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REGIONAL STRATEGY ON REGULATION OF MEDICAL PRODUCTS IN THE AFRICAN REGION, 2016–2025

Report of the Secretariat

EXECUTIVE SUMMARY

1. Medical products play a critical role in the management and prevention of diseases, thereby saving millions of lives globally. These benefits are compromised in the African Region by circulation of products of non-assured quality due mainly to weak regulatory capacity, particularly weak post-market surveillance. In addition, timelines in reviews and approvals of clinical trials, and registration of products delay access to medical products of good quality.

2. WHO has been supporting regulatory systems strengthening through several collaborative initiatives. These include the African Vaccine Regulatory Forum, the African Medicines Regulatory Harmonization initiative, harmonization projects in regional economic communities and the African Medicines Agency. However, countries still face challenges in governance of their regulatory systems, as well as low human, financial and technical resource capacity required for functional National Medicines Regulatory Authorities (NMRAs). Therefore, most NMRAs do not have the capacity to complement these regional efforts, leading to limited impact at country level.

3. This regional strategy therefore aims at ensuring that NMRAs are strengthened to effectively fulfil their mandate. It prioritizes interventions that will improve governance of regulatory systems, enhance collaboration, harmonize standards and facilitate implementation of joint regulatory activities and strengthen capacity of NMRAs to improve access to medical products of good quality.

4. The Regional Committee considered and adopted this strategy and the related resolution.

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ABBREVIATIONS

AMA	African Medicines Agency
AMRH	African Medicines Regulatory Harmonization
AU	African Union
AUC	African Union Commission
AVAREF	African Vaccine Regulatory Forum
EAC	East African Community
ECOWAS	Economic Community of West African States
GMP	good manufacturing practices
NEPAD	New Partnership for Africa's Development
NMRA	National Medicine Regulatory Authority
REC	regional economic community
RCOREs	Regional Centres of Regulatory Excellence
SADC	Southern African Development Community
SSFFC	substandard/spurious/falsely labelled / falsified/ counterfeit
UHC	universal health coverage
WHA	World Health Assembly
WAHO	West African Health Organization
WHO	World Health Organization

INTRODUCTION

1. Medical products include medicines, vaccines, diagnostics, blood and blood products, non-vaccine biologicals and medical devices, which contribute to saving millions of lives globally. Medical products must fulfil the international requirements of quality, safety and efficacy and be available, affordable, properly prescribed and used rationally. Functional regulatory systems ensure that medical products consistently meet international standards and are monitored from clinical evaluation to licensure and use. Therefore, regulatory systems are an essential component of the health systems, and strengthening them contributes to Universal Health Coverage (UHC) and to better health outcomes.

2. Regulatory systems strengthening is one of WHO's mandates.[1] The Sixty-third session of the WHO Regional Committee for Africa adopted a technical document on strengthening the capacity for regulation of medical products in the African Region[2] that emphasizes prioritization of regulation in countries and enhancement of the status of National Medicines Regulatory Authorities (NMRAs). The African Vaccine Regulatory Forum (AVAREF) was established by WHO as a platform for strengthening regulatory capacity for clinical trials and harmonization of regulatory practices through joint reviews.[3] WHO also supports initiatives in the Region to strengthen regulatory collaboration through joint assessments for Marketing Authorization.

3. In addition, regulatory personnel from countries have been trained to prevent and control substandard/spurious/falsely-labelled/falsified/counterfeit (SSFFC) medical products.[4] Countries in the Region are now reporting incidents on SSFFC medical products to the Global Surveillance and Monitoring System to protect public health.

4. Regulatory harmonization and convergence is promoted as an important component of regulatory systems strengthening in the Region. The African Medicines Regulatory Harmonization (AMRH) initiative is supporting NMRAs of regional economic communities (RECs) for harmonization of regulatory standards. In 2015, a roadmap for the establishment of the African Medicines Agency (AMA), agreed to by African Ministers of Health,[5] was endorsed by the African Union (AU) Executive Council. The roadmap sets key milestones for establishing AMA.

