# Capacity Development of National Regulatory Authorities in the Greater Mekong Subregion to Facilitate the Elimination of Malaria

Public Brief Report

This work is funded under the work program of the Regional Malaria and Other Communicable Disease Threats Trust Fund (RMTF) which was set up at ADB in December 2013 with the specific remit to support developing member countries to develop multi-country, cross-border, and multisector responses to urgent malaria and other communicable disease issues. The RMTF's financing partners are the Government of Australia (Department of Foreign Affairs and Trade), the Government of Canada (Department of Foreign Affairs, Trade and Development), and the Government of the United Kingdom (Department for International Development).

## Background

### *Goal to eliminate malaria*

The World Health Organization (WHO) reports that there were 216 million cases of malaria worldwide in 2016, where the vast majority occurred in the WHO African region (194 million, 90%), followed by the South-East Asia region (14.6 million, 7%)[1]. Malaria, spread among people through the bites of infected female *Anopheles* mosquito, is a life-threatening disease. Children under five are the most susceptible to mortality related to malaria infection. The fight to eliminate malaria has taken extensive global health efforts by countries worldwide, WHO, and other non-governmental organizations (NGOs), reducing global malaria incidence by 18% between 2010 and 2016. By WHO region, South-East Asia registered the largest decline by 48%.

However, malaria elimination efforts in the Asia-Pacific are complicated by the emergence of anti-malarial resistance. In five Association of South-East Asian Nations (ASEAN) member states in the Greater Mekong Subregion (GMS; Cambodia, Lao PDR, Myanmar, Thailand and Viet Nam), resistance to artemisinin – a core medicine in the treatment against the *Plasmodium falciparum* strain of malaria – has been detected. This reduces the effectiveness of the medicine to treat malaria, and threatens to undermine ongoing malaria elimination efforts within the region, as well as increase the risk of the disease spreading to new areas or re-emerging in areas where malaria had been previously eliminated. Artemisinin resistance in the GMS has been attributed to multiple factors including but not limited to the widespread distribution of poor quality and counterfeit medicines to treat malaria, misdiagnosis and inappropriate practices of managing malaria infection, such as the indiscriminate use of artemisinin-based therapies.

Aligned with the WHO Global Technical Strategy for malaria (2016-2030) that seeks to accelerate progress towards global malaria elimination, the sub-regional WHO Strategy for malaria elimination in the GMS (2015-2030) was adopted by the GMS Ministers of Health in 2015 with the primary aim to eliminate *P. falciparum* malaria from the region by 2025[2]. In support of these efforts to combat malaria in the GMS, the Asian Development Bank (ADB) along with the Asia Pacific Leaders Malaria Alliance (APLMA) have committed to supporting and driving initiatives towards malaria control and elimination. Further, the ADB Regional Malaria and Other

[1] World Health Organization. World Malaria Report 2017. November 2017.
[2] World Health Organisation. Strategy for Malaria Elimination in the Greater Mekong Subregion (2015-2030). 2015.

Communicable Disease Threats Trust Fund (RMTF) supports developing member countries in developing suitable approaches to address concerns of malaria cases that are not responsive to conventional treatments and other communicable disease issues.

*A key enabler: Strengthening regulatory systems*

Enhancing the capability of national regulatory authorities (NRAs) – the national bodies with the mandate to oversee and regulate health products in their country on the basis of the product's quality, safety and efficacy – is one of the key enablers of malaria elimination efforts in the GMS. Strengthening the regulatory functions of a NRA enables timely access by populations to quality-assured, safe and effective medicines and medical devices for the treatment of malaria and other diseases, and contributes to enhancing overall health security. The scope of these functions spans across the product lifecycle, encompassing the oversight of clinical trials, assessment of health product applications for use in the country, monitoring the safe use of health products and the inspections of facilities. Conversely, poor regulatory capacity often results in delays to accessing essential health products, low assurance of quality, and poor controls over the quality and authenticity of health products – issues that contribute to the problem of artemisinin resistance in the GMS. Therefore, it is important that gaps in the regulatory systems of the NRAs are identified to effectively build their capabilities.

*Collaboration to strengthen regulatory systems and enhance access to good quality, safe, and effective health commodities*

From October 2015 to December 2017, ADB engaged the Duke-National University of Singapore Medical School's Centre of Regulatory Excellence (Duke-NUS CoRE) to collaborate on a project aiming to assist the GMS countries to strengthen regulatory systems and build a stronger response to malaria. CoRE was set up in 2014 to promote regional regulatory excellence for health products and related health systems and policy issues through education, consultancy, and think tank activities promoting policy innovation. This collaboration brought together ADB's networks, resources and expertise with CoRE's regional influence, expertise in regulatory capacity building for therapeutic products, and strength in education and training, to build regulatory capacity in the GMS with the common goal of supporting malaria elimination.

