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WHY AFRICAN COUNTRIES SHOULD PRIORITIZE THE REGISTRATION OF MATERNAL, NEWBORN, AND CHILD HEALTH MEDICAL PRODUCTS

A CALL TO ACTION

November 2024

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This document is made possible by the generous support of the American people through the US Agency for International Development (USAID) Contract No. 7200AA18C00074. The contents are the responsibility of Management Sciences for Health and do not necessarily reflect the views of USAID or the United States Government.

WHY AFRICAN COUNTRIES SHOULD PRIORITIZE THE REGISTRATION OF MATERNAL, NEWBORN, AND CHILD HEALTH MEDICAL PRODUCTS

A CALL TO ACTION

A Call to Action to Improve Maternal, Newborn, and Child Health Product Registration

- Barriers to product registration, ranging from an onerous or expensive registration process to a lack of advocacy for better registration policies, contribute to inadequate access to lifesaving products.
- Many opportunities exist for different stakeholders to reduce such registration barriers by investing in legal, organizational, and procedural changes, with national regulatory authorities playing a critical role. However, financial and/or technical contributions from governments, donors and implementing partners, manufacturers, research institutions, and even civil society are also vital to these efforts.
- One improved action can contribute to an enabling environment for registration that improves access to maternal, newborn, and child health products.

Despite global progress in reducing maternal and child mortality rates, both are still unacceptably high in low- and middle-income countries (LMICs). In fact, in 2020, Sub-Saharan Africa and Southern Asia alone accounted for 86% of maternal deaths worldwide and more than 80% of the under-five deaths.[1] Gaps in the quality of care—including poor access to medicines, vaccines, and medical devices—contribute significantly to illness and death among women, newborns, and children.

National Regulatory Authorities (NRAs) perform the fundamental role of ensuring the efficacy, safety, and quality of medical products that circulate in national markets, including those used for maternal, newborn, and child health (MNCH). One of their primary functions is to provide marketing authorization, or registration, for a medical product after evaluating the manufacturer's data. Although the registration process rests within the NRA, many other stakeholders play important roles in a product's access. For example, manufacturers can be deterred from submitting their products to the NRA for registration by the typically low profit margins of MNCH products and an onerous or expensive NRA product registration process—an assessment of nine countries (7 in Africa and 2 in Asia) by the US Agency for International Development (USAID) Medicines, Technologies, and Pharmaceutical Services (MTaPS) Program[2] identified registration timeframes from six months to four years due to NRAs' inadequate funding and human resources and the legal constraints to reliance on external regulatory decisions. As a result, some countries did not have critical MNCH products registered, such as oxytocin 10-IU/ml injections. In addition, other factors strongly influence access to

[1] UNICEF. 2023. Maternal mortality. https://data.unicef.org/topic/maternal-health/maternal-mortality/.
[2] Briggs J, Kikule K, Walkowiak H, Guzman J. 2021. Improving access to maternal, newborn, and child health products in low- and middle-income countries: considerations for effective registration systems. Arlington, VA: Management Sciences for Health, Inc. Available at: https://www.mtapsprogram.org/our-resources/improving-access-to-maternal-newborn-and-child-health-medical-products-in -low-and-middle-income-countries-considerations-for-effective-registration-systems/.

MNCH medical products; for example, ministries of health struggle with inaccurate product demand forecasts, financial limitations, and inadequate procurement procedures that lead to stockouts. Also, policy makers often lack the data to create policies that facilitate efficient registration, procurement, and distribution processes. Finally, MNCH medical products are not always used appropriately by health care providers and patients, such as not adhering to treatment guidelines or not taking the full dose prescribed.

As these examples highlight, many factors affect access to quality MNCH medicines and other health products; however, this document pinpoints the actions that stakeholders can take to increase registration specifically, because limited product registration—especially for certain formulations—increases the likelihood of shortages or stockouts, particularly if a product has manufacturing problems or is withdrawn from the market. To address these critical issues, health stakeholders must take immediate action to overcome barriers to the timely marketing authorization of MNCH medical products.