5. The regional strategy aims to build on achievements and regional efforts to provide a perspective for strengthening capacity of Member States to regulate medical products. It identifies the challenges to be addressed and proposes the targets that need to be reached through priority interventions.

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1 Resolution WHA67.20, Regulatory system strengthening for medical products. In Sixty-seventh World Health Assembly, Geneva, 19–24 May 2014. Resolutions, decisions and annexes. Geneva, World Health Organization, (WHA67/2014/REC/1; http://apps.who.int/gb/ebwha/pdf_files/WHA67/A67_R20-en.pdf. Accessed on 26 January 2016.

2 WHO Regional Committee for Africa, Sixty-third session Agenda item 11: Strengthening the capacity for regulation of medical products in the African Region, Brazzaville, Republic of Congo, 2–6 September 2013.

3 Maiga D, Akanmori BD, Chocarro L. Regulatory oversight of clinical trials in Africa: Progress over the past five years. Vaccine 2009; 27:7249–7252.

4 Resolution WHA65.19, Substandard/spurious/falsely-labelled/falsified/counterfeit medical products. In Sixty-fifth World Health Assembly, Geneva, 21–26 May 2012. Resolutions, decisions and annexes. Geneva, World Health Organization, (WHA65/2012/REC/1; http://apps.who.int/gb/ebwha/pdf_files/WHA65-REC1/A65_REC1-en.pdf#page=25. Accessed on 26 January 2016).

5 WHO/AUC, Commitment on the Establishment of the African Medicines Agency: Setting milestones towards its establishment, adopted by First African Ministers of Health meeting jointly convened by the AUC and WHO, Luanda, Angola, 14–17 April, 2014.

SITUATION ANALYSIS AND JUSTIFICATION

Situation analysis

6. Between 2005 and 2015, Member states with NMRAs in place increased from 40 (87%) to 45 (96%) and 16 (34%) of these are autonomous or semi-autonomous (unpublished data from WHO). In some countries, administrative entities empowered as regulators (for example, NMRAs) are units under departments of the ministry of health. While 40 (85%) countries have developed legislation for medical products, only 7 (15%) NMRAs are legally mandated to perform all the five critical regulatory functions.[6] In addition, legislations governing the mandate of NMRAs do not cover all medical products.

7. The capacity to perform specific regulatory tasks varies across countries.[7] The majority of NMRAs do not have the full capacity to regulate medical products due to persistent shortage of human, technical, logistical and financial resources. Only 15 (32%) NMRAs register medical devices or control their importation. Twenty-one countries[8] have in place full-time regulatory personnel conducting assessment of quality and preclinical data. However, capacity to assess clinical data and analyse them for decision-making is particularly lacking.

8. The timeline for clinical trial approval or marketing authorization of products is often over one year, still too long particularly for products with prior approval via standards recommended by WHO including WHO prequalification. The low performance of NMRAs in Africa contributes to people not being able to access good quality, safe and efficacious medical products.

9. Due to weak performance of NMRAs, there is increasing circulation of SSFFC Medical products in the African Region, which is currently leading in reporting to the WHO rapid alert system.[9] Surveys to date show quality failure rates of up to 28% in some cases.[10] Thirty four (72%) countries have quality control laboratories in place, at different stages of development and 21 (63%) of them are engaged in market surveillance.

10. Initiatives for regulatory harmonization and convergence are promoting the pooling of expertise and sharing of experiences among countries, and the RECs. However, the AVAREF and AMRH initiatives are not yet covering all RECs. The EAC, ECOWAS and SADC are now engaged in joint reviews for registration of medicines, and the same RECs practice mutual recognition of regulatory decisions. These initiatives are however not yet aligned so as to accelerate harmonization of regulatory requirements and regulatory convergence in the Region.

Justification

11. Despite the multitude of regulatory systems strengthening initiatives in the Region, there are still a number of challenges. These include inability to provide clinical trials oversight, marketing authorization, post-market surveillance for medical products, and the increasing

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6 WHO. Development of Country Profiles and monitoring of the pharmaceutical situation in countries. http://www.who.int/medicines/areas/coordination/coordination_assessment/en/. Accessed on 26 April 2016.

