

Accelerating patient access to medicines in the Economic Community of West African States, the Southern African Development Community and the organization for the coordination of the fight against endemic diseases

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The role played by properly functioning regulatory systems towards enhancing access to essential medicines for patients is crucial. This is especially the case in Africa which has seen progressive growth in the regulatory environment. At the center of this growth has been the African Medicines Regulatory Harmonization (AMRH) initiative. This initiative seeks to strengthen regulatory capacity and encourage harmonization of regulatory requirements – with the ultimate aim of expanding access to quality, safe, and effective medicines for patients in need in Africa. A lot of progress has been made during the last years, with initial focus on the East African Community, where harmonization related regulations have already been implemented. The same is now being rolled out in other regions such as West Africa and the Southern African Development Community.

Removing bottlenecks and reducing redundancies in regulatory processes that slow access to medicines for patients in need today is critical. In this sense, collaboration between the World Health Organization and relevant stakeholders, including the research-based pharmaceutical industry, on collaborative registration procedures that support fast and efficient review and approval of essential medicines in Africa is essential.

African regulatory harmonization offers many benefits to regulatory authorities, patients in Africa and industry alike – and most critically for the protection of public health.

Keywords: AMRH strategic plan; Africa Medicines Regulatory HARMONIZATION; Economic Community of West African States (ECOWAS) and the ECOWAS Regional Pharmaceutical Plan; Southern African Development Community (SADC); Organization coordinating endemic diseases in Central Africa (OCEAC); Regional Economic Communities (REC); Agreements for Mutual Recognition; National Medicines of Regulatory Authorities (NMRA); GMP inspection; Africa Medicines Agency (AMA); New Partnership of Africa Development (NEPAD)

1. Introduction

The African continent has undergone various alignments and changes over the last five decades. Among these developments have been the establishment of regional economic blocks, also known as Regional Economic Communities (RECs). The RECs were formed independently, and are comprised of geographical groupings of African countries as a means of promoting the integration of common regional

interests and processes. Among the key areas of recent collaboration and alliance within each block there has been a common goal of improving the healthcare sector within their respective regions. These developments are not only important to each region, but also to all Africa as well, since the RECs provide an opportunity for collaboration across the African Union's (AU).¹

In this regard, it should be noted that the AU, through its technical arm, the New Partnership for Africa's Development (NEPAD) Agency,² has established a medicines regulatory harmonization initiative with the ultimate aim of establishing one central regulatory body in Africa, the African Medicines Agency (AMA). This initiative dubbed the African Medicines Regulatory Harmonization (AMRH) Programme³ has established a roadmap towards realizing this goal through the intermediate steps being taken by the various RECs.

The World Health Organization (WHO) is also playing a strong role in the AMRH Programme by providing technical assistance in the development and implementation of harmonized processes via supporting technical working groups within the AU. Four technical working groups were officially constituted in 2012 where a respective African member state national medicines regulatory authority (NMRA) took the technical lead in the development of regional guidelines, with the support of another member state NMRA. These working groups focus on the utilization of a common technical document (CTD); along with shared good manufacturing practices (GMPs); information management systems (IMSs); and quality management systems (QMSs) [1].

This article will look at three African RECs – the Economic Community of West African States (ECOWAS), the Southern African Development Community (SADC) and the Organization de Coordination pour la Lutte Contre les Endémies en Afrique Centrale (OCEAC) – and discuss how they are working closely with their respective member states' NMRAs in developing regional medicines registration harmonization proposals to increase patients' access to quality, safe and efficacious medicines. In addition, this article will also discuss how these developments, many of which are complementary, can facilitate the AMRH Programme moving forward.

The AMRH's initiatives are also further described, along with the AMRH's progressive implementation efforts in these regional economic communities [1].

2. Economic Community of West African States (ECOWAS)

The ECOWAS is the regional economic organization for West Africa, headquartered in Abuja, Nigeria. It is composed by the following countries: Benin, Burkina

¹African Union (AU) <http://www.au.int>.

²New Partnership for Africa's Development (NEPAD) Agency www.nepad.org.

³African Medicines Regulatory Harmonization (AMRH) Programme <http://www.nepad.org/content/african-medicines-regulatory-harmonisation-armh-programs>.