This, therefore, is a call to action to health stakeholders on the African continent, including NRAs, ministries of health, donors, development partners, and civil society, to prioritize the registration of MNCH medical products as part of a strategy to provide access to the products that are essential for effective MNCH services and averting preventable deaths.

COMPELLING EVIDENCE ON WHY AFRICAN COUNTRIES SHOULD PRIORITIZE ACCESS TO MNCH MEDICAL PRODUCTS

The UN Commission on Life-Saving Commodities for Women and Children published an eye-opening assessment in 2012 illustrating how many lives are lost unnecessarily for lack of affordable health products; for example, simple treatment of pneumonia with amoxicillin and of diarrhea with oral rehydration solution and zinc could save more than 3.3 million children over five years.[3] Hypoxia, postpartum hemorrhage, and eclampsia are also leading killers of newborns and mothers—deaths that are easily preventable or treatable.

Investing less than $2.6 billion in 13 MNCH commodities—only $8 per person—would save the lives of more than ***6 million mothers and children*** in five years.

Lack of donor or private-sector investment. Compared to high-profile diseases such as HIV/AIDS, malaria, and TB, where significant funding goes to procurement of key commodities, donors contribute little to the procurement of MNCH medical products, leaving those purchases reliant on insufficient public-sector funds coupled with limited private-market investment in local manufacturing. In northern Nigeria, for example, where eclampsia was associated with up to 40% of maternal deaths, there are no local magnesium sulfate manufacturers.[4] In addition to low margins, manufacturers are also unwilling to invest in the resources needed to register MNCH products due to unpredictable market demand and the fragmented market for MNCH medical

[3] UN Commission on Life-Saving Commodities for Women and Children. 2012. Commissioners' report: September 2012. New York: United Nations. Available at: https://www.unfpa.org/sites/default/files/pub-pdf/Final%20UN%20Commission%20Report_14sept2012.pdf.
[4] UNFPA. 2012. Medicines for maternal health: key data and findings. Available at: https://www.unfpa.org/sites/default/files/pub-pdf/Key%20Data%20and%20Findings%20Maternal%20Health%20Medicines-FINAL.pdf.

products. At a 2022 SADC/ZaZiBoNa[5] regional forum for NRA officials and MNCH product manufacturers led by MTaPS, manufacturers cited several factors that prevent them from using regional reliance mechanisms to register MNCH products, including:

- Lack of knowledge or awareness of regional or national regulatory requirements
- Language disparities
- High registration fees
- Unclear dossier approval timelines

Questionable quality products in circulation. Pharmaceutical regulatory inefficiencies and limited investment to ensure that mothers and children on the African continent have access to high-quality, safe, and effective MNCH products can have fatal consequences, such as the recent cases of death of children due tainted cough syrup.[6] The World Health Organization (WHO) reported that 10.5% of medical products circulating in LMICs are substandard or falsified,[7] and up to 70% of medical devices in LMICs are partially or entirely inoperable,[8] often because specifications do not meet requirements. These deficiencies impede service delivery and patient outcomes, particularly for MNCH medical products, which require unique regulatory considerations. The African Medicines Regulatory Harmonization (AMRH) initiative established in 2009 to fight the proliferation of sub-standard and falsified medical products in Africa, supports African Union member states in building effective regulatory systems through harmonization and capacity-building. Its primary focus is on developing harmonized technical and procedural guidelines for the registration of medical products. The AMRH also facilitates Good Manufacturing Practice (GMP) inspections, quality management systems, clinical trial oversight, safety monitoring, and information management systems. This is achieved through a multistakeholder governance framework that engages NRAs, Regional Economic Communities, and development partners.

