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Regulatory System Strengthening report insights: Proposed priorities for funders

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Introduction

This briefing note highlights **ten key priorities** that funders should consider if they want to support the African continent's aim to provide equitable access to safe and effective vaccines and significantly increase local production of these in the next decade. For effective regulatory system strengthening in Africa, investments should collectively address the needs at the national, regional and continental level, building on existing initiatives and priorities as guided by the African Medicines Regulatory Harmonisation initiative (AMRH) and the Partnership for African Vaccine Manufacturing (PAVM).

The proposed priorities are mapped to three overall objectives:

1. The African Medicines Agency (AMA) adding value to users and Member States, providing services that are additional to those already found or evolving on the continent and avoiding duplicating requirements
2. All African countries participating in reliance to improve the oversight of vaccines across the lifecycle, particularly in epidemic contexts
3. All vaccine-producing countries reaching WHO Maturity Level-3 status

1. Background

Wellcome published a report in July 2022 on [Strengthening Regulatory Systems in low- and middle-income countries \(LMICs\)](#) with a specific focus on improving the regulatory ecosystem for vaccines in Africa. The report highlights the achievements in regulatory systems strengthening over the past decade, defines the remaining challenges, and outlines the opportunities for investment by funding partners. These opportunities are aligned with the ambitions of the Partnerships for African Vaccines Manufacturing (PAVM) Framework for Action (2022), the workplan of the African Medicines Harmonisation Initiative (AMRH), the goals of the African Medicines Agency (AMA) and the African Union's ambition to substantially increase the availability of African-produced vaccines on the continent by 2040¹.

This briefing note highlights ten key priorities for regulatory systems strengthening in Africa for funding partners to consider for both immediate and longer-term investments. The research was undertaken in 2020 and 2021 which involved desk research and discussions with stakeholders. Apart from selected technical interventions directed at vaccines, the recommendations would support strengthening of the overarching regulatory system for all medical products². For effective regulatory system strengthening in Africa, investments should collectively address the needs at the national, regional and continental levels, building on existing initiatives and priorities as set out by AMRH and PAVM. Therefore, international funding partners should coordinate their funding and engagement in alignment with AMA/AMRH and PAVM work plans. Our proposed research agenda has been developed in consultation with stakeholders to support policy and technical decision-making by AMRH and its partners. This requires support for its implementation.

2. Key priorities for funders

Table 1 summarises the key funder priorities including objectives, the priorities and required scale of investment.

Table 1. Summary of the key funder priorities

| Objective | Priorities | Scale of investment | Investment duration | Target / recipient |
|--|---|---------------------|---------------------|------------------------------------|
| The African Medicines Agency needs to add value to users and Member States, supporting AMRH in developing services that are additional to those already found or evolving on the continent and avoiding duplicating requirements | 1. Optimise the legal basis for regulatory harmonisation and convergence including fundamental review of the African Union (AU) Model Law and supporting countries with domestication | \$\$ | Long term | Continental (AMRH/AMA > MPRR/UNDP) |
| | 2. Build capabilities within National Regulatory Authorities (NRAs) and AMA aligned to the WHO Global Competency Framework for the regulatory workforce, to enhance future workforce retention and sustainability | \$\$ | Long term | All levels (RCOREs, partners, WHO) |
| | 3. Expand process for product lifecycle management to include post-approvals changes (PACs) | \$ | Short term | Continental |

