Pharmaceuticals such as Aciclovir are registered through national regulatory authorities to ensure their safety, quality, and efficacy. Photo credit: Jiro Ose

Strengthening Medical Products Registration in the Asia Region

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Building the Capacity of National Regulatory Authorities to Strengthen Their Medical Regulatory Systems

Background

The United Nations Sustainable Development Goals (SDG 3) call for universal health coverage, including financial risk protection, access to quality essential health care services and access to safe, effective, quality, and affordable medicines and vaccines for all. By regulating the safety, efficacy, and quality of pharmaceuticals, vaccines, blood and blood products, and medical devices, national regulatory authorities (NRA) play a key role in helping countries achieve SDG 3.

NRAs are responsible for ensuring the efficacy, safety, and quality of medical products—including medicines and vaccines—that circulate in their countries. One key function of NRAs is registration of, or granting marketing authorization to, medicines and other health products before they are allowed to be imported, distributed, sold, or supplied in the country. This process involves reviewing technical data on product quality, safety, and efficacy, as well as conducting regulatory inspections of manufacturing sites. As part of its work on the global level, the US Agency for International Development (USAID) Medicines, Technologies, and Pharmaceutical Services (MTaPS) Program (2018–2025) supports countries in regulatory system strengthening (RSS). This support is aligned with the World Health Organization (WHO) global benchmarking tool (GBT) indicators that measure the maturity of the participating NRAs. The WHO GBT provides a global metric that allows WHO and regulatory authorities to assess the overall maturity of a

regulatory system on a scale of 1 (existence of some elements of a regulatory system) to 4 (operating at advanced level of performance and continuous improvement). Building the capacity of the NRA regulatory workforce to effectively carry out regulatory functions is an important step in improving the GBT maturity level of WHO member states.

USAID partners with the Association of Southeast Asian Nations (ASEAN) Pharmaceutical Product Working Group (PPWG) and Southeast Asia Regulatory Network (SEARN) to strengthen the medical regulatory systems in the Asia region. USAID works through its implementing partners, MTaPS and the Promoting the Quality of Medicines Plus (PQM+) program, to support regional and country efforts to strengthen medical products regulatory systems. By helping ASEAN and SEARN member countries to strengthen the capacity of their NRAs to effectively fulfill their regulatory role, USAID contributes to improving access to quality-assured, safe medical products in the region. MTaPS and PQM+ collaboratively leverage their respective areas of focus and expertise to address regulatory challenges across ASEAN member states by supporting RSS via regional and subregional initiatives.

Within this collaboration, MTaPS' technical assistance focuses on promoting regulatory convergence and reliance, optimizing medical product registration processes and building resilience at the country and regional levels, and advancing the global medical product regulation learning agenda in the region.[1]

Problem Statement

NRAs use the medical products registration process to ensure that the public can access safe and effective medicines and related supplies, while providing protection from harmful or ineffective medicines. However, an onerous, opaque, or ineffective registration process can discourage manufacturers from registering their medical products in a country, which can, in turn, decrease competition among suppliers, limit access to new medical products, and increase the risk of stockouts, all of which can contribute to reduced access to quality medicines. Furthermore, insufficient or ineffective regulation or enforcement in medical product registration can allow poor-quality and unsafe products to enter the market. Efficiency is also a challenge in low- and middle-income countries (LMICs); limited resources (including specialized personnel) and long backlogs of medical product dossiers pending evaluation, can result in four-to-seven–year timelines for registration of new medicines and vaccines.[2]

- **ASEAN MEMBER STATES*** include Brunei, Cambodia, Indonesia, Myanmar, Laos, Malaysia, Philippines, Singapore, Thailand, and Vietnam.
- **SEARN**** is composed of NRAs from Bangladesh, Bhutan, Democratic People's Republic of Korea, India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka, Thailand, and Timor Leste.

* MTaPS supported all ASEAN member states except Singapore.

** MTaPS supported all SEARN member states at the regional level, but provided country-level support to only Bangladesh, Nepal, and the Philippines.

Most of the NRAs in ASEAN and SEARN member countries struggle with inadequate regulatory frameworks and insufficient resources to implement them. As a result, NRAs may not be able to conduct all their regulatory functions, including market authorization, as effectively or efficiently as they should. To improve the NRAs' regulatory function, countries must address fragmented national regulatory requirements, strengthen organizational capacity, and improve regulatory knowledge and skills in the NRA workforce.

