Knowledge Brief

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Regulatory Systems Strengthening for Medicines in Africa: Shining a Spotlight on the World Bank Group's Decade-Long Contributions

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KEY MESSAGES:

- The African Medicines Regulatory Harmonization (AMRH) initiative, a multistakeholder partnership, focuses on improving fragmented regulatory systems in the region to ensure faster access to safe, efficacious, and good quality medicines and vaccines.
- With support from the Bill and Melinda Gates Foundation, the World Bank Group set up a trust fund in 2011 to support AMRH work.
- Since then, significant improvements have been made across the region, including notable decreases in timelines for the registration of medicines, more harmonized registration systems, and an enhanced focus on quality management and transparency in the drug registration process.
- The COVID-19 pandemic has shown that harmonized and well-established regulatory systems are critical to ensure access to safe, efficacious, and good quality medicines and vaccines.
- The establishment of the African Medicines Agency, the next chapter in the AMRH initiative, provides the opportunity to continue institutionalizing this important medicine regulatory system's strengthening work, while increasing country ownership and ensuring sustainability.

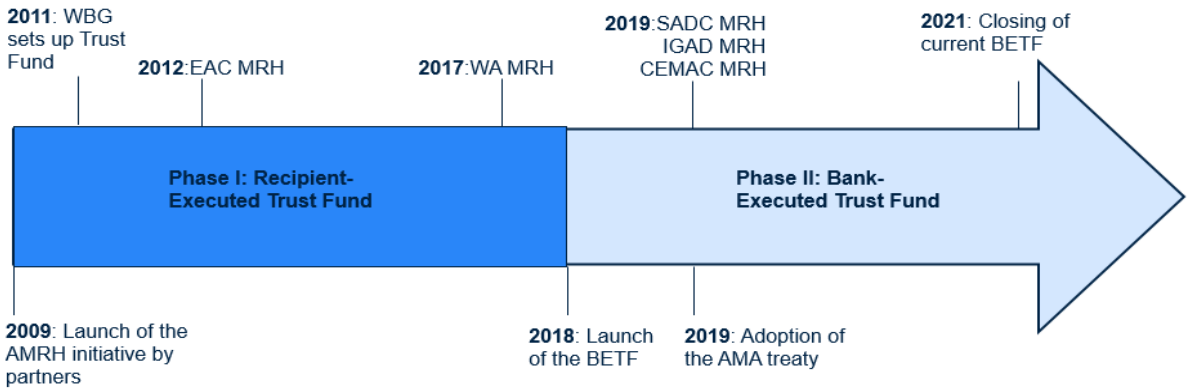
Introduction

Ten years ago, the World Bank Group (WBG) committed its support to helping African countries strengthen their medicines regulations, governance, and accountability in the pharmaceutical sector of their health care systems.

Strengthening the medicines regulatory environment is a well-established prerequisite for increasing access to safe, efficacious, and good quality medicines, and for the successful development of a functioning pharmaceutical industry. While affordability remains the cornerstone of access (WHO 2020), other factors play a role in hindering access to quality medicines. In Africa, these barriers can be attributed, in part, to "weak or non-coherent regulatory standards and requirements among countries; lengthy medicine registration processes that lead to delays in approval decisions; technical capacity and capability; overall resource constraints; and failure to leverage regulatory review activities already performed by better-resourced regulatory authorities and the World Health Organization (WHO)" (Ndomondo-Sigonda et al. 2018).

At the WBG, ensuring that such barriers are removed so that every person can lead a healthy, productive life is central to our shared goals of ending poverty and boosting our shared prosperity. In 2011, to help make life-saving health products more accessible in poor countries, the WBG with generous funding from the Bill and Melinda Gates Foundation (BMGF), set up a trust fund to support the African Medicines Regulatory Harmonization (AMRH) initiative (Figure 1).