## Strategies and Approaches

With the priority focus to eliminate malaria in GMS, the project's overall goal was to promote the availability of safe and effective health commodities appropriate to internationally agreed guidelines for malaria and other communicable disease threats. CoRE set out to evaluate and help strengthen the regulatory capability and effectiveness of the GMS NRAs, expand CoRE's collaboration, contribution and capacity into the GMS, and leverage regional platforms and other stakeholders to achieve the overall goal. Moreover, engagement with NRAs and health policy-makers initiated fostering of opportunities for greater convergence of regulatory requirements within the region.

The main objectives of the project were to:

1. Conduct assessments to identify needs and gaps in the health product regulatory systems in the GMS, with a focus on anti-malarial commodities;
2. Develop country and regional roadmaps for regulatory system strengthening, defining priorities for attention; and,
3. Initiate capacity building programmes to address constraints to accessing quality-assured, safe and efficacious medicines for patients in these countries.

The project consisted of two main phases. Phase I involved a needs assessment exercise, including conduct of a literature review, development and utilization of a regulatory system profiling instrument (RSPI), and development of country-specific and regional roadmaps based on the identified needs. Phase II built on the Phase I outputs to develop a sustainable capacity building plan aimed at strengthening NRA capabilities, thereby contributing to efforts to enhance access to quality, safe and efficacious health products, including anti-malarial commodities. Table 1 describes the key steps, activities and outputs of the project.

**Table 1. Steps and activities for enhancing regulatory functions in the GMS**

| Step | Activities | Key Outputs |
|---|---|---|
| 1 | **Conduct a Literature Review**<br>• Structured review of publicly available information on the existing regulatory landscape of the GMS | • Gaps in knowledge hindering the planning of capacity building programmes were identified and guided the development of the profiling tool |
| 2 | **Develop the Regulatory System Profiling Instrument (RSPI)**<br>• Review of existing tools, including the WHO Data Collection Tool, for reference in customizing one for the GMS<br>• Pilot of a draft instrument in an ASEAN regulatory authority to assess usability<br>• Construction of the final version of the RSPI, and an abridged version for use in minimally resourced NRAs | • A new tool was developed to cater to the requirements of this project in profiling the NRAs<br>• Inputs from external stakeholders were solicited and incorporated into the reports for the NRAs<br>• The RSPI can be regarded as a complementary aid to the WHO Data Collection Tool, since references were drawn from the latter |
| 3 | **Profile the Needs of NRAs in the GMS**<br>• Administration of RSPI - questionnaires and interviews with NRA staff and external stakeholders<br>• Collation of information to develop reports and roadmaps | • Areas for regulatory strengthening and needs for training were identified<br>• Country specific assessment reports and roadmaps for regulatory systems strengthening were developed and discussed with the individual NRAs |
| 4 | **Regulatory Capacity Building**<br>• Development of training materials and workshop agendas for selected topics (pharmacovigilance and medical device regulation)<br>• Collaboration with interested parties for a coordinated approach in regulatory systems strengthening in the GMS | • In-country training workshops were conducted for both central and provincial NRA staff of selected NRAs<br>• Selected training materials were translated into the local working languages to facilitate learning<br>• Regional workplan for the GMS was developed in collaboration with other parties e.g. World Health Organization, Asia Pacific Leaders Malaria Alliance, Therapeutic Goods Administration of Australia |

## Significant Outputs, Contributions and Achievements

The project has generated key outputs that can be utilized in other countries and regions, or expanded through wider regional and international platforms, thus amplifying their value.

*Utility of a regulatory profiling tool*

With assistance from an expert panel, the RSPI was developed to elicit more complete and holistic information (adding to or validating limited public domain information in existing literature), in order to provide an informed basis for planning regulatory capacity building programmes for the region. The RSPI assesses a range of key organizational and regulatory functions (Table 2) relevant to the medicines and medical devices arms of NRAs, as well as inputs from external stakeholders

including industry associations, healthcare professional associations, and malaria control departments of health ministries.