Faso, Cape Verde, Ivory Coast, Gambia, Ghana, Guinea, Guinea-Bissau, Liberia, Mali, Niger, Nigeria, Senegal, Sierra Leone and Togo. The ECOWAS was founded with the mandate of promoting economic integration in all fields of activity within its constituting countries. However, the diversity of culture and languages (French, English and Lusophone) within the region have in general presented challenges in the past, resulting in disparate medicines registration processes and patient access within this region. Therefore, the current main objective of the ECOWAS is to overcome these hurdles through greater cooperation within the region to enhance the convergence of regulatory requirements.

In 2014, the West African Health Organization (WAHO) (WHO's regional agency in West Africa) developed the ECOWAS Regional Pharmaceutical Plan (ERPP) [2]. The ERPP provides a clear roadmap to support the harmonization of robust medicines regulatory systems in the ECOWAS. The ERPP's vision is to improve the quality control of laboratories and centers of excellence for the local production of medicines and the support of local clinical trials, as well as, strengthening the medicines regulatory harmonization processes, while recognizing the need for enhanced collaborations with global stakeholders to facilitate the production and distribution of high quality standard medicines. The full implementation of the ERPP objectives will take some time since they involve overcoming local manufacturing challenges, establishing robust regulatory systems, creating centers of excellence for quality control laboratories, and generating an ecosystem which enables pharmaceutical sector growth. Hence, the ERPP objectives have been defined as a long term vision up to the year 2025.

As a first step, the ECOWAS is focusing on the quality control of regional laboratories and centers of excellence for the local production of medicines. In 2015, the ECOWAS launched the AU's AMRH Programme focusing on the development of national and regional roadmaps for GMPs. Some regional accreditation initiatives are also planned to strengthen the regional GMPs and to help further shape the regulatory harmonization efforts in Africa.

This effort is intended to build upon various pharmaceutical supply programs previously initiated in the region by WAHO. Since 2010, WAHO has initiated several programs to strengthen the capacity of quality control (QC) laboratories in selected ECOWAS' countries [2]. Among these WAHO programs are: the development of guidelines and training manuals for laboratory quality management systems; the training of laboratory managers and staff in the utilization of these manuals and guidelines; and the selection of five QC laboratories to upgrade and support attainment of ISO 17025 certification and the subsequent elevation to the status of centers of excellence for the testing of medicines. Despite WAHO's efforts, only two countries (Nigeria and Ghana) have been qualified as laboratories of control in alignment with ISO standards. Thus, more work on WAHO's programs to strengthen the capacity of QC laboratories is envisioned to be implemented/take place.

Over the past five years, a number of programs have been initiated by the WAHO in collaboration with the ECOWAS to strengthen the manufacturing capacity of selected pharmaceutical firms and the supply of anti-malarial and anti-retroviral drugs

within the region [2]. To foster the ECOWAS's commitment towards improving the local pharmaceutical production of medicines, the 14th African Assembly of Health Ministers endorsed the "ECOWAS Charter on Public Private Partnership Initiative for Local Pharmaceutical Production of Priority Essential Medicines" in Praia, Cape Verde in April 2013. The WAHO has also supported the development of the guidelines for the ECOWAS/WAHO's Certification Scheme for Finished Products, Raw Pharmaceutical Materials and Pre-qualification Requirements for the evaluation of pharmaceutical manufacturers for market authorization.

In addition, within the ECOWAS region, the CTD format has been developed for the registration of medicines, pharmacovigilance, and inspections among other specific and technical fields. The harmonization of local regulations, in alignment with the regional ones, will facilitate joint review and mutual recognition of the regulatory activities (e.g. medicines registration and approval) conducted by the different NMRAs within the ECOWAS region. These efforts were facilitated by earlier work performed by the West African Economic and Monetary Union (WAEMU), also known by its French acronym, UEMOA. The WAEMU had worked beforehand with eight Francophone countries within Africa on a CTD format. Following the 2014 resolution, backed by the WHO to consolidate harmonization activities under the WAHO within the region, the WAEMU and its past CTD efforts helped to finalize a region-wide CTD format which was approved at the ECOWAS Ministers of Health Meeting in April 2016.

In the last five years significant improvement in several regulatory affairs and quality activities have been achieved within the ECOWAS REC in alignment with the AMRH Programme goals. Looking ahead, the WAHO, in collaboration with its regional member states and partners, is in the process of organizing the 2nd ECOWAS Good Practices Forum in Health in October 2016 in Ivory Coast. This Forum will serve as a platform to further identify key strategic issues on good practices, and innovative approaches to develop future recommendations and resolutions to the ministers of health of the ECOWAS REC.