Figure 1: Key Milestones of the AMRH Initiative



Source: Adapted from presentation on "The AMRH Program: Overview of World Bank Support, Achievements and Planned Activities" by L. Philippe Kagan et.al., November 18, 2021.
Notes: EAC MRH = East African Community Medicines Regulatory Harmonization; WA MRH = West Africa Medicines Regulatory Harmonization; SADC MRH = Southern African Development Community Medicines Regulatory Harmonization; IGAD MRH = Intergovernmental Authority on Development Medicines Regulatory Harmonization; CEMAC MRH = Economic and Monetary Community of Central Africa Medicines Regulatory Harmonization; BETF = Bank-executed trust fund; AMA = African Medicines Agency.

Two years before WBG's involvement, the AMRH initiative was launched by a consortium of partners[1] to expedite market authorization to facilitate alignment of national legislative frameworks with the African Union (AU) Model Law on Medical Products Regulations. The AU Model Law guides member states and regional economic communities (RECs) in harmonizing regulatory systems and in providing an enabling environment for the development and scale-up of health technologies. As laid out in the treaty adopted on February 11, 2019, by the AU Commission, the AMRH initiative serves as the foundation for the establishment of the African Medicines Agency (AMA). Moving from 55 countries acting independently to six RECs with centralized regulatory functions through AMA, brings many benefits, especially for countries with limited regulatory resources to carry out oversight activities.

A decade later, a dynamic movement toward more harmonized registration systems, improved overall efficiency in medicine registration, and an enhanced focus on quality management and transparency in the drug registration process has been established in Africa, thanks to the AMRH initiative. Additionally, this important work has increased collaboration, information, and work-sharing among RECs, which are important components for strengthening supply chain integrity and for thwarting the spread of substandard and falsified medicines.

In this paper, we discuss the remarkable achievements of the AMRH Trust Fund managed by the WBG over its decade-long existence. We showcase the range of technical support and strong partnerships undertaken by the WBG, in collaboration with its program partners, the World Health Organization (WHO) and the African Union Development Agency (AUDA-NEPAD), to support the AMRH initiative. We discuss some lessons learned from project implementation and conclude by highlighting some opportunities for future donor engagement in the area of medicines regulatory systems–strengthening in Africa.

Background

Africa has only 16 percent of the world's population and yet bears a disproportionately higher share of diseases: communicable, maternal, nutritional, and newborn diseases continue to dominate and present significant challenges for the health care systems in the region (World Bank 2013). Adding to this grim reality, the lack of regular access to essential medicines is particularly concentrated in Africa (WHO 2004). Without the availability of quality-assured, affordable drugs and vaccines in sufficient quantities, broader global health efforts such as universal health coverage (UHC) and the attainment of the Sustainable Development Goal (SDG) 3.8[2] are doomed to fail.

[1] The consortium of partners includes the Pan-African Parliament, African Union Development Agency (AUDA-NEPAD), the World Health Organization (WHO), Bill and Melinda Gates Foundation (BMGF), United Kingdom's Foreign, Commonwealth and Development Office (formerly DFID), and the Clinton Health Access Initiative (CHAI).

[2] Sustainable Development Goal (SDG) 3, Target 3.8 reads: "Achieve universal health coverage (UHC), including financial risk protection, access to quality essential health care services, and access to safe, effective, quality, and affordable essential medicines and vaccines for all." https://unstats.un.org/sdgs/metadata/?Text=&Goal=3&Target=3.8 (accessed June 28, 2021).

The pathway from drug product development to a drug's appropriate use by consumers is a complex, lengthy undertaking that is fraught with a high degree of unpredictability. The value chain involves many touch points with regulatory authorities, including licensing of facilities and personnel, clinical trial approvals, marketing authorization, factory inspections, reporting and management of side effects, and post-approval changes. Each step in the process has the potential of compromising drug quality due to tampering or delays if robust regulatory controls, within the context of an appropriate legal framework, are not applied.

