



Building Foundations for Robust Quality Assurance Systems in Myanmar

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Background



In recent years, Myanmar has made dramatic progress in combatting malaria. The number of malaria cases in the country has plummeted from more than 2 million cases in 2010 to approximately 142,000 cases in 2016.¹ However, Myanmar still carries one of the highest malaria burdens of any country in the Greater Mekong Subregion (GMS) of Southeast Asia, and 60 percent of the population remains at risk of contracting the disease.²

Although Myanmar has made significant strides toward reducing its malaria burden, the disease remains a critical public health priority, mainly as a result of the development and potential spread of drug resistance. In particular, resistance to the drug artemisinin, a critical component of first-line treatment regimens, has been observed in the *Plasmodium falciparum* malaria parasite in Myanmar and in several other GMS countries.^{3,4} Further spread of artemisinin resistance could potentially unravel the progress made to date and would threaten the wellbeing and lives of the 30 million people in Myanmar who are at risk of contracting malaria.⁵

A number of interacting factors have likely contributed to the development of drug resistance, including poor dispensing practices and availability of artemisinin monotherapies, especially in informal markets.⁶ Even when the medicines are available to patients, their quality may not be assured. In addition to leading to treatment failure and unnecessary adverse events, poor-quality medicines likely contribute to and drive the development of drug-resistant malaria.^{7,8} They also exacerbate the loss of productivity and income that individuals face as a result of illness, waste scarce resources, and erode public confidence in health systems.

Robust and effective regulatory and quality assurance systems help to detect poor-quality medicines and allow national medicines regulatory authorities to take

evidence-based regulatory actions to protect local populations. In Myanmar, to meet the growing needs of its population, the national medicines regulatory authority—the Department of Food and Drug Administration (DFDA)—is expanding rapidly, working to open field offices and laboratories in every region and state in the country. As DFDA grows, it is critical for the agency to strengthen its quality assurance systems, which help protect the local population from substandard and falsified antimalarial medicines. This includes developing a robust network of quality control (QC) laboratories; institutionalizing a system for routine post-marketing surveillance; and streamlining other regulatory functions and processes, such as medicines evaluation and registration, inspections, and licensing.

Poor-quality antimalarials can lead to unnecessary adverse events and treatment failure, and contribute to the development of drug-resistant malaria.

Strategic Approach

To support the the Government of Myanmar in building capacity to properly ensure the quality of antimalarial medicines, USP's Promoting the Quality of Medicines (PQM) program, funded by the U.S. Agency for International Development (USAID) and the U.S. President's Malaria Initiative (PMI), began working directly with the Myanmar Mission in September 2014 to provide technical assistance to DFDA. The major focus of this assistance was strengthening the network of QC laboratories to be able to accurately and reliably test the quality of medicines, with the aim of earning ISO/IEC 17025 accreditation.

Although ISO/IEC accreditation was a major goal of PQM's initial support, the PQM program has long recognized that the challenges associated with poor-quality medicines are rarely adequately addressed by focusing only on one area of support. Instead, PQM takes a holistic approach that aims to strengthen and improve the systems, structures, and processes that promote product quality. This approach recognizes the dynamic and cross-cutting relationships among different components of the health system, and therefore seeks to address product quality issues in a sustainable manner

using systems-based thinking and solutions. As a result, PQM is equipped to provide a wide range of support to increase access to quality-assured medicines and strengthen quality assurance systems. In practice, this means providing tailored support not only to national QC laboratories, but also to national medicines regulatory authorities, the local manufacturing industry, and other key stakeholders throughout the supply chain as necessary. PQM also aims to raise awareness about the importance of quality medicines and enhance coordination and information-sharing among key stakeholders.

In Myanmar, PQM's systems-strengthening approach was used to address potential areas for improvement for the QC laboratories as well as DFDA.⁹ This multipronged effort has aimed to support the country's *National Strategic Plan for Intensifying Malaria Control and Accelerating Progress towards Malaria Elimination, 2016–2020* and PMI's *President's Malaria Initiative Strategy, 2015–2020*. DFDA's ability to effectively monitor the quality of and appropriately regulate medicines is paramount to these and other efforts to eliminate malaria in the GMS.



Analytical laboratory staff at DFDA in Nay Pyi Taw learn how to perform dissolution testing.

Photo credit: Dr. Lu Lu Kyaw/PQM

Safeguarding Medicines Quality: Strengthening the Network of QC Laboratories

Through funding from the USAID/Myanmar Mission, PQM began working to support several QC laboratories in Myanmar—namely, those in the cities of Nay Pyi Taw, Mandalay, and Yangon. Because the laboratory in Nay Pyi Taw functions largely as a central laboratory where technicians often receive training before being dispatched to other laboratories, and since it had the highest number of qualified laboratory staff, it was mutually decided that the Nay Pyi Taw facility should be the first laboratory to attempt accreditation.