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[1] Regulatory convergence is a voluntary process whereby the regulatory requirements in different countries or regions become more similar or "aligned" over time. [FDA. Regulatory harmonization and convergence. Silver Spring, MD: US Food and Drug Administration, 2015. Available from: http://www.fda.gov/BiologicsBloodVaccines/InternationalActivities/ucm271079.htm.]
Regulatory reliance is defined as the act whereby the national regulatory authority (NRA) in one jurisdiction may take into account and give significant weight to assessments performed by another NRA or trusted institution, or to any other authoritative information in reaching its own decision. [WHO. WHO expert committee on specifications for pharmaceutical preparations: fifty-fifth report (WHO Technical Report Series, No. 1033). Annex 10: Good reliance practices in the regulation of medical products: high level principles and considerations. 2022. Available from: https://apps.who.int/iris/bitstream/handle/10665/340323/9789240020900-eng.pdf.]

[2] Delivering Quality-Assured Medical Products for All 2019–2023: WHO's five-year plan to help build effective and efficient regulatory systems (WHO/MVP/RHT/2019.01). Geneva: World Health Organization.
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Technical Approach

MTaPS' technical approach to RSS relies on identifying gaps using global metric tools such as the WHO Global Benchmarking Tool and providing technical assistance through the following:

- Partnering with regional networks to enhance collaboration by supporting NRAs to align their regulatory processes, including regulatory convergence of technical standards, reliance, and harmonization, within the region.
- Working with interested NRAs to improve their regulatory capacity, streamline regulatory processes, and adopt international best practices in medical product registration/marketing authorization.

Stakeholder Engagement

In strengthening capacity for medical product registration as part of overall RSS in Asian member countries, MTaPS collaborates with the ASEAN PPWG and SEARN, as well as the USAID PQM+ program and WHO Regional Office for South East Asia (SEARO).

In 2019, MTaPS performed a mapping exercise to identify key entities (initiatives, networks, and other stakeholders) at the regional and subregional levels to establish partnerships and to build capacity of existing regional platforms to enhance convergence and harmonization. Through this exercise, MTaPS identified 18 entities, including ASEAN and SEARN, which were selected for engagement due to their strategic position of bringing together several Asian member states for regional cooperation.

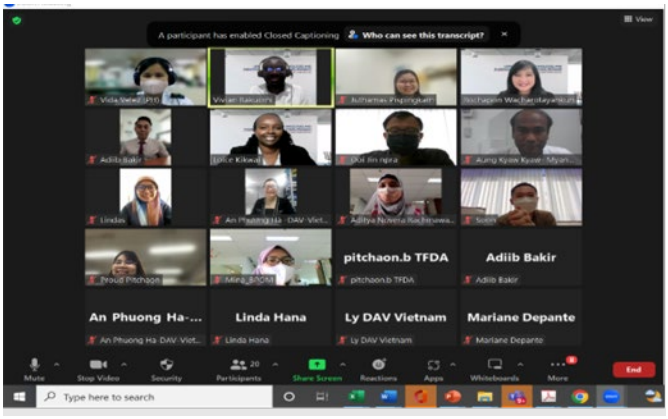
Intervention

MTaPS engages in regional and subregional initiatives to build harmonized, sustainable, and resilient medical products regulatory systems in Asia. Key MTaPS interventions have included the following:

Competency mapping of NRAs

In 2021, MTaPS conducted an exercise to map the competency of NRAs in Nepal, Bangladesh, and the Philippines using a workshop-based approach grounded in the WHO global competency framework for regulators of medical products. The mapping focused on the core and functional competencies/skills required for product evaluation (reviewers), safety monitoring, inspection, and enforcement (inspectors), laboratory quality control (analysts), and whether NRA staff had these skill sets. MTaPS engaged with NRAs to get their input into validation of the mapping results, develop training plans, and support the NRAs to implement interventions to address the identified competency gaps.

Capacity-building workshops (virtual)



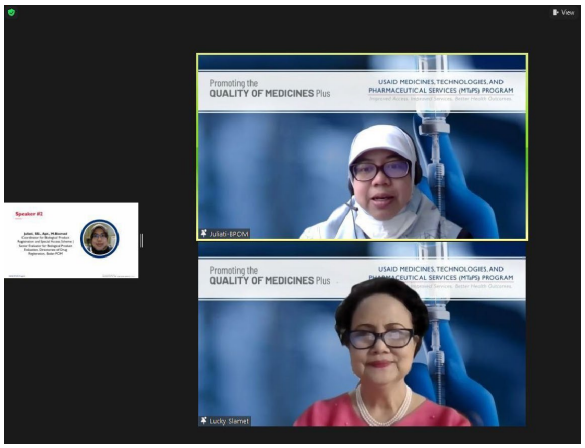
ASEAN member state participants attend training on good review practices for the dossier evaluation process. Photo credit: MTaPS

