Informal Consultation with Partners on Emergency Response to Artemisinin Resistance in the Greater Mekong Subregion

11-12 February 2015
Bangkok, Thailand

World Health Organization
Western Pacific Region
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MEETING REPORT

INFORMAL CONSULTATION WITH PARTNERS ON EMERGENCY RESPONSE TO ARTEMISININ RESISTANCE IN THE GREATER MEKONG SUBREGION

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NOTE

The views expressed in this report are those of the participants of the Informal Consultation with Partners on Emergency Response to Artemisinin Resistance in the Greater Mekong Subregion and do not necessarily reflect the policies of the conveners.
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Keywords:

/ Artemisinins / Mekong Valley / Malaria – prevention and control / Communicable disease control
SUMMARY

Over the past few years, national governments in the Greater Mekong Subregion (GMS) have achieved a great deal of success in leading the fight against malaria. Countries have made significant progress in reducing malaria case numbers, working in partnership with World Health Organization (WHO) country offices, the Regional Hub of the WHO Emergency Response to Artemisinin Resistance (ERAR), donors and other key stakeholders. National programmes are now revising their malaria strategies from containment to the goal of elimination.

However, significant challenges remain. The simultaneous appearance and spread of malaria multidrug resistance, including ACT resistance in several foci is a major obstacle to eliminating malaria, not only in the GMS. Resistance to artemisinin and other partner drugs may pose a very real threat of malaria becoming untreatable.

The move to regional economic integration through the Association of Southeast Asian Nations (ASEAN) Economic Community has resulted in large-scale movements of populations within and across borders, which can further contribute to the spread of resistant malaria parasites, thus contributing to an even greater challenge to eliminating malaria. Reaching mobile and migrant populations is often difficult due to geographical limitations as well as legal issues that often prevent migrants from crossing at official check points. In addition, porous borders facilitate the flow of undocumented migrants between areas with different transmission intensity and untapped resistance patterns.

Overcoming these and other challenges to malaria elimination in the GMS requires a multipronged approach. The WHO ERAR Hub worked closely with all partners to facilitate an improved, technical response and better coordination. Through ERAR, WHO and other stakeholders advocate for adequate financial resources with built-in flexibility to enable innovative interventions and to improve donor coordination, avoiding any duplication and thereby maximizing impact.

WHO ERAR has also galvanized efforts towards strengthening surveillance to facilitate real-time reporting, strengthening the capacity of those involved in combatting malaria and ensuring adequate numbers of health facilities are sharing information needed for program planning and management. Other coordination activities included strengthening regional mechanisms for drug regulatory authorities, facilitating policy dialogue for the development of an appropriate governance mechanism and supporting operational research for improved tools to eliminate resistance. Improving cross-border cooperation and collaboration, maintaining malaria drug resistance and elimination high on the political agenda, and helping countries to adapt global strategies to country settings also benefited from increased attention among ERAR Stakeholders, as a result of ERAR Hub coordination activities.

Forum participants agreed that malaria multidrug resistance, including ACT resistance should no longer be seen only as a regional issue but as a threat to the entire global community. There is a sense of urgency and a need to tackle more aggressively the malaria drug resistance situation in priority, by eliminating *P. falciparum* as soon as possible. The general consensus was that all stakeholders work together to ensure that efforts are aligned with the WHO *Global technical strategy for malaria 2016-2030*, and *Strategy for malaria elimination in the Greater Mekong subregion 2015–2030*, launched during the 68th session of the World Health Assembly.
1. INTRODUCTION

1.1. Background

The WHO ERAR Regional framework for action 2013-2015, launched in April 2013, defined 15 essential actions along four priority areas. The Framework is aimed at stepping up efforts to preserve artemisinin-based combination therapies (ACTs) as an effective tool to treat *P. falciparum* malaria, the deadly form of the disease, and ultimately eliminate malaria. Implementation of the framework is estimated to cost around US$ 175 million per year.