Before initiating technical assistance, PQM sought to thoroughly understand the key challenges faced by the Nay Pyi Taw laboratory in effectively carrying out its mandate. A preliminary assessment carried out by PQM in July 2015 revealed that major infrastructure improvements were needed before efforts toward accreditation could begin. This included establishing a proper storage area for chemicals, installing essential laboratory features, securing a continuous supply of electricity, and completing other refurbishment projects. Following a presentation of the assessment findings, DFDA leadership reallocated funds to support the necessary laboratory upgrades and oversaw the subsequent implementation.

Following the completion of the laboratory infrastructure upgrades, PQM revisited the Nay Pyi Taw laboratory in March 2016 to begin strengthening the quality management system (QMS) and compliance with the ISO/IEC 17025 standard. PQM helped the laboratory identify several areas requiring strengthening before accreditation, including QC testing methods, good documentation practices, data integrity, procurement and calibration of essential equipment, and internal audits.

Building Capacity through the Collaborative Learning Model

To help build staff capacity in these areas, PQM supported the laboratory by conducting a series of didactic and practical trainings on analytical laboratory techniques and QMS. In order to maximize this effort, PQM used a Collaborative Learning Model in which technicians and staff from the Mandalay and Yangon laboratories also attended trainings alongside laboratory staff from

Nay Pyi Taw. This helped to reinforce learning across all three laboratories and enable the Mandalay and Yangon laboratories to make improvements and progress toward accreditation, even as PQM was primarily focused on supporting accreditation of the Nay Pyi Taw laboratory.

The Collaborative Learning Model facilitates the transition of trainees to become trainers after technical and managerial competencies have been built. Those trained under this model act as trainers and in turn train other colleagues at their local laboratory. This model allows in-country technical teams to develop a professional network, compare and share skills and practices, and advance competencies across their institutions. The Collaborative Learning Model has been successfully applied in other PQM countries, including Nigeria and Kazakhstan.¹⁰ Using this model, PQM held 9 trainings for 177 laboratory staff in Myanmar on an array of relevant topics (see Box 1).^{*} PQM also supported the development and/or revision of 114 standard operating procedures and 1 quality manual, which were then adopted and shared with the Mandalay and Yangon laboratories. By sharing procedures and documents across laboratories, Myanmar effectively standardized these materials nationwide and supported all three laboratories in taking a major step toward compliance with international standards.

Box 1. Technical and Managerial Topics Covered during PQM's Training Workshops

- Analytical methods: HPLC, dissolution, loss-on-drying, among others
- Equipment calibration and maintenance
- Data management and integrity
- Laboratory safety
- Risk management
- Internal audit

^{*} Number is a tally of participants attending each training event and includes individuals who may have been trained more than once.



New staff at DFDA prepare reagents for dissolution testing.
Photo credit: Dr. Lu Lu Kyaw/ PQM

In the third quarter of FY16, with PQM providing support as needed, DFDA's Nay Pyi Taw laboratory successfully conducted its first internal audit and completed a root-cause analysis of the observations identified. It also successfully developed and implemented a plan to address all corrective and preventive actions to remedy the audit observations. These accomplishments were a major milestone that individual and organizational capacity at the Nay Pyi Taw laboratory had been strengthened and that accreditation was within reach.

Modernizing Laboratory Equipment and Establishing Mechanisms for Calibration

A major hurdle to address prior to accreditation was the laboratory's outdated and out-of-calibration equipment. Through PMI funding, PQM supported the laboratory in

selecting and procuring a high-performance liquid chromatography (HPLC) system and a dissolution apparatus, two essential pieces of equipment at the heart of quality control testing and necessary for the scopes of accreditation that the laboratory was planning to seek.

To ensure that the laboratory not only had these essential pieces of equipment but also had the means to effectively calibrate and maintain the equipment, PQM supported the laboratory staff in engaging a certified calibration services provider to assist with the calibration requirements of ISO 17025. The calibration provider has since supported the laboratory in calibrating 47 pieces of equipment.¹¹

Strengthening DFDA's Quality Assurance Systems

Concurrently with efforts to ensure the Nay Pyi Taw laboratory would be in a position to earn accreditation, PQM also worked with DFDA to build institutional capacity. With the accreditation of its first laboratory, DFDA would be poised to begin strengthening its post-marketing surveillance program. To support this effort, PQM worked with DFDA to revise and update its reporting systems, build a cadre of trained and qualified inspectors, and implement risk-based measures that help to detect poor-quality medicines while optimizing the use of agency resources.