**Table 2. Key functions assessed by RSPI**

| |
|---|
| ▪ **Overall Regulatory System** |
| ▪ **Human Resources** |
| ▪ **Marketing Authorization** |
| ▪ **Licensing of Medicines/Medical Devices Establishments** |
| ▪ **Inspections of Medicines/Medical Devices Establishments** |
| ▪ **Post-marketing Surveillance** |
| ▪ **Control of Medical Products Promotion and Advertising** |
| ▪ **Regulatory Quality Control Laboratory** |
| ▪ **Pharmacovigilance and Medical Device Vigilance** |

While there are existing tools to profile regulatory functions, such as the WHO Data Collection Tool, the RSPI's predominant value is that it is an interview-based qualitative assessment instrument that collates the inputs of NRA staff as well as key external stakeholders to provide an overview of a NRA in relation to the regulatory ecosystem in which it operates. This allows a validation of the needs and gaps, using the inputs and perspectives obtained from the various external stakeholders. Conducting future similar assessment exercises in other countries of ASEAN and beyond would also potentially provide useful comparative information of the regional regulatory environment on a wider scale.

Given the limited timeframe of this project, the true impact of the activities to enhance regulatory capacities can only be observed through continued tracking and monitoring of the various activities aimed at strengthening regulatory systems in the GMS. One area of opportunity involves extending the utility of the RSPI to be used as a monitoring tool, with appropriate refinements. Familiarity with the administration of the tool among the GMS countries during this project would make it potentially easier to apply it for monitoring purposes.

*Deeper understanding of the regulatory environment in the GMS*

Findings from the administration of the RSPI were collated into individual country assessments, detailing the gaps and needs of the regulatory systems, and returned to the respective NRAs.

When analyzed across the five countries, common key gaps and challenges across medicines and medical devices regulatory systems in the GMS were observed (Figure A).