7 Strengthening Pharmaceutical Systems (SPS) Program. Safety of Medicines in Sub-Saharan Africa: Assessment of Pharmacovigilance Systems and their Performance. Submitted to the US Agency for International Development by the Strengthening Pharmaceutical Systems (SPS) Program. 2011. Arlington, VA: Management Sciences for Health.

8 Algeria, Botswana, Burkina Faso, Benin, Cameroon, Côte d'Ivoire, Democratic Republic of Congo, Ethiopia, Ghana, Kenya, Madagascar, Mali, Namibia, Nigeria, Senegal, Sierra Leone, South Africa, Tanzania, Uganda, Zambia and Zimbabwe.

9 WHO Surveillance and Monitoring System. http://www.who.int/medicines/regulation/ssffc/surveillance/en/ . Accessed on 20 February 2016.

10 WHO/EMP/QSM/2011.1, Survey of the quality of selected antimalarial medicines circulating in six countries of sub-Saharan Africa. http://apps.who.int/medicinedocs/documents/s17835en/s17835en.pdf. Accessed on 26 January 2016.

circulation of SSFFC medical products. This situation persists mainly because the NMRAs that are responsible for regulation at country level are lacking in some countries and are still weak to complement the initiatives developed at regional level to harmonize and pool regulatory expertise.

12. Adressing the above highlighted challenges related to weak clinical trials oversight, marketing authorization, post-market surveillance for medical products will require additional local resources, government leadership and commitment for NMRAs and alignment between harmonization initiatives. The technologies and tools available, including real-time information platforms represent new opportunities to reach the targets. Building on existing efforts, this regional strategy aims at providing guidance for strengthening regulatory systems at country level.

THE REGIONAL STRATEGY

Aim

13. The aim of the regional strategy is to guide Member States to strengthen NMRAs to fulfil their regulatory functions for improving access to medical products which meet international standards of quality, safety and efficacy.

Objectives

14. The main objectives are to:

(a) Improve governance of regulatory systems for medical products in Member States.

(b) Strengthen capacity of NMRAs to perform comprehensive regulatory functions.

(c) Increase implementation of regulatory functions.

(d) Reduce incidence of SSFFC medical products in the Region.

(e) Strengthen regional regulatory harmonization and convergence.

Targets

15. The strategy has targets to be reached in the African Region by 2018, 2020 and 2025, based on 2015 baseline data.

16. *Governance*

All Member States will have functional NMRAs with governing bodies and quality management systems in place by 2025.

17. *Capacity of NMRAs*

(a) Member States carrying out assessment of quality and preclinical data of medical products increased from 35 (75%) by 2020 to at least 45 (96%) by 2025.

(b) Member States regulating medical devices increased from 15 (32%) to at least 24 (51%) by 2020 and from 25 (53%) to at least 40 (85%) by 2025.

18 *Implementation of regulatory functions* by all Member States

(a) Member States to attain a timeline for assessment of clinical trial applications or marketing authorization applications of medical products of a maximum of six months by 2025;

(b) Member States to be regularly performing market surveillance of all medical products circulating in their market by 2018.

19. *Combating SSFFC medical products* by all Member States

(a) Member States to have access to certified or prequalified quality control laboratories by 2018;

(b) Member States to have functional pharmacovigilance systems by 2025;

(c) Member States to report regularly Individual Case Safety Reports to the WHO Collaborating Centre for International Drug Monitoring by 2018.

20. *Harmonization and convergence*

(a) The joint reviews of clinical trial applications performed by AVAREF Member States will have increased from 3 to 10 each year, starting in 2020.

(b) The RECs engaged in mutual recognition of regulatory decisions will have increased from 2 (29%) to 7 (100%) by 2018.

(c) The AMA is established and functional by 2018, and coordinating regulatory harmonization at continental level and promoting international regulatory information exchange by 2020.

Guiding principles

21. The principles that will guide the implementation of this strategy will be the following:

(a) **Good governance** to ensure transparency and accountability and supervisory mechanism that respect independent decisions of NMRAs based on current scientific evidence.