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Table 1. Summary of the key funder priorities (continued)

| Objective | Priorities | Scale of investment | Investment duration | Target / recipient |
|---|---|---------------------|---------------------|---|
| All African countries to participate in reliance to improve the oversight of vaccines and medicines across the lifecycle, particularly in epidemic contexts | 4. Develop regulatory best practices for emergency use contexts and pathways for reliance, including improving ability to rely on ML4 agencies | \$\$ | Medium term | Continental (AVAREF) / AMRH |
| | 5. Develop a Regulatory Information Management System (RIMS) that brings together national, regional and continental activities | \$\$ | Medium - long term | Continental and regional (predominantly) and national |
| | 6. Support development of regulatory pathways for clinical trial approval, incorporating ethics review and ensuring data availability from trials | \$\$ | Medium term | Continental (AVAREF), regional, national |
| | 7. Build NRA capacity to ensure uptake of a continental pharmacovigilance system | \$\$ | Medium – long term | National (regional and continental support) |
| | 8. Support WHO PQ programme in cold chain oversight and NRA capacity for Good Distribution Practice oversight | \$\$ | Short term | NRAs |
| All vaccine-producing countries to reach WHO Maturity Level-3/4 status | 9. Prioritise NRAs in manufacturing countries to identify and address critical bottlenecks preventing them from achieving WHO Maturity Level-3/4 status | \$\$\$ | Medium – long term | Global (through WHO) and national |
| | 10. Support the development of an African network of regional reference laboratories to conduct lot release (and batch testing for small molecules) via a hub and spoke model | \$\$\$ | Medium - long term | Regional; continental and national |

Scale of investment based on expected monetary value required to support priority, as defined by:

- \$ for activities costing up to \$1 million
- \$\$ for activities costing between \$1-6 million
- \$\$\$ for investments over \$6 million

Timeline defined by:

- Short-term: up to 2 years
- Medium-term: 2-5 years
- Long-term: 5-10 years

Objective 1:

The African Medicines Agency needs to add value to users and Member States, providing services that are additional to those already found or evolving on the continent and avoiding duplicating requirements

Context

The AMA has been founded on the principles of scientific robustness, transparency, accountability, international standards, reliance and convergence. The AMA will help to facilitate coordination of selected regulatory activities and further harmonisation and cooperation across Member States, Regional Economic Communities (RECs) and global reference authorities to support NRAs with oversight of medical products for routine and emergency use.

As of October 2022, 23 countries have now ratified the AMA Treaty. A joint workplan between AUC and AMRH has been developed that includes a roadmap for the AMA's first years, setting up AMA's core activities and developing AMA business processes. The foci of the AMA will be limited initially, and the current treaty does not provide for any binding decisions. Funders should support the AMRH and AMA to systematically examine issues which might challenge the effectiveness of the Agency and its constituent parts in the oversight of vaccines and medicines.

Priorities

1. Optimise the legal basis for regulatory harmonisation and convergence including fundamental review of AU Model Law and supporting countries with domestication

- a. Appraise options for reforming the legal basis for reliance to make uptake mandatory and conduct a review of stakeholder incentives for uptake of reliance pathways and related activities.
- b. Review the AU Model Law to ensure it is fit-for-purpose.
- c. Roll-out of a programme for domestication of the AU Model Law (or its successor, should there be one).

- d. Develop a streamlined framework to harmonise and coordinate ethics review of clinical trials applications to prevent slowing of trial approval times. This should include promoting concurrent rather than sequential decision-making (via AVAREF), with a focus on ethics board standards and harmonisation procedures.

2. Build capabilities within NRAs and AMA aligned to the WHO Global Competency Framework for the regulatory workforce, to enhance future workforce retention and sustainability

- a. Develop a capability building and retention strategy based on an agreed professional framework for the regulatory workforce and regional baseline assessments of gaps and needs.³
- b. Support regional assessments of human resource needs and development of an educational and training strategy for the continent.
- c. Facilitate a comprehensive view of retention beyond the AU Model Law, through facilitating financial sustainability of NRAs (e.g. through appropriate user fee structures) to ensure NRAs can allocate funds to improve conditions for regulatory professionals and support career development.

3. Expand an end-to-end process to support product lifecycle management

- a. Harmonise procedures across regulators for timely post-approval changes (PACs) to be approved to support registration at national level and to prevent stockouts due to unauthorised PACs – especially of vaccines – requiring timely disclosure of variations by manufacturers to regulatory authorities.
- b. Develop harmonised requirements across NRA for quality, efficacy, labelling, packaging, safety and post-approval changes for biologicals & diagnostics.