Building Local Capacity to Detect Poor-Quality Medicines

Regulatory inspectors play a pivotal role in post-marketing surveillance programs—conducting a range of inspection activities that help detect potential problems and the entry of poor-quality medicines across the pharmaceutical supply chain. To support Myanmar's cadre of regulatory inspectors, PQM conducted a training workshop for 24 inspectors from across 14 local states/regions in May 2016. In line with the Collaborative Learning Model used to support the laboratory, PQM designed the event as a train-the-trainer workshop so that participants would be equipped to return to their states/regions and repeat the training for other colleagues. Eleven topics were covered, including the quality assurance and quality control of medicines, inspections at different levels of supply and distribution chains, good inspection practices, and appropriate sampling strategies. A practical inspection exercise was performed in the town of Lewe to evaluate the performance of the inspectors. A post-workshop knowledge assessment found that 83 percent of the participants had increased their knowledge on the subject matter.¹²

To further expand DFDA's post-marketing surveillance capacity, PQM supported DFDA in acquiring and rolling out 20 GPHF-Minilab™ units at various field sites. The GPHF-Minilab™ is a field-based screening tool that can help detect poor-quality medicines and can reduce the testing burden and backlogs faced by some QC laboratories. Because field testing using GPHF-Minilab™ is much less expensive than full quality control testing,

these types of field-based screening tools can help regulatory authorities detect poor-quality medicines while optimizing resources and making the most of limited budgets. PQM advocates that field-based screening tools be used as part of a multilevel, risk-based testing program that comprises visual inspection, field-based screening, and compendial testing.¹³ Toward this end, PQM supported 2 training-of-trainers sessions with a total of 35 DFDA staff on the appropriate use of GPHF-Minilab™.

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Results and Achievements

With PQM's support, the QC laboratory in Nay Pyi Taw was ready for an accreditation visit from the ANSI/ASQ National Accreditation Board (ANAB) based out of the United States. PQM helped the laboratory in facilitating and coordinating ANAB's pre-assessment audit in October 2016. Given the advanced level of preparedness of the laboratory's QMS and laboratory analysts, the lead assessor changed the pre-assessment visit into an official accreditation assessment and audit.¹⁴ Following the visit, ANAB officially granted ISO 17025 accreditation to the Nay Pyi Taw laboratory, the scope of accreditation covering 10 different types of tests. With PQM's support, DFDA successfully transformed an old, under-equipped, and outdated laboratory into an ISO 17025 accredited laboratory that is now performing tests for donors, international organizations, and national health programs, and is the only ANAB-accredited laboratory in Southeast Asia.

PQM's experience in supporting accreditation for laboratories in other countries has shown that the process typically takes about 2 years. In Myanmar, this timeline

was significantly shorter (approximately 12 months), due in large part to the commitment of DFDA leadership and Nay Pyi Taw laboratory staff. DGDA leadership showed consistent involvement and investment—participating in key meetings, providing oversight of laboratory activities, and even reallocating funding to ensure the laboratory was able to continue to make progress toward accreditation. Similarly, the laboratory staff was demonstrably committed in making improvements to the laboratory, as exemplified by their willingness to become trainers for other colleagues and foster a culture of learning and collaboration across the Nay Pyi Taw, Mandalay, and Yangon laboratories. This culture of continuous improvement is critical to the sustainability of the achievements made to date and helped the Nay Pyi Taw laboratory maintain its accreditation status in 2017. Finally, the decision by ANAB to change the pre-assessment visit into an official audit reduced the time to accreditation by several months, as the laboratory did not have to plan an additional visit.



DFDA staff members at a metrology and dissolution training facilitated by PQM.
Photo credit: PQM

Figure 1. Major Milestones in PQM's Support to DFDA



In addition to earning accreditation at the Nay Pyi Taw laboratory, DFDA has expanded its institutional capacity in several other ways as well. Following PQM's training and support in rolling out GPHF-Minilabs™, DFDA is now using the screening tool in all states and regions in the country and at several border points to support enhanced post-marketing surveillance of medicines quality. DFDA has also developed a cadre of individuals who can train and retrain colleagues on key regulatory and laboratory subjects, including use of the GPHF-Minilab™, basic laboratory techniques, and essential aspects of a QMS.

These accomplishments are critical steps forward for DFDA and are helping to lay the groundwork for a more robust post-marketing surveillance system within the agency. DFDA has increased its capacity to test the quality not only of antimalarial medicines but also of many other medicines that can be tested within its scope of accreditation, making the country as a whole safer from the dangers of poor-quality medicines.

The laboratory staff was demonstrably committed in making improvements to the laboratory, as exemplified by their willingness to become trainers for other colleagues and foster a culture of learning and collaboration across the Nay Pyi Taw, Mandalay, and Yangon laboratories.