(b) **National ownership, leadership and stewardship** for a consistent increase of financial, human, infrastructural and other resources for strengthening national regulatory systems.

(c) **Partnerships and collaboration for pooling regulatory expertise and resources as well as** sharing **information** among NMRAs and relevant stakeholders.

(d) **Resilience** through evidenced-based decisions, implementation of strategies, appropriate levels of funding, good regulatory and financial management practices, adequate oversight, strong community participation and a multisectoral approach which are critical components of regulatory systems for medical products.

Priority interventions

22. **Improve governance** of regulatory systems so that NMRAs have responsibility to oversee regulation of all medical products, from research and development to use. Therefore, it is important to establsih NMRAs where they do not exist. For this purpose, NMRAs should be provided with adequate legal framework and mechanisms that ensure their independence and accountability in scientific decision-making. In order to ensure a continuous improvement in the

performance of NMRAs, they should be autonomous with independent governing bodies and quality management systems. A platform for policy dialogue and coordination among stakeholders will enhance government leadership in the area of regulation of medical porducts.

23. Good governance is esssential to ensuring that NMRAs are effective and credible with public confidence through:

(a) Enactment of comprehensive laws, establishment of appropriate regulations and policies to cover all medical products.

(b) Comprehensive assessment of their regulatory systems and development of mitigation plans to close identified gaps.

(c) Development and implementation of procedures that prevent conflict of interest of their staff and others such as external experts involved in regulatory activities.

24. **Strengthening capacity of NMRAs** for effective implementation of regulatory functions requires qualified human and adequate financial resources. A sustainable funding mechanism will be an asset for the NMRAs to recruit and maintain regulatory personnel. Adequate technical resources should be available to enable the NMRAs to rely on existing technologies, including real-time information platforms. Countries should prioritize institutionalization of training and postgraduate courses in regulatory sciences. This will create a critical mass of regulators capable of carrying out assessment of quality, preclinical and clinical data. The WHO Collaborating Centres and Regional Centres of Regulatory Excellence (RCOREs) should be used as training hubs in regulatory sciences.

25. To attract and retain adequate and skilled human resources for regulatory work, countries should engage in:

(a) Creation of clear career pathway and progression for personnel, and the provision of incentives to attract and retain them.

(b) Creation of a budget line and appropriation of funds for regulation of priority medical products within the national health budgets.

(c) Allocation of adequate financial resources to cover NMRAs' operations; and establishment of procedures for the collection and use of financial resources generated by the NMRAs.

(d) Improvement of access to available technologies and tools for real-time sharing of information, including computerization of regulatory procedures.

(e) Creation of a mechanism to track progress in implementation of critical regulatory functions and enforcement of regulatory decisions.

26. **Increasing implementation of regulatory functions** is deeply linked to the performance of the NMRAs and the range of products that are regulated. This should be enhanced through:

(a) Expansion of NMRAs' regulatory responsibility to cover all products.

(b) Purposeful funding to support local manufacturers to comply with requirements for good manufacturing practices (GMP) and WHO prequalification standards.

(c) Close collaboration with regional and international platforms for review of clinical trial applications, particularly for trials conducted in multiple countries.

(d) Fast-tracking marketing authorization of products with prior approval via standards recommended by WHO including WHO prequalification through collaborative procedures.

27. **Reducing the incidence of SSFFC medical products** is critical to maintain trust in health systems in the African Region. Premarketing authorizations and WHO prequalification of medicines are important to reduce failure rates on quality testing.[11] However, a functional pharmacovigilance system should be in place and all stakeholders involvement is required for intensifying the measures against SSFFC medical products. This will involve close collaboration between immunization programmes, national pharmacovigilance centres, NMRAs and other stakeholders to ensure monitoring of the safety of medical products.

28. In combating SSFFC medical products, Member States should also be engaged in:

(a) Taking appropriate measures to address the high cost of medicines that limits access, and the illicit entry of medicaments due to porous borders, while maintaining the integrity of the supply chain.

(b) Monitoring of alerts on SSFFC medical products to improve risk management for informed decision-making to strengthen market surveillance and protect public health.