Objective 2:

All African countries to participate in reliance to improve the oversight of vaccines and medicines across the lifecycle, particularly in epidemic contexts

Context

Relying on work done by other ML4 authorities is now a cornerstone of modern medical products regulation. The WHO has demonstrated how reliance is an important aspect of an efficient and effective regulatory system⁴. To avoid duplication of effort and wasting of limited resources, regulatory authorities worldwide are moving towards a model of reliance and work-sharing which enables national authorities to concentrate efforts only on functions that cannot be, or have not been, conducted by other ML4 authorities. To oversee the local production of vaccines on the continent, national regulators should not only operate at ML3 but work collaboratively through work-sharing arrangements and reliance.

In epidemic contexts, regulators in Africa have opportunities to use 'facilitated regulatory pathways' which enable them to use the opinions or decisions issued by other regulatory authorities and expedite approvals or authorisations for emergency use.⁵

Priorities

4. Develop regulatory best practices for emergency use contexts and pathways for reliance, including improving ability to rely on ML4 agencies

- a. Support AVAREF/AMRH to promote uptake of facilitated regulatory pathways⁶ that accelerate the assessment and approval of medical products by resource-limited authorities, by providing them with access to scientific assessments and opinions that inform a benefit-risk assessment for licensure and registration.
- b. Support promotion of the AVAREF emergency joint review process for clinical trials applications.
- c. Support AMRH to institutionalise the framework for emergency use authorisations for other products by SRAs/reference authorities used with the WHO Emergency Use Listing for COVID-19 vaccines.

5. Develop an RIMS that brings together national, regional and continental activities

- a. Support roll-out of digital RIMS, through the AMRH Technical Committee for RIMS, to enhance efficiency and effectiveness of work.

6. Support development of regulatory pathways for clinical trial approval, incorporating ethics review and ensuring data availability from trials

- a. Invest in linking databases for clinical trials and removing information gaps for a shared platform, building on prior efforts by the European and Developing Countries Clinical Trials Partnership (EDCTP)
- b. Support the African Vaccine Regulatory Forum (AVAREF) to expand their scope and review of complex trial designs such as adaptive trials and human challenge studies.

7. Build NRA capacity to ensure uptake of a standardised pharmacovigilance system

- a. Provide bilateral support to countries to build capacities to respond to adverse events reporting in other countries, including through broadening the scope and overall impact of the AMRH's 3S (Smart Safety Surveillance) initiative

8. Support WHO PQ products and develop best practices for supply chain oversight through strengthening NRA capacity

- a. Invest in WHO PQ's capacity to oversee cold chain equipment. The cold chain equipment and administration devices program is a critical aspect in WHO PQ but currently focuses on guidance and does not have the scale necessary to support vaccine deployment.
- b. Invest in cold chain equipment, develop Good Distribution Practice (GDP) and support uptake of guidelines across countries.

Objective 3:

All vaccine-producing countries to reach WHO Maturity Level-3 status

Context

To provide assurance about the safety and quality of medicines and vaccines in circulation, regulatory authorities perform a series of activities along the lifecycle of a product. Maturity Level-3 (ML3) is the minimum level of competency required to provide adequate regulatory oversight. The WHO assesses regulatory authorities using its Global Benchmarking Tool, which provides consistency and allows for structured Institutional Development Plans to be developed that, with help from the WHO and other partners, the regulatory authorities can implement and work towards to reach ML3. Egypt, Ghana, Tanzania and Nigeria have already attained ML3 status for medicines. However, to-date only Egypt and South Africa have this designation for vaccines and biological products.

All countries in the African Union (AU) need to have a functional regulatory authority that is compliant with the AU Model Law and engaging in regulatory reliance to maximise efficiencies. Countries wishing to produce vaccines for export need to be operating at ML3 for vaccines, converging with global standards which requires, among other factors, the ability to conduct lot release through National Control Laboratories or reliance, a requirement above and beyond what is required for oversight of small molecule generic therapeutic products.