Challenges and Lessons Learned

Creating a culture of learning and continuous improvement

A key challenge in developing the institutional capacity of DFDA and its QC laboratories is ensuring a deep cadre of experienced and appropriately trained individuals to staff key DFDA and laboratory positions. Like many regulatory authorities in low- and middle-income countries, DFDA suffers from high attrition as staff members often move to other positions or prefer to take positions in their home states or regions.

To help combat this challenge, PQM employed the Collaborative Learning Model to transfer technical knowledge in a sustainable way. This meant that when PQM provided trainings to the Nay Pyi Taw staff, staff from the laboratories in Mandalay and Yangon would also attend so that the knowledge was shared across the three laboratories. The trainings were also designed as train-the-trainer sessions so that all attendees could go on to train other individuals at their respective laboratories.

Not only does this reinforce the learning for the trainer, but it also builds a cadre of trainers who can reinforce learnings for each other if attrition occurs.

The Nay Pyi Taw laboratory trainers are now conducting trainings with the Mandalay and Yangon laboratories on their own, with minimal PQM involvement. This same model was used to support the rollout of GPHF-Minilabs™ in which PQM provided initial trainings in 2013 and 2014, and DFDA has taken ownership of the trainings and continues to train new staff. Continued utilization of the Collaborative Learning Model will be imperative as DFDA continues to expand its footprint in each state and region.

Establishing mechanisms for regular and effective coordination and communication

In Myanmar, coordination among various implementing partners was insufficient. In the past, only one coordination meeting among DFDA, the World Health Organization, PQM, and other partners occurred each year. PQM helped to streamline respective work plans

and coordinate more closely with partners to maximize resources and the outcomes of each partner's activities.¹⁵ PQM also ensured regular communication with DFDA senior management to engage on important issues that required their immediate attention (e.g., follow-up on the renovation of the laboratory building and procurement of a back-up generator). This regular and consistent follow-up was essential in achieving ISO 17025 accreditation.

Planning for sustainability

Ensuring that the achievements made by DFDA and the Nay Pyi Taw laboratory are maintained is a major challenge that PQM has been working collaboratively with DFDA to address, in part by considering ways to optimize financial resources.

Unlike some regulatory authorities in low- and middle-income countries, DFDA has established a specific budget for its QC laboratories, and has increased and reallocated funds to support the effective functioning of its QC laboratories. Future reaccreditation fees and associated costs have been planned for in annual DFDA budgeting activities. In close collaboration with experts from PQM, DFDA is also working to build internal capacity to conduct high-cost activities such as instrument maintenance and calibration. Shifting from using external service providers to developing the internal capacity to meet these needs themselves will reduce costs and allow DFDA to support expansion and accreditation of QC laboratories in other states and regions.

In 2018, PQM also provided technical assistance to DFDA to revise the outdated cost structure for quality control testing at the Nay Pyi Taw QC laboratory. Priority was given to establishing testing fees for antimalarials, as the laboratory is managing the quality testing of medicines being used by the Defeat Malaria Program, a key implementing partner supported by USAID/PMI.

Future Directions



As DFDA continues to expand its laboratory network and strengthen its ability to carry out key regulatory functions, the advances made to date provide the foundations for a stronger national quality assurance system. However, to build capacity to test other types of medicines and health products, DFDA and its laboratories will require support in the introduction of new technologies and analytical methods (e.g., gas chromatography and mass spectrometry). Additionally, the regulation of complex medical products, such as biologics, will be a key challenge for DFDA and is an area where additional support may be required. With PQM's support, DFDA is already taking on these challenges and has begun testing the quality of long-lasting insecticidal nets at

the Nay Pyi Taw laboratory to support the fight against malaria.

In the future, DFDA has the potential to strengthen not only its post-marketing surveillance capacity, but also other key regulatory functions, such as premarketing evaluation, product registration, licensing, and control of pharmaceutical advertising and marketing. Progressively strengthening in these areas would be facilitated by revising the outdated pharmaceutical law, continuing to build human resource capacity, increasing the number of accredited laboratories, and raising public awareness about the dangers of substandard and falsified medicines and health products.

New staff at DFDA in Nay Pyi Taw participating in a metrology training facilitated by PQM. Photo credit: Dr. Lu Lu Kyaw/PQM



Endnotes

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About PQM

The Promoting the Quality of Medicines (PQM) program is a cooperative agreement between the U.S. Agency for International Development (USAID) and the U.S. Pharmacopeial Convention (USP). PQM helps to strengthen medicines regulatory authorities and quality assurance systems and supports manufacturing of quality-assured priority essential medicines for malaria, HIV/AIDS, tuberculosis, neglected tropical diseases, and maternal and child health.

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