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Strengthening Health Products Regulatory Systems to Enhance Access to Quality Health Products in the Asia-Pacific

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Abstract

Asia-Pacific is a region of fast growing opportunity for biomedical research and marketing of new health products by pharmaceutical and medical device companies. While national regulatory authorities have the responsibility to ensure timely access to innovative, effective and safe therapies, many face capacity and resource constraints that limit their ability to guarantee a robust regulatory system capable of licensing and monitoring novel medicines and medical devices, and tackling substandard and falsified products. The region's regulatory landscape is also fragmented with country specific requirements that create barriers to entry for new health products. To help address these challenges, the Duke-National University of Singapore's (Duke-NUS) Centre of Regulatory Excellence (CoRE) was established in 2014 with the strategic goals to strengthen the region's regulatory agencies through capacity development, regulatory convergence, work sharing, and nurturing networks for leadership and systems innovation. A smart and mature regulatory system in Asia-Pacific is pivotal to promote biomedical innovation and enhance equitable, sustainable access of populations to quality health products that are safe and efficacious.

Keywords

Regulatory systems strengthening; regulatory convergence; regulatory excellence; Asia-Pacific; regulatory innovation.

Background

As standards of living and the quality of health care rise across the Asia-Pacific region, so does demand for pharmaceuticals, medical devices and other medical commodities (broadly referred to as health products). The region's spending on healthcare is expected to grow by an annual average of 6.6% from 2015 to 2019, making it one of the fastest growing medicines and medical devices markets globally.^{1,2} Reflective of these trends, a rise in the quantity, diversity and complexity of applications filed across multiple jurisdictions for marketing authorisation of health products can be anticipated.

This surge in the number of products entering the Asia-Pacific market should ideally be accompanied by a greater regulatory preparedness at the national and regional level to ensure timely access to effective and safe therapies. However, outside the high-income Asia-Pacific countries such as Japan, Singapore and South Korea, many of the region's medicines and medical device national regulatory agencies (NRAs) are neither adequately structured nor resourced to promote optimal access to health products. Companies planning to introduce new health products into this market thus need to manage the varying levels of investment risks and rewards that arise from this regulatory heterogeneity.

In a project supported by the Asian Development Bank, the Centre of Regulatory Excellence (CoRE) at the Duke-National University of Singapore Medical School (Duke-NUS) conducted an assessment of regulatory systems gaps in South-East Asian member states of the Greater Mekong Subregion.^{3,4} Key issues identified included the lack of sufficient qualified staff and sustainable financing. Whereas the U.S. Food and Drug Administration, for example, has more than 3,000 staff in its Center for Drug Evaluation and Research alone (out of a 14,000-strong workforce), NRAs in South-East Asia tend to have staff strengths ranging from only 30 to 300, but are still responsible for the full spectrum of pre- and post-marketing activities.⁵

NRAs in the region are also limited by inappropriate legislative and policy frameworks, lack of autonomy to hire necessary staff, and inadequate enforcement capabilities. Unlike the European Union, Asia-Pacific does not have centralised or uniform assessment processes for marketing authorisation. Interpretation of international standards varies among NRAs, creating undue regulatory burden for marketing authorisation applicants. Without greater coordination and collaboration among national NRAs and partner stakeholders, the overall effectiveness and efficiency of the regional regulatory system will continue to be constrained.

Why regulation matters in the context of Asia

A robust regulatory system enables safe, tested and reliable supplies of health products to be released into the health system. This is especially important in Asia-Pacific, where the expansion of universal health coverage (UHC) - equitable access to quality health care without undue financial burden - is predicted to occur in tandem with the growing prevalence of chronic diseases that comes with population ageing.² The ability of UHC to effectively improve health outcomes and fuel economic prosperity hinges upon reliable sources of safe and effective health products reaching the market free from unwarranted bureaucratic delays.⁶ When regulatory systems are weak and demand is strong, resulting market distortions foster an underground market for unregulated supplies of medicines and medical devices, including substandard and falsified products, and encourage criminal activities and corruption. These distortions result in poor healthcare systems, constrained therapeutic options and under-detection of serious adverse events.