Low-priority registration leads to shortage of quality-assured MNCH products. Despite the knowledge of the relative simplicity and affordability of saving lives, compared with other medicines, countries still fail to prioritize the registration of lifesaving MNCH medical products, leaving them with an inadequate number of authorized products that are susceptible to stockouts. Furthermore, in countries with weak regulatory enforcement, the market may fill those gaps with substandard or falsified products. PEPFAR and the US Food and Drug Administration product approval processes, along with the WHO Prequalification of Medicines Programme (PQP), ensure access to quality antiretrovirals, which has been a critical contribution to fighting the AIDS epidemic[9]; however, the WHO PQP does not include most MNCH products, which reduces the availability of the data that countries rely on to procure high-quality medicines and commodities.

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[5] SADC (Southern African Development Community) has 16 member states. ZaZiBoNa is a collaboration between NRAs in Zambia, Zimbabwe, Botswana, Namibia, South Africa, Tanzania, Democratic Republic of Congo, Mozambique, and Malawi (active countries) as well as Eswatini, Angola, Seychelles, Madagascar, Comoros Islands, Lesotho, and Mauritius (nonactive).
[6] https://www.who.int/news/item/23-01-2023-who-urges-action-to-protect-children-from-contaminated-medicines
[7] https://www.who.int/news/item/28-11-2017-1-in-10-medical-products-in-developing-countries-is-substandard-or-falsified
[8] Malkin R, Keane A. Evidence-based approach to the maintenance of laboratory and medical equipment in resource-poor settings. Med Biol Eng Comput 2010;48:721–6. Available at: https://doi.org/10.1007/s11517-010-0630-1.
[9] Chahal HS, Capella P, Presto R, et al. Impact of the US Food and Drug Administration registration of antiretroviral drugs on global access to HIV treatment. BMJ Global Health 2018;3:e000651. https://doi.org/10.1136/bmjgh-2017-000651.

To save lives by improving access to high-quality MNCH commodities, global health partners and countries' health authorities, including ministries of health and NRAs, must take deliberate steps to prioritize MNCH medical product registration.

CALL TO ACTION

As mentioned, there are many opportunities to facilitate the product registration process that would motivate suppliers of the quality-assured MNCH medicines needed to implement WHO recommendations, such as oxytocin and magnesium sulfate, to enter national markets. While NRAs are the cornerstone of the registration process, other stakeholders play critical roles; for example, NRAs cannot register a product that a manufacturer has not submitted, but this situation is unlikely to improve without creating a more enabling environment for investing in MNCH products. Civil society can advocate for policy changes that contribute to a more enabling environment. This call to action describes the specific steps that all stakeholders can take to leverage those opportunities and invest in legal, organizational, and procedural changes.

NRAs should:

- Work with ministries of health to establish policies, regulations, and guidelines to prioritize MNCH product registration that will ensure their access in the national health system. MNCH medicines should be added to the list of other priority health program medicines, such as those for malaria, TB, HIV/AIDS, and cancer, which are subject to accelerated evaluation to expedite market entry and contribute to saving lives.
- Consider waiving or reducing registration fees for key MNCH products to further encourage manufacturers to register a variety of quality products, thereby helping to prevent stockouts.
- Align their regulatory systems with international best practices, such as use of Good Review Practices and quality management systems, to ensure the efficient review of dossiers that meet regulatory requirements.
- Establish mechanisms to register all MNCH products, including donated medical items and those acquired through alternative procurement mechanisms, ensuring that the products are available on publicly accessible databases of registered MNCH products.
- Collaborate with regional platforms to review regulatory frameworks for marketing authorization to ensure that countries can take advantage of reliance and recognition mechanisms to adopt decisions made by reference NRAs, including quality Good Manufacturing Practices inspection outcomes. These mechanisms include the WHO collaborative registration procedure and prequalification program, facilitated registration pathways, and advanced regulatory authority assessments.
- Streamline registration processes and provide predictable approval timelines using regional and continental reliance networks and frameworks, such as those of the Southern African Development Community/ZaZiBoNa, the East Africa Community, and the Economic Community of West African States Medicines Regulatory Harmonization initiative, and by taking advantage of work sharing and joint review activities to register MNCH medicines.
- Adopt a harmonized process (e.g., Common Technical Document format for submission of product data and information[10] or ZaZiBoNa evaluation procedure) to clarify manufacturer expectations.