Besides government contributions and other bilateral agreements, the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund) has pledged US$ 100 million over three years to fund operations in priority areas affected by artemisinin resistance in five GMS countries through the Regional Artemisinin Initiative (RAI). Countries include Cambodia, the Lao People’s Democratic Republic, Myanmar, Thailand and Viet Nam.

ERAR received funding from the Bill & Melinda Gates Foundation (BMGF) and the Department of Foreign Affairs and Trade of Australia (DFAT), and has established a regional hub in Phnom Penh, Cambodia to coordinate initiatives in artemisinin resistance containment and elimination in the GMS. The goal is to preserve the effectiveness of artemisinin-based combination therapies by containing and ultimately eliminating artemisinin resistant *P. falciparum* parasites from the GMS. As part of the oversight mechanism, the ERAR Forum of Interested Parties was established and is comprised of all stakeholders involved in the implementation of the ERAR Framework.

Annual meetings on containment and elimination of artemisinin resistance represent an opportunity for the Forum to review the progress, issues and challenges in implementing an effective response to the threat posed by artemisinin resistance in the GMS, and to discuss opportunities and future directions, with the full participation of senior government officials from GMS countries, WHO, donors and other partners and stakeholders.

The first ERAR annual meeting was held on 11–12 February 2015 in Bangkok, Thailand, as an informal consultation with all stakeholders in the GMS. The meeting was led by the ERAR Regional Hub, in collaboration with the WHO Regional Offices for the Western Pacific and South-East Asia, GMS countries and partners. ERAR, along with governments and key stakeholders, is in the process of developing a GMS Malaria Elimination Strategy in response to new evidence emerging from the region. This includes the identification of multiple foci of artemisinin resistance in the GMS that emerged both independently and through geographic spread, and multidrug resistant malaria in western Cambodia. Further, the proceedings from the meeting will inform the ERAR annual report on malaria elimination, to be shared with partners and posted on the ERAR website.

The informal consultation represented a significant milestone after the 9th East Asia Summit held in November 2014, where leaders set the goal of a malaria-free Asia Pacific by 2030. Consequently, the theme for the meeting was “moving forward with accelerated malaria elimination in the Greater Mekong Subregion.”

The key goals of the consultation meeting were to review the progress and challenges in implementing the ERAR Framework, and to provide a forum to refine the GMS Malaria Elimination Strategy.
1.2. Meeting objectives

The objectives of the meeting were to:

1) review progress, share lessons learnt and identify solutions to challenges in the implementation of ERAR Framework 2013–2015;
2) discuss planned key activities of the ERAR project for 2015;
3) provide a forum for discussion and refinement of the GMS malaria elimination strategy; and
4) discuss implementation arrangements including roles and responsibilities for malaria elimination in the GMS by 2030.

Expected outputs of the meeting are:

1) ERAR implementation progress towards artemisinin resistance elimination targets (both at country and regional level) reviewed and directions for 2015 and beyond defined;
2) GMS Malaria Elimination Strategy updated with inputs from ERAR wider constituencies with options on governance (technical and managerial) for a coordinated implementation GMS Malaria Elimination Strategy discussed.

2. PROCEEDINGS

2.1. Progress of ERAR Hub, ERAR Coordination and Key Achievements

Dr Mulombo presented the key achievements of ERAR in 2014 including high-level advocacy, commitment and leadership of national governments and institutions, with the support of key stakeholders, particularly those from national malaria control programmes (NMCPs). He noted that WHO, through its convening power and neutrality, had been instrumental in generating the necessary momentum to keep artemisinin resistance and malaria elimination high on the political agenda. WHO will build on these achievements to pursue its crucial role in effective coordination of the GMS malaria elimination campaign.