At the same time, in line with international trends, regional perspectives of health products regulation and inter-relationships with other sectors are changing. Although the fundamental role of NRAs continues to be the protection of public health, it is increasingly acknowledged that risk-based and innovative regulation can be a significant enabler in supporting the development of dynamic and sustainable health care systems.^{7,8} Overly cautious regulation can restrict access to needed therapeutic commodities and may negatively impact quality of life and socio-economic development. Globally, mature NRAs are developing new regulatory paradigms that promote a

balance between public health protection and innovation. Such regulators aim to be relevant, responsive and open to appropriate collaboration with different stakeholders in the regulatory ecosystem.

Asia-Pacific regional regulatory systems challenges

The regulatory landscape in Asia-Pacific, particularly in the developing economies, faces three major challenges:

1. Insufficient regulatory knowledge and capacity

The workforce inadequacies that constrain NRAs stem from a dearth of regulatory training programmes and a lack of recognition for this professional skillset.^{9,10} Most training happens on the job, and the inadequacy of formal training opportunities affect the quality and timeliness of regulatory decisions.¹¹ With growing demand for more advanced therapeutic options amongst emerging Asia-Pacific economies, local regulatory capacity needs to be ramped up to ensure that populations have safe, timely access to new health products. As global supply chains for health products expand, regulators would benefit from joint capacity building and technical cooperation to effectively and efficiently carry out their responsibilities across product life cycles.¹²

2. Fragmented national regulatory requirements

Regulatory systems and authorities across different jurisdictions are at different levels of maturity and still evolving. Despite the availability of regional regulatory guidelines such as the Association of South-East Asian Nations (ASEAN) Common Technical Dossier and Requirements, NRAs across the region still tend to impose country-specific requirements, over and above what is specified in regional guidelines.^{13,14} Companies attempting to penetrate Asia-Pacific markets face the challenges of keeping abreast with differing requirements and finding appropriate expertise to manage this diversity.

3. Lack of regulatory science and policy innovation

Most NRAs are not appropriately incentivised to take informed risks in innovating or implementing new regulatory paradigms. They may not be sufficiently exposed to newer regulatory systems initiatives, such as adaptive licensing and reliance, to appreciate what this would require within their local contexts, nor possess the requisite strategic and advocacy skills to propose appropriate models for implementation to higher levels of government.

Addressing challenges to strengthen regional regulatory systems

Various initiatives to address capacity issues have been attempted in the past, including from major non-governmental organisations and partners such as the World Health Organization (WHO) and the Asia-Pacific Economic Cooperation (APEC) forum. However, this has proven difficult to sustain without established neutral organisations or platforms committed to coordinating and promoting collaboration in capacity building and policy innovation.

The significant need for capacity development of regulatory professionals was highlighted to Singapore's Economic Development Board in 2013, when several large multi-national companies looking to establish or expand their Asia-Pacific presence encountered major difficulties in finding qualified staff. This prompted the provision of seed funding for the establishment of CoRE at Duke-NUS in Singapore in 2014. With a wider interest in the Asia-Pacific region but a specific focus on South-East Asia, the centre aims to enhance regulatory capability and scientific excellence for health products through three strategic areas: education and training, applied research, and policy innovation. CoRE provides a neutral academic platform to strengthen regional networks amongst stakeholders through collaborations, nurturing thought leadership in innovative regulatory science, and developing training roadmaps for regulatory-capacity strengthening that reference international benchmarks but are customised to regional needs. To achieve this, CoRE is committed to fostering capacity development, regulatory convergence, work sharing, and networks for leadership and innovation.