From 2020 to 2023, due to COVID-19 and to allow for participation by more NRAs, MTaPS conducted a series of virtual capacity-strengthening workshops as follows:

- *Good manufacturing practices (GMP) for pharmaceutical manufacturers workshop, conducted jointly with the JSS Academy of Higher Education and Research, Mysuru, India in December 2020.* Pharmaceutical manufacturers are required to achieve GMP certification before they are able to register their products. Participants learned about international GMP norms and standards from the US Food and Drug Administration (FDA), European Medicines Agency (EMA), WHO, and compared them with the Indian GMP and developed strategies to apply international GMP norms. The course also covered the importance of stability testing for active pharmaceutical ingredients (API) and finished pharmaceutical products and explained how stability studies are conducted.
- *Capacity-strengthening session for evaluation of COVID-19 vaccine dossiers for assessors in Bangladesh and Nepal in December 2021.* The training equipped participants with practical skills on how to evaluate a vaccine dossier with a special focus on COVID-19 vaccines, including the regulatory framework; key principles for the evaluation of non-clinical, clinical,

manufacturing, and quality data; summary of product characteristics/product information; and a review of a real dossier. Participants were also provided with a systematic outline and approach on how to review a dossier and prepare an assessment report of findings and recommendations.

- *Workshop on convergence of technical standards for medical product registration for Bangladesh and Nepal NRA staff in July 2022.* The workshop focused on orienting NRA personnel on the need for convergence of technical standards and guidelines for medicine registration. As part of this training, a framework for joint assessment of medical products between NRAs of Bangladesh and Nepal was proposed, and the countries agreed to engage in collaborative activities.
- *Regional training of trainers course on the evaluation of biological products, including vaccines, conducted in collaboration with PQM+ in December 2022.* The workshop targeted NRA staff in the marketing evaluation division from all ASEAN member states, except Singapore. The objective of the course was to enhance knowledge and understanding of the current global regulatory requirements to be considered during product evaluation for registration of biologics and vaccines and to equip them with skills to further cascade the training as regional experts.



MTaPS facilitators provide training on evaluation of medicines. Photo credit: MTaPS

- *Regional training on good review practices (GRevPs) for the dossier evaluation process for Indonesia, Thailand, Malaysia, Myanmar, Vietnam, Laos, Brunei, and the Philippines in January 2023.* The workshop aimed to improve knowledge of the essential principles of WHO guidance on GRevP and GRelP guidelines, applying the principles of collaborative review procedures (CRP) for the review of medicines, and evaluation of real-world case studies during dossier evaluation. Participants gained skills to support quality assessments and timely decision making on marketing authorization for medicines.

In addition to these regional capacity-strengthening activities, MTaPS provided support for RSS through country-level technical assistance in Bangladesh, Indonesia, Nepal, and the Philippines. These activities included supporting capacity building in pharmacovigilance (PV) and medicine registration functions; developing and updating policies, regulations, and guidelines; implementing OpenRIMS for medicine registration and PV; supporting safety data evaluation for decision making; working to strengthen good pharmacy practices; developing a quality management system, developing regulations for medical devices; and implementing the corrective action preventive action (CAPA) plan to address the WHO GBT findings for maturity level assessments.[3]

Results and Achievements

With technical support from MTaPS and partners, NRAs in a total of 11 countries were exposed to global and regional experiences and gained knowledge on key concepts for medical products registration, had the opportunity to practice key processes for medical product registration, and learned specialized skills in evaluation of vaccines (including COVID-19 vaccines) and biological products. More than 180 people, including NRA staff and pharmaceutical manufacturers, improved their understanding of medical product registration and related topics. For example, post-course questionnaires in the capacity-building training on the evaluation of vaccine dossiers from NRA officials from Bangladesh and Nepal demonstrated their knowledge improved on the evaluation of quality, safety, and efficacy data of a vaccine dossier, particularly on the non-clinical and clinical data evaluation and post-authorization approval changes or requirements.

Through capacity-strengthening activities, the NRAs from the ASEAN countries/SEARN network have built connections with one another, which will allow for

[3] OpenRIMS is an open-source Regulatory Information Management System (RIMS). RIMS serves to automate and digitalize the processes and work routines at an NMRA. https://wiki.openrims.org/index.php/Main_Page

continued collaboration and exchange of information to support medicine harmonization across the region. A pool of experts has been established in 9 countries to serve as a regional resource and to conduct training on assessment of vaccines and biological products. These interventions align with the WHO GBT indicator MA03 (human resources to perform registration and marketing authorization activities), which tracks progress on the number, competency, skills, and knowledge of NRA staff undertaking these activities to be well resourced and have adequate expertise to undertake reviews.