National medicines regulatory authorities (NMRAs) are the gatekeepers to the medicines regulatory system. Their mandate is to ensure that drugs circulating in the market are of good quality and safe for use. However, baseline studies conducted in 2009 revealed that while some countries in Africa have robust and functional NMRAs, others have regulatory systems that are virtually nonexistent (Ncube, Dube, and Ward 2021). Thus, it is not surprising that marketing authorization (MA) and clinical trials authorization (CTA) for global health products such as vaccines and medicines experience significant delays ranging from four to seven years in comparison to other more resourced regions of the world (Ndomondo-Sigonda et al. 2018). It is this highly fragmented landscape that drug manufacturers must operate in, many of whom end up being deterred from entering the market in the first place.

Launched in 2009, the AMRH initiative rightly focuses on improving the fragmented regulatory system for product registration in Africa by changing from a country-focused approach to a collaborative-regional one (Ndomondo-Sigonda et al. 2018). With many NMRAs being underresourced and lacking the capacity to carry out essential regulatory tasks, AMRH's medium of change is to bring regional entities such as the RECs and regional health organizations (RHOs), alongside NMRAs, to harmonize technical requirements and guidelines for registration of medicines, and to conduct the typical functions of regulators, such as joint regional dossier assessments and Good Manufacturing Practices (GMP) inspections. The goal is to have faster registration cycle times starting with generics and extending to other product categories. Adopting harmonized regional approaches to medicines regulations benefits all stakeholders because it offers NMRAs unique opportunities to share responsibilities and to build capacities for the vast majority of processes and functions needed. Most importantly, enhanced collaboration and coordination benefits patients by ensuring that the best possible science, standards, and practice drive the regulatory process, resulting in improved safety, innovation, and access to medicines.

The World Bank Group's comparative advantages in employing innovative financing strategies, pooling donor funding, and driving projects through its field-based management capabilities were critical in getting the AMRH initiative off the ground in 2011. Starting with an initial contribution of US$12.5 million from the BMGF, the WBG set up the AMRH Trust Fund and quickly mobilized additional funding from other donors including the United Kingdom's Foreign Commonwealth and Development Office, US Government/President's Emergency Plan for AIDS Relief (PEPFAR), and GAVI, increasing its programmatic budget from US$12.5 million to about US$35.0 million over the last decade. In 2012, the first grant was awarded to the East African Community (EAC). Thereafter, the trust fund expanded its support to four more regions by 2019, namely, the Economic Community of West African States (ECOWAS), the Southern African Development Community (SADC), the Intergovernmental Authority on Development (IGAD), and the Economic and Monetary Community of Central Africa (CEMAC). Additionally, AUDA-NEPAD and WHO joined the WBG as program partners, bringing their coordination/advocacy prowess and technical know-how, respectively, to benefit the regions. Thanks to the unwavering support of these program implementation partners, impressive gains in improving medicines regulatory systems have been recorded.

Achievements

Regional collaboration and information-sharing were significantly enhanced following the implementation of the regulatory harmonization initiative. With AMRH Trust Fund support, the regional projects succeeded in bringing together regulators in the different RECs and pooling resources and expertise to assess pharmaceutical products dossiers and to fast-track registration of essential medicines. As a result, steering committees have been established as platforms for ensuring regular dialogue among member states, for project oversight and approval of main decisions. This also ensures sustainability of the initiative even after donor support ends. Technical expert working groups in the different regulatory functions[3] were also created and harmonized regulatory criteria through the development of guidelines and procedures. Due to requirements standardization, medicines registration timelines were significantly reduced, potentially accelerating access to essential medicines. For instance, in EAC and SADC, the timeline for registration greatly decreased from 24 months on average to 10 to 12 months on average.[4] Furthermore, regulators participated in joint activities such as joint assessments[5] of medicines' dossiers and joint GMPs inspections.[6] For example, the Southern African Development Community Medicines Regulatory Harmonization (SADC

[3] According to the WHO, the main pharmaceutical functions are (i) product registration; (ii) licensing of manufacturing, importation, and distribution; and (iii) control of medicine promotion and information.
[4] World Bank, "EAC Implementation Completion Report," August 2018.
[5] Joint assessments are defined as collaboration among member states in regions to assess quality, efficacy, and safety of medicines before granting marketing authorization.
[6] Good Manufacturing Practices (GMPs) are the practices required to conform to the guidelines recommended by agencies that control the authorization and licensing of the manufacture and sale of pharmaceutical products. They are set by the International Consortium for Harmonization (ICH).