3. Southern African Development Community (SADC)

The SADC is a REC comprising 15 member states: Angola, Botswana, Democratic Republic of Congo, Lesotho, Madagascar, Malawi, Mauritius, Mozambique, Namibia, Seychelles, South Africa, Swaziland, Tanzania, Zambia and Zimbabwe. Established in 1992, the SADC is committed to regional integration and poverty eradication within Southern Africa through economic development and ensuring peace and security.

During the SADC Health and HIV and AIDs Ministers joint meeting held in November 2013 an agreement was reached to review and update the SADC regional registration guidelines to streamline them with internationally recognized standards (e.g., the International Council for Harmonization of Technical Requirements for

Pharmaceuticals for Human Use – ICH, or WHO, among others) for the registration of medicines, and the use of a CTD format within the region [3]. The updated version of the SADC regional registration guidelines, along with the CTD format were approved by the SADC Ministers in January 2015 [4]. Since then, member states have adopted the SADC regional registration guidelines at the diverse national level. The adoption of a CTD format and regional registration requirements facilitate submit applications for the registration of medicines in a common single format within the SADC region, and enhances cooperation between the SADC's NMRAs. Moreover, regulators in the SADC region, through the ZAZIBONA Initiative, have been collaborating together towards better medicines registration processes to improve access to quality medicines.

Updating and harmonizing regulatory standards to create one regional market and facilitate mutual recognition is just one part of the draft Strategy on Regional Manufacturing of Essential Medicines and Health Commodities (2016–2020), which supports the pharmaceutical component in the SADC's Industrialization Strategy and Roadmap 2015–2063 [5]. A harmonized regulatory process, including a harmonized GMP certification, is essential for facilitating the approval of new products, and increasing the market uptake for locally produced products.

Despite the work done to date, the SADC's NMRAs recognize the continued challenges the pharmaceutical industry faces with respect to the varying regulatory requirements within the region [6]. While the regional registration guidelines have been updated and a harmonized SADC CTD format approved, common product information, labelling format and harmonized GMPs requirements are lacking.

To this end, the SADC, in partnership with the NEPAD, the WHO and the World Bank, organized a workshop in April 2016 for regulators and representatives of the pharmaceutical industry to discuss the harmonization of medicines registration and GMPs certification within the region. The work is in line with the approved SADC Pharmaceutical Business Plan 2015–2019 [7], the SADC Industrialization Strategy (2015–2063) [4] and the draft Strategy on Regional Manufacturing of Essential Medicines and Health Commodities (2016–2020) [3]. The objective of the SADC workshop, held in South Africa in April 2016, was to review the AMRH progress achieved on the regulatory convergence initiatives regarding labelling and GMP requirements, along with further actions needed, and the status of the implementation of the approved SADC registration guidelines and CTD format, and GMP standards by SADC member states.

Common GMP standards are considered essential within the region to ensure the protection and promotion of public health, production of medicines and health commodities. While the WHO GMPs guidelines are generally used or referred to as the standard within the SADC region, there is a non-uniform application of these standards across the region leading to the existence of diverse GMPs guidelines across the SADC region. Further, with respect to international recognition of quality assurance mechanisms used within Africa, at this time, South Africa's Medicines Control Council (MCC) is the only African NMRA that has been granted membership in the

Pharmaceutical Inspection Convention and Pharmaceutical Inspection Cooperation Scheme (PIC/s).⁴

To help address differences in the application of GMPs within the regions, along with other observed divergences in regulatory practices, the SADC has identified the following key strategic priorities to be addressed in 2016–2019 [6]:

1. Create an environment that will maximize the research into production capacity of local and regional pharmaceutical industry in terms of generic essential medicines;
2. Strengthen regulatory capacity by assessing NMRAs to identify critical areas of weaknesses in control and registration;
3. Develop strategies to strengthen selected NMRAs;
4. Utilise the harmonised SADC medicine regulation guidelines; and
5. Set up of technical working group to facilitate the implementation of the roadmap was agreed as a next step.

4. Organization for the Coordination of the Fight against Endemic Diseases (OCEAC)

The OCEAC is a regional Economic community comprising the following countries: Cameroun, Congo, Gabon, Equatorial Guinea, Chad, and Republic Central Africa.

In its beginnings (between 1965 and 1983) the OCEAC was responsible for: 1) setting and coordinating all programs of action for the control and eradication of major endemic epidemics in the Central African Region (e.g. tuberculosis, malaria, intestinal parasites), and 2) following up studies and conducting research to succeed in the fight against endemic epidemics.

