%	6.67	%	20	%

Yes = functional website; **No** = No functional website; **Yes/No** = development of a website is on-going

Vacant spaces = **U** = no available information on that parameter in the literature consulted or the regulatory authority was not in existence or they were not part of the sample size for those studies in the literature.

Table A9 Comparison of NMRA in ECOWAS in the 2005, 2010, 2017 reports engaging in harmonization and international collaboration.

7. Harmonization and International Cooperation					
2005		2010		2017	
Country 1	U		U	U	0
Country 2	U		U	Yes	1
Country 3	U		U	U	0
Country 4	U		U	Yes	1
Country 5	U		U	Yes	1
Country 6	U		U	Yes	1
Country 7	U	information on harmonization and International Cooperation not captured by the 2010 report of the WHO	U	Yes	1
Country 8	U		U	Yes	1
Country 9	U		U	Yes	1
Country 10	U		U	Yes	1
Country 11	U		U	Yes	1
Country 12	U		U	Yes	1
Country 13	U		U	Yes	1
Country 14	U		U	Yes	1
Country 15	U		U	Yes	1
Total	1	Total	1	Total	13
%	6.67	%	6.67	%	86.67

Yes = participating in harmonization initiative; No = Not participating in harmonization initiative

Vacant spaces = U = no available information on that parameter in the literature consulted or the regulatory authority was not in existence or they were not part of the sample size for those studies in the literature.