1. Capacity development

CoRE's aim is to address regulatory systems challenges from a strong educational and capacity development base that provides credibility for thought leadership and innovation in regulatory systems strengthening. To this end, it is rolling out a modular curriculum for working regulatory professionals in NRAs, industry and research institutes. Participants will be able to gain a Graduate Certificate and eventually a Master's degree through part-time project work, online learning and workshops, seminars and conferences over three to five years. The learning approach builds on the successful Duke-NUS model for medical training but adapted to cater to working regulatory professionals.¹⁵

2. Work-sharing

With many regulators under-resourced and struggling to keep pace with rapid advances in the volume and complexity of the products before them, the need for cooperation amongst NRAs has never been greater. Training organised by CoRE addresses technical and scientific issues that support potential work-sharing, especially for pre-market product assessment. After many years of in-principle support for such a concept, the ASEAN Pharmaceuticals Product Working Group has formally introduced a joint assessment scheme amongst its ten member states in the hope of strengthening each member NRA's technical capacity and forging mutual reliance amongst them without undermining existing national decision-making processes. With support from WHO, the procedures for this were published in 2016 on the website of the National Pharmaceutical Regulatory Agency of Malaysia, the lead country for this initiative.¹⁶

3. Regulatory convergence

Capacity building programmes such as those being offered by CoRE support convergence of the region's regulatory systems and lowering barriers posed by existing disparate requirements and interpretation of technical standards. This is in line with international trends. WHO is promoting a similar global level approach as it seeks to improve coordination and reduce duplication in systems-strengthening initiatives offered by various academic institutions and non-

governmental aid organisations*. Nonetheless, expectations on the pace of convergence should be tempered by the fact that bureaucracies often maintain the status quo, and the absence of harmonisation organisations with the authority to enforce regulatory alignment among NRAs.¹⁷

4. Leadership, innovation and networks

Developing leaders with relevant scientific understanding and strategic perspectives is critical to ensure long-term sustainability of regulatory systems. It is also important to inculcate creativity among regulators that leads to innovative and implementable ideas for NRAs in a rapidly-evolving regulatory ecosystem. To encourage such innovation, workshops and roundtables organised by academic centres such as CoRE, and which also involve industry experts and academics, enable regulators to explore technical and policy solutions in safe-harbour settings. Opportunities are also needed to pilot new regulatory approaches in collaboration with industry, academia and non-governmental partners in an environment of mitigated risk. In finance, the regulatory “sandbox” approach allows trialling of innovative frameworks. An equivalent paradigm needs to be developed for health products regulation, where concerns about patient health and safety can also be managed.

5. Coordination with health technology assessment agencies

Regulators will also have to increasingly address the affordability of new innovative health products. As more Asia-Pacific countries implement UHC, more stringent cost-containment policies based on value-driven evidence are being introduced.² Traditionally, health technology assessment (HTA) is performed independently from NRAs and only after marketing authorisation has been granted. Lack of government or third-party funding as a result of a new product’s inability to meet requirements set by the HTA agency can have a negative impact on its accessibility.^{18,19} Trends in more developed markets to bridge licensing and HTA processes point

* WHO’s Essential Medicines Department launched the Coalition of Interested Parties in June 2017. CoRE is part of this global network for regulatory systems strengthening that comprises capacity building providers and partners to promote consistency and coordination in training initiatives.

to a similar need in the Asia-Pacific so that industry, NRAs and HTA bodies can work together early to facilitate market entry of health products.¹⁹

Conclusion

The Asia-Pacific region faces a range of regulatory systems challenges. To effectively address regulatory systems gaps, it is imperative to ensure that the vision of regulatory systems strengthening takes account of concerns of the different stakeholders, and then develop safe settings in which they can interact to collectively address common scientific, technical and policy issues. Relevant capacity and capability building is a vital foundation. However, this must then translate into defining solutions grounded in the practical realities of the socio-political-economic arenas in which NRAs, industry and academia function, and where building and sustaining trust are fundamental. The ability to converge, work-share and innovate are important enablers, and the role of informed leadership is vital. Regulatory excellence does not mean unattainable regulatory perfection but is an ongoing collective journey. The ultimate destination is to unlock the potential of what good and smart regulation can offer to promote biomedical innovation in the Asia-Pacific region.

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