The involvement of OCEAC in the AMRH Programme began in July 2015. NEPAD is coordinating the AMRH Programme within the region and has empathized the on-going collaboration between the OCEAC and WHO.

At the AMRH 5th Advisory Committee Meeting held in Dakar in May 2016, Dr. Aime Djitafo Fah, Coordinator of the OCEAC's Regional Sub-Program Harmonization of National Pharmaceutical Policies in Central Africa, introduced the OCEAC's governance structure and a brief background report on the progress made in the medicines regulatory harmonization field (e.g. the development of registration guidelines) in this region since 2006. During his presentation, Dr. Aime Djitafo

⁴PIC/S is an international collaboration initiative, comprised of 48 participating authorities across the globe. PIC/S membership is dependent upon the demonstration of GMP inspection systems comparable to that of the PIC/S. PIC/S mission is *to lead the international development, implementation and maintenance of harmonised Good Manufacturing Practice (GMP) standards and quality systems of inspectors in the field of medicinal products*", which can facilitate mutual recognition of inspections amongst members. www.picscheme.org.

Fah highlighted the importance to continue the advocacy and coordination efforts towards the implementation of the AMRH Programme in Central Africa; and reiterated OCEAC's willingness to continue collaborating with ECCAS. During the AMRH 5th Advisory Committee Meeting, it was also discussed the implementation plan for the period 2014–2018 which focuses on the following priority areas [8]:

1. Conduct joint training on guidelines;
2. Establish regional ethics committee to facilitate local clinical trials;
3. Establish a Regional Commission on pharmacovigilance; and
4. Draft legislation to assist combating counterfeit medicines.

There are significant ongoing efforts on cooperation between the Economic Community of Central African States (ECCAS) and the OCEAC on the implementation of the AMRH Programme in the Central African region. The collaboration framework and roadmap for the AMRH roll out in the Central Africa region will be signed in 2016 by NEPAD Agency, WHO, and OCEAC.

High level discussions regarding the implementation of the AMRH Programme in the Central African region were held in 2015 during the 4th AMRH Advisory Committee Meeting under the leadership of the *Economic Community of Central African States* (ECCAS) and OCEAC.

Other efforts underway include the Harmonization of National Pharmaceutical Policies in Central Africa to help align the current different regulations and practices governing pharmacies in order to opt for an identical and common policy in the countries of the Central African sub-region.

In recognition of the existing efforts to advance the pharmaceutical sector in the Central African region, the AMRH Programme undertook to engage ECCAS and OCEAC with a view to develop a framework and a roadmap for the implementation of AMRH in the Central African Region [8].

5. Common topics to the three RECs

5.1. GMP standards and GMP inspections

A common theme within the ECOWAS, SADC and OCEAC is the need to harmonize quality standards and cooperative agreements for the mutual recognition of member states' GMP inspections and master batch records (MBRs). Currently, GMP inspections and MBRs have not been implemented harmoniously leading to remarkable regulatory discrepancies between the different NMRA in these RECs.

During the last AMRH Advisory Committee held in May 2016 in Dakar one of the key topics discussed was the implementation of GMPs Roadmaps through the AU Pharmaceutical Manufacturing Plan for Africa (PMPA) [8]. The overall goal of this meeting was to develop regional GMP approaches to reach alignment and harmonization of national GMP roadmaps within the PMPA and AMRH Frameworks. The

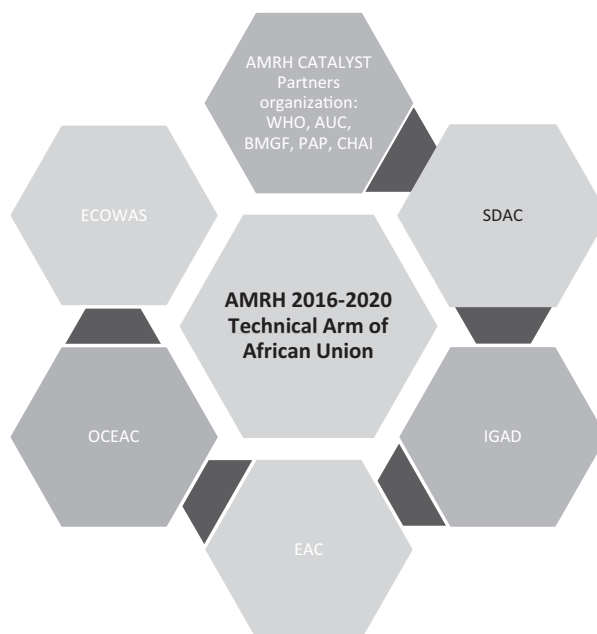


Fig. 1. Africa networking platform.

core objectives of the GMPs roadmap are to identify existing regional GMPs certification schemes, and support RECs to develop strategies and approaches to achieve universal GMP standards by the local pharmaceutical manufacturers in Africa.