[10] Common Technical Document is a standard set of specifications for an application dossier for the registration of medicines.

- Actively participate in medical product-related harmonization initiatives and work to strengthen regional reliance mechanisms, such as the continental harmonization through the AMRH initiative, of marketing authorization tools, procedures, and guidelines that will pave the way for increasing access to quality, safe, and effective MNCH products in Africa.
- Establish electronic systems to better manage and track registration applications for essential medicines, including those for MNCH.
- Put in place realistic requirements for renewing registration status, which is a key factor in maintaining availability of quality MNCH products on the market.
- Implement post-market surveillance for MNCH medical products to deter the spread of substandard and falsified products.

Governments and ministries of health should:

- Allocate appropriate budgets for the regulation of medical products, including those for MNCH.
- Domesticate the AU Model Law on Medical Products Regulation. The Model Law provides a comprehensive template for regulatory harmonization of medical products across the continent to improve access to medical products that are safe, efficacious, and of assured quality.
- Ratify the African Medicines Agency (AMA) Treaty which builds on the AMRH initiative and came into force in 2021, to address the fragmentation in regulatory decision-making that compromises the quality of medical products and delays the introduction of new products. AMA will operate as a specialized agency of the African Union, and aims to streamline and harmonize regulatory processes, thereby accelerating access to essential medical products throughout Africa.
- Develop and implement local pharmaceutical manufacturing strategies and policies to help satisfy public health needs by diversifying the sources of MNCH products, where economically feasible.
- Establish an essential medicine list that includes priority MNCH products to align with the country's health care priorities and assess the list's implementation and impact over time. Additionally, conduct sensitization campaigns to inform health care providers about the updated list and encourage tracking of the use and accessibility of MNCH medical products.
- Explore the possibility of broadening the range of MNCH medical products procured from agencies such as UNICEF and UNFPA to expand access to competitively priced products of assured quality.
- Foster sustainable private-public partnerships by establishing forums for continuous dialogue and collaboration to enhance import, export, manufacturing, and procurement of MNCH medical products through a well-defined regulatory framework.

Donors and development partners should:

- Provide technical and financial support to LMICs to follow health policies, guidelines, and regulations that prioritize the registration of MNCH pharmaceuticals.
- Help NRAs to develop institutional development goals and appropriate financing mechanisms that enhance registration of MNCH products.
- Support regional and continental platforms such as the AMRH Initiative and the AMA once fully operationalized to prioritize and streamline registration of MNCH medicines and to advocate for mutual recognition of country approvals through harmonization.
- Review and support expansion of the list of MNCH items eligible for WHO PQP approval.

- Engage governments, health care professionals, researchers, and patient advocates to gather feedback on identifying priority MNCH medical products. This input will support regulators in using robust evidence to prioritize the registration of MNCH products.

Manufacturers should:

- Harness existing regulatory procedures for expedited product registration, including submitting applications through continental and regional platforms and participating in the WHO collaborative registration procedure process.
- Ensure the quality and safety of MNCH medical products in adherence to international quality standards and regulations to guarantee these products' effectiveness and patient safety.

Research institutions should:

- Produce valuable evidence and insights that support sound decision making about registering specific MNCH medical products based on public health priorities.

Civil society should:

- Engage in policy dialogue and advocacy to support regulatory systems strengthening as well as harmonization of medicines regulation.
- Advocate for regulatory policies to improve registration systems that help increase access to safe and quality-assured medical products to improve the health of vulnerable populations such as mothers, newborns, and children.
- Share information about best practices and knowledge to enhance regulatory capabilities.
- Advocate for allocation of resources to support NRAs and ministries of health.