(c) Joint prequalification of suppliers of medical products within the framework of harmonization projects of the RECs.

(d) Reliance on certified or prequalified quality control laboratories for systematic control of authorized medical products.

(e) Active investigation, prosecution and confiscation of the assets of those responsible for the manufacture and distribution of SSFFC medical products.

29. **Strengthening regulatory harmonization and convergence** will improve regulatory efficiency and avoid duplication of efforts**.** Therefore, initiatives supporting regulatory systems strengthening in the Region should prioritize harmonization and alignment of their interventions at country, REC and continental levels. This should be guided by their needs identified by the situation analysis and development of harmonization projects in RECs which are not yet implementing a harmonization programme. As part of these initiatives, the AMA will promote cooperation, harmonization and mutual recognition of regulatory decisions.

30. The NMRAs should take advantage of regional efforts such as AVAREF, AMRH and AMA to efficiently fulfil their mandate through:

(a) Recognition of decisions made by other NMRAs such as for GMP inspection of foreign manufacturing sites and marketing authorizations.

(b) Pooling of regulatory expertise through joint and assisted reviews of clinical trial applications and registration dossiers.

(c) Establishment of coordination mechanisms among RECs to harmonize their programmes, and subsequently those of Member States within the RECs.

(d) Expansion of AMRH initiative and AVAREF to cover all countries in the Region.

(e) Initiation of strong advocacy and communication strategy that enable AMA to elicit buy-ins.

[11] El-Jardali F, et al. Interventions to combat or prevent drug counterfeiting: a systematic review. BMJ Open 2015; 5: e006290. doi:10.1136/bmjopen-2014- 006290.

Roles and responsibilities

31. **Member States shall:**

(a) **Set the agenda for strengthening regulatory systems** for medical products in countries including assessment and ensuring government leadership in development and implementation of policies and plans.

(b) **Ensure availability of adequate human, financial and technical resources** for the NMRAs' operations.

(c) **Ensure the creation of a budget line and appropriation of adequate funds** for regulation of medical products within the national health budgets.

(d) **Participate in regulatory** harmonization and convergence initiatives to share best practices and pool regulatory expertise.

(e) **Create mechanisms** to track progress and generate evidence on regulation of medical products in Africa.

(f) **Establish effective information systems** for implementation of strategies to ensure adequate market surveillance of medical products.

(g) **Develop, review and update their medicine legislation** based on the African Union Model Law on medical products regulation.

32. ***The World Health Organization and other partners shall*:**

(a) **Support countries in development and implementation of policies and plans aimed at** regulatory systems strengthening.

(b) **Support countries to** adopt and adapt evidence-based policies, WHO norms and guidelines, and align their regulatory practices with international recognized standards.

(c) **Support initiatives and networks** for harmonization and convergence of regulatory practices, including establishment of the AMA.

(d) **Support countries to establish** their pharmacovigilance systems**.**

(e) **Support countries to adopt tools** for monitoring progress on regulation of medical products.

(f) **Support countries to develop** regulatory capacity for food and related products.

RESOURCE IMPLICATIONS

33. Each country should allocate adequate resources from their annual national health budget for the implementation of this strategy. The cost of WHO support to Member States in implementing this Strategy for the next decade is estimated at US$ 40 million.

MONITORING AND EVALUATION

34. A comprehensive monitoring and evaluation tool and framework, with a set of indicators for monitoring both region-wide and country targets, will be developed by 2017. These shall be used by WHO to evaluate implementation of the strategy every two years. WHO will support Member States to regularly review the implementation of the strategy.

35. A progress report on implementation of the regional strategy will be presented to the WHO African Regional Committee every two years, starting in 2018.

CONCLUSION

36. Despite the progress made by countries in regulating medical products in the WHO African Region, several challenges remain. It is expected that this strategy will ensure that Member States have legally-mandated and functional NMRAs to regulate and provide access to medicines which meet international standards of quality, safety and efficacy for all who need them, while promoting harmonization across the RECs and leading to operationalization of the AMA.

37. The Regional Committee considered and adopted this strategy and the related resolution.