The International Federation of Pharmaceutical Manufacturers & Associations (IFPMA) position paper *GMP Inspections and the Provision of Batch Records in Sub-Saharan Africa* stresses that GMPs inspections are a fundamental path that NMRAs can use to ensure the production of high quality pharmaceutical products [9]. Recognizing stringent regulatory authorities (SRAs) and the mutual recognition of African NMRA inspections and implementation of the above mentioned practices may be a more resource efficient way of providing assurance with GMP compliance. A positive inspection report or a valid GMP certificate from an SRA can negate the need for a duplicative inspection.

5.2. AMRH strategic direction

As background, the origin of the AMRH Initiative goes back to 2007 with the assembly of a consortium of key partners (the United Kingdom's Department for International Development or DFID, Bill & Melinda Gates Foundation, NEPAD, Clinton Foundation, and WHO) established to accelerate and ensure medicines regulatory harmonization in Africa. The AMRH Initiative led to the creation of the

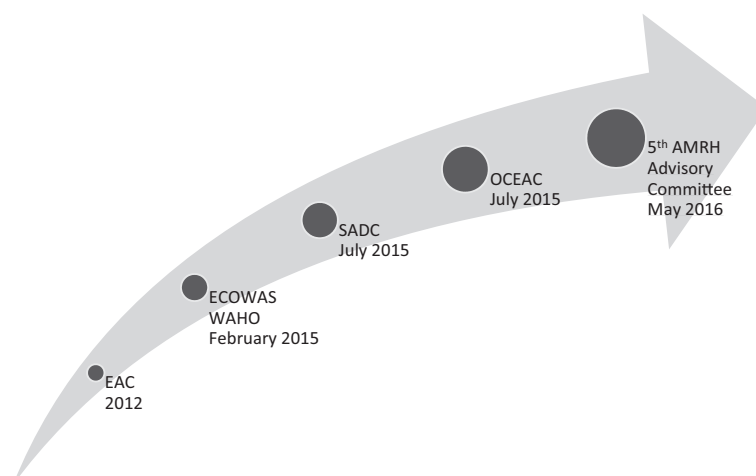


Fig. 2. Chronological overview of the AMRH implementation.

AMRH Programme in 2010 through which the NEPAD, as the technical arm of the AU, in collaboration with partnering stakeholders, is supporting African RECs efforts towards regulatory harmonization and increase African patients access to essential medicines. Drawing upon the past experiences around the globe, the Africa Union, its RECs and partnering organizations involved in the African Networking Platform (see Fig. 1) are leveraging lessons learnt from other harmonization models and schemes within ICH, Europe, America and Asia to help Africa to achieve an efficient harmonization process.

The new AMRH Programme Strategic Plan for 2016–2020 will build upon past efforts (see Fig. 2) and is intended to provide continued support to the NEPAD and its collaborating partners to ensure the implementation of the AMRH Programme over the next five years.

IFPMA, through its African Regulatory Network (ARN) activities, supports the implementation of the AMRH Programme by sharing IFPMA member companies' extensive and global technical expertise in pharmaceutical development and manufacturing. Ongoing communication amongst all stakeholders is essential, and the African Regulatory Conference, supported by the ARN, provides a platform to bring NMRAs, the biopharmaceutical industry, and other stakeholders together to share, collaborate and establish clear milestones towards regulatory harmonization in Africa to improve patients' access to quality drugs.

6. Conclusion

The individual activities conducted by the ECOWAS, SADC and OCEAC are intended to help collectively to lay the ground work for the implementation of the

AMRH Programme over the next five years. The envisioned benefits of the AMRH Programme include: increased patient access to quality medicines; optimized labelling requirements that enable packaging sharing across member states, thus facilitating the distribution and supply of needed medicines across the continent; and harmonized GMP standards for sharing GMP Certificates provided to regulators to reduce duplicative inspections. In parallel, to support the AMRH Programme, the AU, WHO, and NEPAD are collaborating to ensure the endorsement of the establishment of the AMA by the Summit of AU Heads of State and Government in 2018.

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