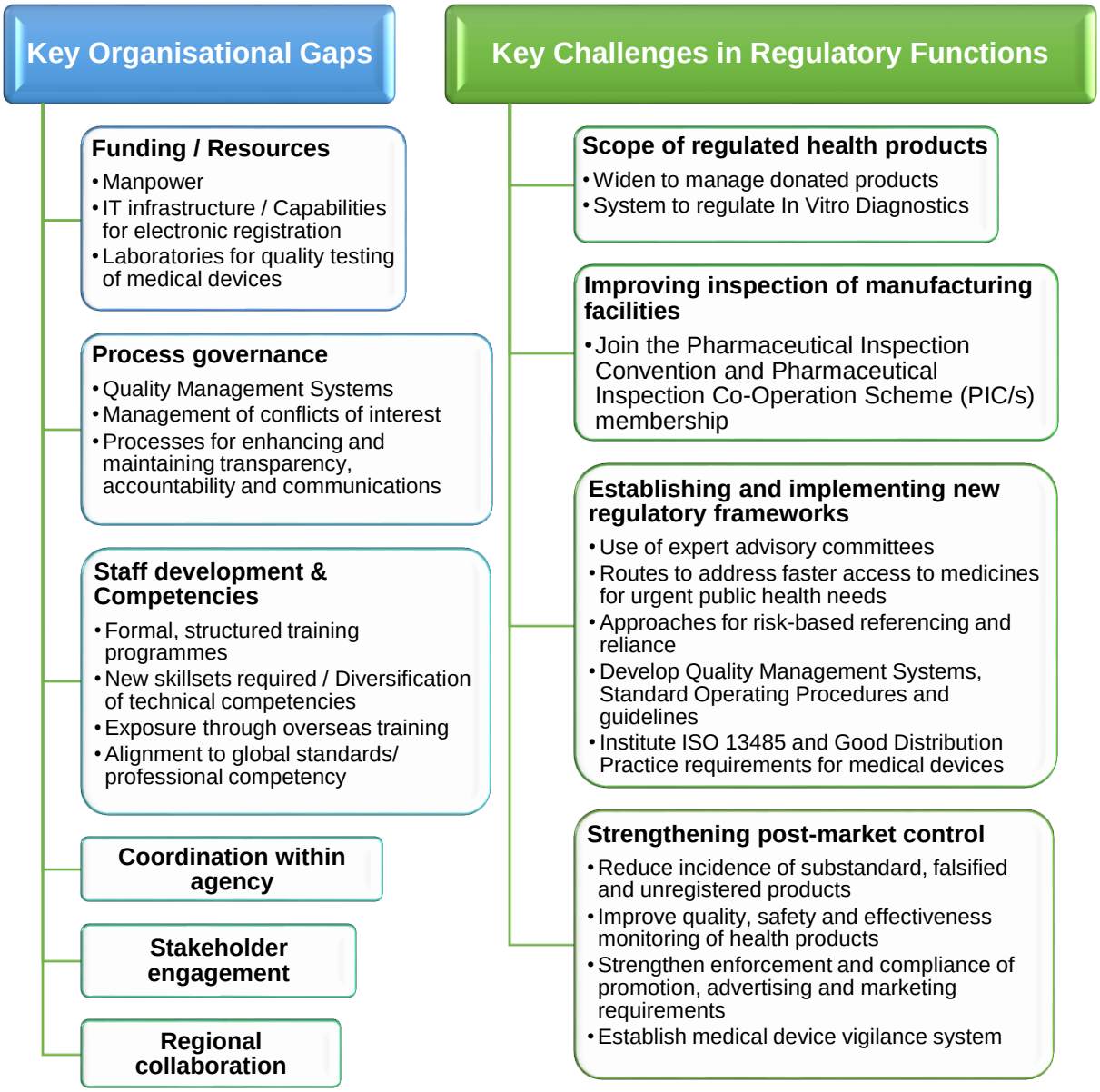


**Figure A. Key gaps and needs in the GMS for regulating medicines and medical devices**

The country assessment reports are a rich resource providing an overview of the perspectives and expectations of regulatory stakeholders in each GMS country. Drawing from the knowledge obtained about the regulatory gaps and needs in the GMS, roadmaps were constructed for each

NRA to support their efforts in regulatory system strengthening. Individual GMS NRAs can continue to use these roadmaps to monitor their progress in addressing identified gaps in their countries' health product regulatory systems. The materials generated from the profiling exercise could also be used to develop proposals to the NRA's parent ministry or funders to support plans for regulatory system strengthening, in addition to facilitating efficient use of resources by minimizing duplication of efforts.

*Regionalization and coordination of regulatory systems strengthening approaches*

As an initial step to explore feasible options for a regional approach to regulatory system strengthening, a regional roadmap for regulatory systems strengthening interventions across the region was developed. The regional roadmap laid out priority areas, goals, and roles of stakeholders across seven key domains covering regulatory and organizational functions, as well as stakeholder communication and regional collaboration (Figure B).

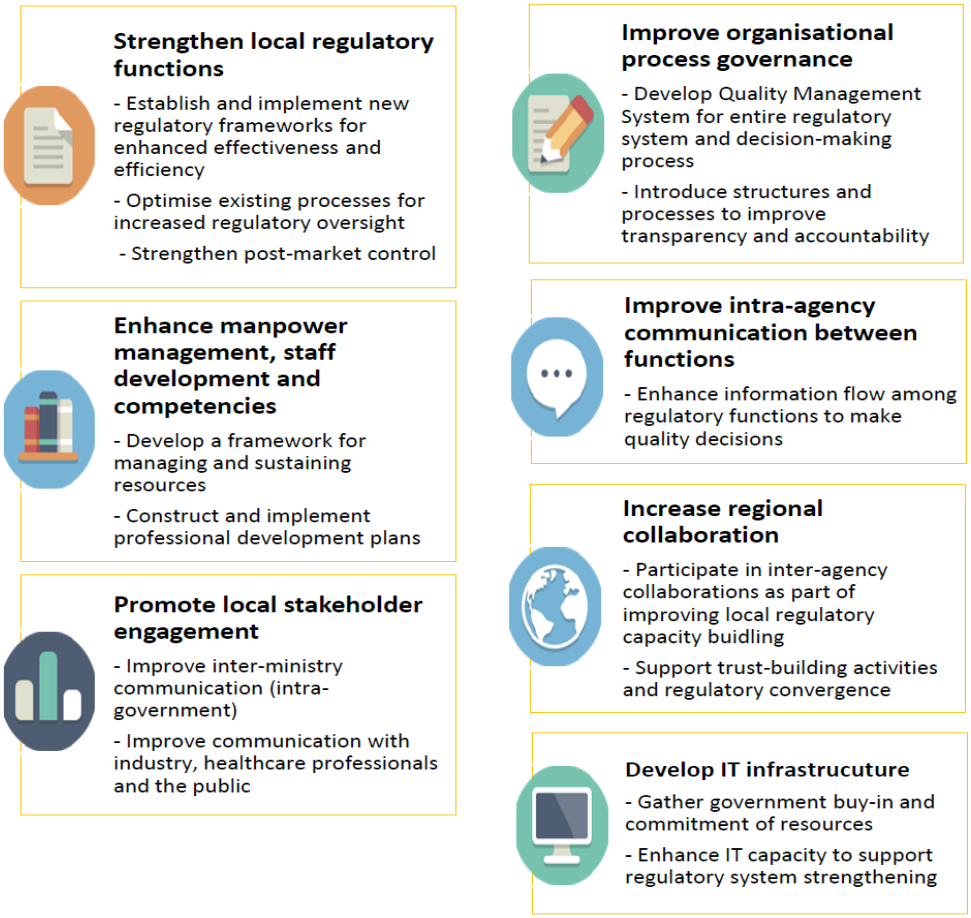


**Figure B. Regional Roadmap for Regulatory Systems Strengthening in the GMS**

The regional roadmap facilitates the coordination of capacity building programmes, reducing duplicative efforts and providing a focal point for planning the use of resources, and fostering collaboration and partnership. Beyond regulatory training, it encourages a holistic approach to regulatory systems strengthening, and emphasizes the need to also address organizational governance issues and communication with external stakeholders. The regional roadmap also serves as a regionally relevant resource for both GMS NRAs and other stakeholders to track wider goals for the region and encourage ongoing progress towards enhanced regulatory capacity.