Priorities

9. Prioritise regulators in manufacturing countries to identify address critical bottlenecks preventing them from achieving WHO Maturity Level-3/4 status

- a. Ensure countries fulfil their Institutional Development Plans (IDPs) created in partnership with WHO, working bilaterally with their national regulatory authorities or through the WHO, to address resource gaps and enable competent oversight of imported medical products by working towards ML3.
- b. Support specific anchor countries⁷ in becoming capacity strengthening partners for other countries in the region through activities such as twinning.

10. Support the development of an African network of regional reference laboratories to conduct lot release (and batch testing for small molecules) via a hub and spoke model

- c. Support scoping, design and roll-out of a network or hub-and-spoke model of regional reference laboratories.
- d. Develop legislative and governance structures to enable countries to conduct lot release and bioequivalence testing through reliance.
- e. Ensure RECs are sufficiently funded to conduct lot release and bioequivalence for non-Prequalified products.

3. List of acronyms

| | |
|---------------|---|
| AMA | African Medicines Agency |
| AMRH | African Medicines Regulatory Harmonisation Initiative |
| AU | Africa Union |
| AUC | Africa Union Commission |
| AVAREF | African Vaccine Regulatory Forum |
| RIMS | Regulatory Information Management System |
| LMIC | Low- and middle-income countries |
| NRA | National Regulatory Authority |
| PAC | Post-approvals changes |
| PAVM | Partnership for African Vaccine Manufacturing |
| PQ | Pre-qualification |
| REC | Regional Economic Community |
| WHO | World Health Organisation |

Call to action

We encourage funders to support improvement in public health and prosperity in Africa to support these areas, through the implementation of the Partnerships for African Vaccine Manufacturing Framework for Action and the African Medicines Regulatory Harmonisation Initiative workplan.

Endnotes:

1. African Union and Africa CDC launches Partnerships for African Vaccine Manufacturing (PAVM), a framework to achieve it, and signs two Memoranda of Understanding (MoUs).
2. Including new chemical entities; advanced therapy medical products, cell- and gene therapies and other complex biological products; in vitro diagnostics and devices; and blood products.
3. Key facilitators include roll-out of a professional development network (such as TOPRA, The Organisation for Professionals in Regulatory Affairs); the strategic implementation of AMRH's Regional Centres of Regulatory Excellence (RCOREs); and renewed efforts to increase domestication of the AU Model Law to ensure authorities can charge and retain user fees and can leverage these to offer adequate remuneration to support professional retention.
4. <https://www.who.int/news/item/29-04-2021-who-publishes-new-guidance-to-promote-strong-efficient-and-sustainable-regulatory-systems>
5. World Health Organisation, Regional Office for Africa. Overview: The AVAREF Joint Review Process. <https://www.afro.who.int/health-topics/immunization/avaref-joint-review-process>.
6. This includes the SwissMedic procedure for scientific advice and Marketing Authorisation for Global Health Products (MAGHP); the EU-Medicines4all (EU-M4all) procedure; the WHO Collaborative Registration Procedures (CRP) by Stringent Regulatory Authorities (SRAs) (including EMA and UK MHRA and over twenty African NRAs) and the WHO Pre-Qualification collaborative registration procedure.
7. Based on existing commitments and achievements in local production, funders may prioritise bilateral support to vaccine-producing countries including Algeria, Egypt, Morocco, Rwanda, Senegal, and South Africa, which have vaccine production facilities either in operation or in the pipeline, and consider support to a second tier of countries with small molecule/generic pharmaceutical production facilities and aspirations to become vaccines producers, including Ghana, Nigeria, Ethiopia, Tanzania, Kenya and Tunisia, or to the WHO in support of these national authorities. These authorities will be required to play an important role in providing technical support to the AMA.

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