As a result of the 2023 workshop on GRevPs, participants drafted a regional framework for adoption of the WHO's GRevPs in registration and marketing authorization which is to be proposed to the ASEAN PPWG. The framework provides guidance to ASEAN for the adoption of WHO's GRevPs standards in registration and marketing authorization as a step toward regional harmonization; application of the framework can lead to application of reliance regulatory pathways among NRAs to accelerate regulatory review processes by abbreviating the elements considered in the review of medicines applications and meeting patients' need for timely access to life-saving medical products.

MTaPS' support also contributed to the development and implementation of the capacity-strengthening plan for the regulatory authority in Nepal and continues to contribute to the development of plans for Bangladesh and the Philippines.

Lessons Learned

- Capacity-strengthening workshops need to be complemented by ongoing mentorship and coaching to support the uptake and application of learned principles and to gauge the benefit of the course to the NRAs.
- It is important to work closely with NRAs to ensure that they nominate staff with sufficient professional experience to benefit fully from the capacity-strengthening courses and are able to implement learned skills and knowledge.
- Regional frameworks and coordination mechanisms are critical in bringing countries together to promote collaboration, convergence, and harmonization.

Pathway to Sustainability

MTaPS has developed frameworks for joint assessment of medical products between the NRAs of Bangladesh and Nepal, and a framework for adoption of WHO's GRevPs in registration and marketing authorization. These frameworks provide guidance and strategies on how to enhance regional collaborations in medicine regulation and information exchange. Conducting competency mapping in the three countries provided a way for NRAs to understand existing gaps and develop a plan to address them. A pool of experts has been established within the region to perform effective product dossier evaluation, including for specialized products like vaccines and biologics, and train other regulatory officers. NRAs have access to the competency mapping tool and can use it on a regular basis to determine progress and regulatory capacity in all functional areas. Regional events allowed participating NRAs to strengthen their relationships with one another for future collaboration and information exchange; for example, Bangladesh and Nepal's NRAs have planned for a joint learning visit on medicine registration.

Conclusions

Medical products registration is a key function for any country to ensure the availability of much-needed medical products and health technologies for its population. Marketing authorization, by extension, protects the public from harm by ensuring that available medical products are safe, effective, and quality-assured. For NRAs to successfully undertake marketing authorization, they must have skilled personnel able to make evidence-based decisions aligned to international best practices to promote confidence in the health system.

Through its technical support and collaboration with the NRAs in the ASEAN and SEARN member countries, MTaPS contributed to stronger regulatory systems across the region in line with the WHO GBT indicators for registration, marketing authorization, and vigilance in NRAs; established regional frameworks; and facilitated regional collaboration for medical product registration.

Moving forward, to strengthen capacity to implement internationally recognized best practices, NRAs will need to establish and implement capacity-strengthening plans that clearly outline a phased approach for staff

training. Continuous quality improvement steps such as mentorship and coaching will be critical to support NRAs in adopting and applying these concepts and principles. Regional networks should develop a regional capacity-building strategy for countries to adopt and implement that clearly outlines how to tap into existing country-level capacity. These networks should also implement frameworks to enhance regional cooperation in medicine registration, including joint assessments, reviews, work sharing, and reliance.

References

MTaPS. Medicines to Markets: Building Effective Medicines Registration System in LMICs [webinar]. 2021. Available from: https://www.mtapsprogram.org/our-resources/medicines-to-markets-building-effective-medicines-registration-system-in-lmics/.

MTaPS. Advancing Regulatory Systems for Improved Access to Safe, Effective, Affordable, and Quality-Assured Medical Products Technical Program Update. December 2022. Available from: https://www.mtapsprogram.org/wp-content/uploads/2023/01/MTaPS-Regulatory-Systems-Strengthening-Technical-Program-Update-December-2022.pdf.

SEARN Network. https://searn-network.org/.

WHO. Global Competency Framework for Regulators of Medicines. 2023. Available from: https://iris.who.int/handle/10665/374053. License: CC BY-NC-SA 3.0 IGO.

WHO. Global Benchmarking Tool (GBT) for Evaluation of National Regulatory System of Medical Products - Revision VI. 2021. Available from: https://www.who.int/publications/i/item/9789240020245.

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About USAID MTaPS:

The USAID Medicines, Technologies, and Pharmaceutical Services (MTaPS) Program (2018–2025) enables low- and middle-income countries to strengthen their pharmaceutical systems, which is pivotal to better health outcomes and higher-performing health systems. The program is implemented by a consortium of global and local partners, led by Management Sciences for Health (MSH), a global health nonprofit.