Given the wide scope of needs and gaps to be addressed for regulatory systems strengthening in the GMS, strong cooperation and collaboration among funding partners, training providers and the GMS countries is necessary to effectively and efficiently improve regional regulatory capacity through consolidated efforts.

## Sustaining the Momentum

Beyond the activities and outputs of the project, it is vital to ensure that regulatory capacity building plans and actions continue to be carried out in a timely manner and monitored to achieve longer term outcomes and progress. Sustainability of the work is not only dependent on the availability and allocation of financial support from funders and manpower resources of training partners, but also relies on the willingness and commitment of the NRAs' leadership, partners and other key stakeholders to work towards common goals. Continued engagement among all players is necessary to monitor and track progress, ensure alignment of strategies and resources, and empower commitments to achieving goals.

*Fostering and sustaining commitment from multiple stakeholders*

Commitment can be further bolstered through leveraging regional platforms and establishing strategic partnerships. These offer opportunities for coordinating and aligning capacity building programmes, sustaining activities with sufficient funding support, and optimizing resources through multi-stakeholder collaboration. A key opportunity extending from this project is the Regional Regulatory Partner (RRP), a platform set up to engage regulatory stakeholders and technical partners to coordinate regulatory capacity building programmes in support of malaria elimination efforts. Information from the regional roadmap in this project has been shared with

WHO and the RRP partners to support the ongoing development of a RRP workplan for regional regulatory capacity building. The collaborative approach at the RRP has also drawn interest from potential funding agencies with similar goals to support malaria elimination efforts, including the Bill and Melinda Gates Foundation and the Australian Department of Foreign Affairs and Trade (DFAT).

CoRE's ongoing involvement at other global and regional platforms will help sustain interest and support for capacity building programmes in the GMS. The WHO Coalition of Interested Partners (CIP) for Regulatory Systems Strengthening, of which CoRE is a founding partner, will potentially draw in wider global resources for systems strengthening efforts in the region. In addition, CoRE's existing involvement with the ASEAN Pharmaceutical Products Working Group (PPWG), the ASEAN Medical Device Committee (AMDC), and APEC Life Sciences Innovation Forum (LSIF) Regulatory Harmonisation Steering Committee (RHSC) will help to align capacity building activities with regional regulatory harmonization initiatives.

As part of the planned activities within this collaboration, CoRE's position as a neutral academic centre within ASEAN has enabled the Centre to support capacity building programmes for GMS NRAs by developing appropriate curricula, training materials and in-country workshops. In particular, pharmacovigilance and medical device regulation have been identified as primary focus areas of training by CoRE for this region. Beyond this project, CoRE will continue to involve GMS NRAs in its training initiatives such as workshops and courses linked to the new Duke-NUS Graduate Certificate in Pharmaceutical Regulation. The learning outcomes of these activities are tied closely to the goals of the individual country and regional roadmaps, supporting greater coordination of efforts for regulatory system strengthening in the GMS.

## The Big Picture: A Comprehensive Approach to Regulatory Systems Strengthening

Regulatory systems strengthening requires a comprehensive approach. In addition to the provision of targeted training, strategies need to address fundamental issues linked to the wider regulatory and socio-economic-political environment in which NRAs operate, in order to drive real change. Amidst the inherent diversity across GMS countries in history, culture, and political systems, there are increasing opportunities to engage in collaborative initiatives through wider

regional platforms and partnerships to implement more holistic and sustainable solutions. This is certainly necessary when aiming to promote greater regulatory convergence, reliance, and good regulatory practice in effective and practical ways at the country and regional levels in the GMS.

To ensure that the initiatives and products from this project have an optimal impact on malaria elimination efforts in the GMS, regulatory capacity building should be regarded as a critical agenda by funding agencies as well as national health policymakers for strengthening health product regulatory systems in order to ensure access of populations to safe, quality and effective medicines and medical devices, including anti-malarials. The outputs from this project support ADB's ongoing initiatives to strengthen health security in the GMS.