MRH) project jointly approved 18 pharmaceutical products for registration in the region, while IGAD granted a positive recommendation for four products. These main regulatory activities aim to guarantee that drug development complies with international standards and brings safe, good quality, and efficacious products to the market. Moreover, the WBG is closely working with the RECs to develop a regional information management system (IMS) for regulators to share confidential information about assessments, inspections, and pharmacovigilance and to avoid potential duplication of efforts.

Support from the AMRH Trust Fund played a critical role in strengthening governance and institutions, efficiency, and transparency at the national level. Through the implementation of Quality Management Systems[7](QMS), NMRAs' efficiency and transparency significantly improved. As a result, quality of work and information-sharing with manufacturers and the public increased, leading to better accountability. The program supported QMS implementation in several NMRAs such as the Gambia, Ghana, Kenya, Tanzania, Uganda, and Zanzibar, all of which have become ISO-certified. In a customer survey, these countries also reported improvements in the quality of services, better clarity of timelines for every stage of the process for medicines regulation, as well as inputs and outputs for each regulatory function. Efficiency and transparency were also enhanced as countries started using IMS at the national level. Regulatory systems were assessed in more than 20 countries in CEMAC, IGAD, and SADC using the WHO Global Benchmarking Tool, their maturity levels were determined, and institutional development plans were prepared for governments to act on. Although, most regulatory authorities were ranked at maturity level 1 (out of 4), the program supported the Ghana Food and Drug Authority (FDA) in reaching maturity level 3. Furthermore, assessments of the respective legislative environments led to the development of draft legislations to align outdated countries' laws with the AU Model Law, paving the way toward the establishment of autonomous medicines regulatory authorities. Some countries in CEMAC have also been using the legislative assessment to advocate for the ratification of the Treaty for the Establishment of the African Medicines Agency (AMA).

Regulators' capacity was strengthened in all the RECs through the support of the AMRH Trust Fund. In collaboration with the WHO, training workshops, curricula in the different regulatory areas, post-marketing surveillance, Integrated Management Systems (IMS), and Quality Management Systems (QMS) were organized. As a result, 1,433 regulators and health personnel across the continent benefitted from these capacity-building activities and had the opportunity to disseminate knowledge in their respective agencies. Strengthening capacity across the continent was critical to minimizing disparities among countries, as it allowed countries to better collaborate, build trust, and move toward a future of mutual recognition of regulatory assessments and decisions.

The AMRH program as a platform for regulatory exchanges has proven to be key for African countries to collaborate on critical issues such as the fight against substandard and falsified medicines but also in terms of pandemic preparedness. AMRH has been an important player in pooling together relevant expertise on the continent in an effort to accelerate the registration and deployment of new COVID-19 tools and interventions. At the onset of the pandemic, the AMRH platform used its strong convening power to enable NMRAs across the continent to meet and share information quickly to address the effects of the disease. During these key interchanges, perspectives and learning on the effective regulation, quality, and safety assurance of in vitro diagnostic (IVD) devices, personal protective equipment (PPE), along with preparations for clinical trials of prospective vaccines in member countries were discussed. The forum helped to hasten steps in the approval of various products, address drug and medical supply shortages, and reduce any existing barriers that could negatively impact supply. It also enabled the quick adoption of WHO COVID-19-related guidelines and boosted support for local production in the various member countries as an additional interventionary measure.

