

Strengthening regulatory systems globally: a crucial step towards pandemic preparedness and response

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The focal point of the United Nations (UN) Sustainable Development Goal 3 is Universal Health Coverage (UHC), meaning all people should have access to quality health services, including access to safe, effective and quality assured medical products, without facing any financial hardship.¹ However, the WHO estimates a 10% prevalence of poor-quality medicines in low-income and middle-income countries (LMICs) which can be partly attributed to a lack of stringent oversight by weak or absent regulatory authorities.² With the onset of the COVID-19 pandemic, several countries reported significant disruptions to essential health services, including access to medical countermeasures (MCMs). Lessons learnt from the pandemic have highlighted the need to enhance regulatory preparedness for public health emergencies, as part of overall UHC strengthening efforts, to ensure timely access to quality medical products. The cohesion between UHC and pandemic preparedness is embedded in the fact that pandemics do not discriminate, affecting all geographies and socioeconomic statuses.³

Regulatory systems support UHC through the evaluation and approval of medical products, post-market surveillance, inspections, communication with stakeholders and legal enforcement of regulations. These functions enable access to safe, effective and quality-assured medical products and can only be achieved through universal adoption of regulatory systems.⁴ During an emergency, regulatory systems can expedite reviews of MCMs to ensure rapid availability; this must be coupled with effective communication to address manufacturer and stakeholder inquiries, connecting healthcare professionals, patients and the public and providing critical information about medical products and their regulation. A strong, pandemic-prepared regulatory system will not only improve access to safe, quality medical products but also public

SUMMARY BOX

- ⇒ The COVID-19 pandemic has highlighted significant gaps in global access to drugs, vaccines and other essential medical countermeasures (MCMs), with many low-income and middle-income countries (LMICs) struggling to get their populations vaccinated due to the inequities in vaccine availability and distribution.
- ⇒ Lessons learnt from the global response have highlighted the need to establish and strengthen vaccine manufacturing capacities, particularly in LMICs to aid in global health security.
- ⇒ Although much emphasis has been placed on establishing, strengthening and diversifying global vaccine manufacturing capacity, few have called for the need to strengthen regulatory systems, which are crucial in overseeing the development and manufacturing of MCMs, as part of overall pandemic preparedness and response efforts.
- ⇒ This commentary provides an overview of the key role of medical product regulatory systems during a health emergency crisis, such as pandemics, and provides concrete justifications for the need to simultaneously strengthen national and regional regulatory systems, especially in LMICs, to ensure access to safe, effective and quality MCMs.
- ⇒ This commentary aims to highlight the need to include regulatory system strengthening, as part of global and national health security and pandemic preparedness frameworks, to ensure that future responses to pandemics close the inequities in vaccine access and availability observed during the COVID-19 pandemic.

confidence in their healthcare system and government.⁵

During the pandemic, the benefits of effective regulatory systems were recognised in countries' ability to rapidly authorise new products, repurpose treatments and clinical trial oversight for vaccines, resulting in faster availability of life-saving countermeasures. For instance, the United States Food and Drug Administration (FDA) demonstrated unprecedented progress in



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pandemic response issuing the first Emergency Use Authorization (EUA) for vaccine distribution in the USA. Additionally, FDA's heightened monitoring and surveillance efforts were critical in identifying safety concerns due to the various countermeasures being used to treat or prevent COVID-19. For example, through monitoring and surveillance, the FDA identified safety concerns regarding the use of hydroxychloroquine and chloroquine as a treatment for COVID-19 and released a Drug Safety Communication, as a result, to alert the public of the risks.⁶ Similarly, the European Union's European Medicines Agency enabled the region to rapidly respond to the pandemic through co-ordination activities to identify and mitigate MCM shortages between countries when global supply chains were disrupted.⁷ Shortages in medical products directly impede access to essential MCMs and negatively impact the overall healthcare system. Weak regulatory systems can suppress medical innovation, heighten the costs of countermeasures and leave countries vulnerable to disparate regulatory pathways and falsified or substandard products. Strengthening regulatory systems to become multifaceted and flexible will help the world progress towards UHC and become better prepared for pandemics.

The essential role of regulatory systems in ensuring access to life-saving medical products has been recognised. Indeed, the WHO assists countries in strengthening their national regulatory systems through the Global Benchmarking Tool and evaluating their 'maturity' on a scale of 1–4; a 'maturity level 3' represents the minimum target for most national regulatory systems which are considered as 'stable, well-functioning and integrated regulatory systems'.^{8 9} However, estimates from WHO revealed that only 26% of Member States have functioning national regulatory authorities⁹ and only seven national regulatory systems from LMICs have achieved maturity level 3 (Egypt, Ghana, India, Indonesia, Nigeria, Tanzania and Vietnam).^{2 10} These numbers are notably concerning considering the COVID-19 pandemic exposed significant inequities in the global health ecosystem such as unequal access to life-saving medical products and the detrimental impact on countries with weak or non-existent regulatory systems. Those countries without well-functioning regulatory systems were largely dependent on the WHO, the COVID-19 Vaccines Global Access (COVAX) Facility or on bilateral donations for medical products, significantly delaying their access and contributing to poor health outcomes.