Outside regional projects, the WBG has also been supporting work in thematic areas that contribute to overall improvements in the pharmaceutical governance sector. In 2019, the Global Steering Committee (GSC) for Quality Assurance of Health Products received support from the trust fund. The GSC serves as a voluntary coalition of major health development and financing agencies working together to enhance supply chain integrity and to combat the challenges associated with falsified and substandard medicines in low- to middle-income countries. Also, the WBG recruited a consultancy firm in 2019 to review the existing AMA Business Plan and Institutional Framework with a view to develop recommendations for a five-year strategy and revised the business plan for the operationalization of AMA. The review successfully addressed many outstanding questions surrounding the precise size, scope, scale, governance, and functioning of the AMA, including its financing model; the product and functional scopes; and the operational transitioning of AMRH activities, structures, and governance to the AMA.

Lessons Learned

Some of the core elements for achieving more consistent and sustainable impact in MRH activities are as follows:

- **Prioritize deeper engagement with countries.** Efforts to engage countries to drive the decision-making process need to be constantly prioritized, as ultimately the success of the regional activity depends on them. Strong NMRA commitment and ownership, especially the involvement of the heads of agencies, are key to strengthening regulatory activities, such as integrating MRH activities into the overall work plan and deliverables of the country's regulatory agency for better workflow and staffing

[7] Quality Management Systems (QMS) can be defined as a set of interacting elements based on procedures, policies, resources, and objectives that are established collectively to guide an organization.

support.

- **Allocate additional resources for institutional strengthening in less-resourced NMRAs to facilitate their eventual full participation in the harmonized system over the long term.** Although, significant support was provided for several capacity-building and twinning initiatives, additional time and investments in human resources and infrastructure, along with securing the necessary political will and support, were necessary to bridge the gap between less-resourced NMRAs and the stronger NMRAs.
- **Encourage regular, open dialogues** with stakeholders such as the pharmaceutical industry to increase accountability and to make the process more transparent.

Conclusion

Taken together, the WBG partnership under the AMRH Trust Fund has contributed immensely to strengthening systems and to improving the overall efficiency of the medicines regulatory landscape in Africa. With the dedicated support of WHO and AUDA-NEPAD, it has built important partnerships with public and private stakeholders and created a vibrant community of regulatory harmonization advocates in the region. During the COVID-19 pandemic, RECs adjusted quickly to carrying out their essential work activities, despite the very challenging context. For example, joint assessments and inspections transitioned completely to a virtual environment and innovative solutions were used to quickly share information and to connect with other stakeholders. This level of dedication speaks volumes about the regions' commitment to the long term and about the sustainability of the AMRH program. Despite these impressive gains, more work needs to be done to fully realize the benefits of regulatory harmonization. For example, there needs to be a standardized electronic submission portal for each region; national regulators need to be more reliable in fast-tracking approval for jointly reviewed products; communication between regulators and manufacturers can be improved; and national-level capacity needs to be strengthened, to name a few priorities. Additionally, a major milestone for achieving a mature regulatory environment is the establishment of AMA, which is yet to be realized.

On October 31, 2021, the WBG officially closed its projects and activities under the AMRH Trust Fund. This planned closure presents many opportunities for redefining the donor and coordinating landscape for MRH in Africa. With their growing capacity and ownership of the MRH agenda, African institutions are poised to capitalize upon this new opportunity and to keep the current momentum to ensure sustainability.

For example, AUDA-NEPAD has been at the forefront of formalizing and operationalizing many of the AMRH's institutional structures and procedures, including the AU Model Law and AMA. Where AMRH donors and international organizations are concerned, the opportunity to engage directly with the regions creates new channels for communication and collaboration. Finally, given the extensive operational and technical knowledge and network built over the last decade, both at global and regional levels, the WBG is also uniquely placed to continue supporting AMRH through collaboration with governments and the donor community. Moving forward, a key priority for improving access to medicines in Africa would be to strengthen their pharmaceutical manufacturing capacity. Through the support of the International Finance Corporation (IFC), the WBG is well-positioned to support the continent toward achieving greater independence in the supply of quality medicines.

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