The stark disparity in access to essential MCMs during the COVID-19 pandemic generated political will and country commitments to strengthen local in-country medicine and vaccine manufacturing capacity. Indeed, in September 2022, the African Union called for a 'New Public Health Order for Africa' to drive global health security and sustainable

health outcomes, with efforts to expand the manufacturing of vaccines, diagnostics and therapeutics in Africa as a top priority.¹¹ However, to ensure the effectiveness of manufacturing and pandemic preparedness and response strengthening, it will be crucial to simultaneously bolster the regulatory systems that underpin such efforts due to the following reasons. First, by strengthening effective regulatory functions and systems, including medicine dossier evaluation, product registration, clinical trial oversight, regulatory inspections, post-market surveillance and EUAs, countries can ensure a resilient medicine and vaccine supply chain. This reduces reliance on bilateral or multilateral donations during crises and strengthens country ownership of the response, aiding in timely access to essential MCMs. Second, building effective national or regional regulatory systems helps ensure quality throughout product development and manufacturing processes, which promotes access to safe and effective medical products and reduces the circulation of falsified and substandard medicines. This in turn generates confidence and public trust in the country's health system and medical products, which can lead to greater public compliance with public health measures and uptake of MCMs.^{5 12 13} Third, the presence of effective national or regional regulatory health agencies with clear regulatory pathways can streamline manufacturer interactions with regulatory agencies, ensuring strong alignment and efficient progress from medical product development to manufacturing to market access with respect to the national or regional context. This is critical during health emergencies, where close co-operation with regulatory authorities during drug or vaccine development is required to accelerate in-country product availability through pathways such as EUAs. Lastly, vaccines, drugs and other medical products produced in manufacturing facilities that are under the regulatory oversight of functional regulatory systems can be exported, procured and purchased by organisations such as Global Alliance for Vaccination and Immunization (GAVI), UN agencies or by other countries. Since these MCMs will be considered safe and effective for public use, the export of MCMs from producing economies can stimulate private sector investment in MCM manufacturing, creating a sustainable financing arrangement supporting local manufacturing efforts in countries. Additionally, by diversifying sources of MCM procurement during pandemics and other public health emergencies, the detrimental effects of vaccine nationalism and export restrictions can be mitigated. This situation was seen during the COVID-19 pandemic wherein vaccine export restrictions significantly delayed the delivery of vaccines from the Serum Institute of India to the COVAX Facility, leaving lower-income economies without access to life-saving COVID-19 vaccines.^{14 15}

Strengthening the overall regulatory ecosystem to ensure a timely and reliable supply chain of safe and effective MCMs involves multiple elements such as establishing the legal and policy framework within which regulatory authorities can function, improving overall infrastructure such as laboratory infrastructure, digital infrastructure and information management systems, workforce strengthening and retention, establishing financing arrangements and incorporating transparency in regulatory processes. In addition to WHO's efforts to improve regulatory system strengthening through the Global Benchmarking Tool,⁸ the United States Pharmacopeia plays a key role to strengthen national regulatory functions to help achieve regulatory maturity in LMIC countries.¹⁶ However, due to the immense financing requirements for establishing and maintaining regulatory systems, competing priorities within countries and other structural disadvantages, government support and political will to invest in regulatory systems can vary considerably. In such situations, the establishment of and investment in regional regulatory systems can play an important role in supporting access to quality, safe and effective medical products in a particular geographic region. For example, the Caribbean Regulatory System serves as the regulatory unit for 15 countries in the Caribbean region forming the Caribbean Community.¹⁷ Additionally, the ratification of the African Medicines Agency (AMA) Treaty in 2019 by countries in the African Union to establish the AMA is another step towards ensuring access to medical products; however, as of February 2023, only 23 countries had ratified the treaty,¹⁸ and additional country commitments to support the AMA are strongly warranted to ensure a strong and resilient regional regulatory system in the African continent. In the aftermath of the COVID-19 pandemic, countries are likely to implement significant reforms in their pandemic preparedness and response plans such as outbreak surveillance systems, vaccine and therapeutic manufacturing capacities and investment in health system strengthening. By prioritising the establishment and maintenance of regulatory system capacities as part of the overall health security and pandemic preparedness framework, countries can be better prepared to respond to the next pandemic. Without adequate leadership, resources and financial arrangements, regulatory systems are incapable of providing equitable access to quality assured MCMs and the most disadvantaged groups will continue to be hit hardest by pandemics and other public health crises.

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