Significant successes during 2014 included development of a web-based GMS malaria database; development of a GMS Surveillance, Monitoring and Evaluation (SME) Strategy and establishment of a Technical Working Group; completion of the revised draft of the Regional Elimination Strategy; expansion of the drug efficacy surveillance network; and generation of strategic information through regular therapeutic efficacy studies (TES) which was used to update tier maps and guide prioritization and resource allocation in the GMS. In addition, the ERAR Hub is now actively engaged in providing managerial expertise and technical assistance to all partners supporting the initiative.

2.1.1.1. Cambodia

Approximately eight million people in Cambodia are exposed to malaria, predominantly in remote forested areas. Strong support from the Ministry of Health and effective collaboration with public health dispensaries, operational districts, health centres, and local authorities has significantly helped in the response and the integration of basic services. Malaria cases declined from 2009 to 2013 but increased from 2013 to 2014 due to high numbers of mobile and migrant populations (MMPs) crossing the borders.

The failure of artemisinin-based combination therapy (ACT) has been identified in five provinces and the 2014 data, though not yet official, is of concern. Also of concern is the asymptomatic carrier population identified after cross-border screening. Approaches to case management involve free diagnosis and treatment in public health facilities and subsidized treatment in the private sector. Despite success in many areas, challenges remain, such as insufficient and inflexible funding; difficulty targeting MMPs for diagnosis and treatment; asymptomatic parasite carrier population, and the challenges of common borders. In addition, the NMCP has found it difficult to take the lead role due to diversion of resources to partners who frequently expand their own networks and targets, rather than providing assistance. The NMCP needs to recruit more staff but has not found donor support to do so and as a result, the salaries and motivation of NMCP staff remains very low.

Discussion

The Chair noted the value of the CNM and also the need to address the issue of motivating staff in the public sector which remains a challenge for many countries in the region. Questions were then raised on the reason for the sudden rise in the number of cases in 2014, the origin of the cases, breakdown by species, location of screening points and screening of asymptomatic cases. Clarification was provided as follows: the increase in cases in 2014 was attributable to movements of MMPs and forest workers; the origin of transmission was mostly from Cambodia to the Lao People's Democratic Republic, although sometimes the reverse occurred.

The majority of cases were detected by rapid diagnostic test (RDT) at the cross-border screening point between the Lao People's Democratic Republic and Cambodia in Champasak Province. With drug resistance occurring in Champasak province, there is concern that high population movements between the two countries could facilitate the spread of resistance.

In addition, the different treatment regimes between the two countries remain a challenge. Breakdown by species revealed an increase in both *P. falciparum* and *P. vivax* but the majority of cases were *P. falciparum*. Asymptomatic screening was conducted at the Pailin checkpoint in Cambodia by village malaria workers. A final question concerned the rationale for conducting D3 surveillance of *P. falciparum* in Tier 2. D3 surveillance is carried out in Tier 2 due to a higher number of malaria cases and to stop the spread of resistance. D0 surveillance is conducted in low prevalence areas for elimination and there is no D3 surveillance for Tier 1.
2.1.1.2. China

China’s elimination timeline is to have zero local cases by 2015 except in the border areas of Yunnan and Tibet, and by 2020 to have a malaria-free nation. China has adopted the “1,3,7” strategy for elimination. This involves the following:

- **D1**: case detection and notification = diagnosis, report and treatment commenced;
- **D3**: case investigation and classification = laboratory confirmation and case classification; and
- **D7**: focus investigation and action = targeted action (reactive case detection; health education; vector control).

Case appropriate treatment has reached 100% in both Yunnan and the rest of the country.

In terms of interventions, indoor residual spray is used in foci vector control activities and long-lasting insecticidal nets (LLIN) distributed along the China-Myanmar border. The “1,3,7” approach has been highly successful and 50% of epidemic countries have passed the elimination assessment. Treatment is available free of charge across the country which has eliminated the market for fake or substandard drugs. However, challenges remain including control of cross-border malaria; laboratory identification of local or imported cases; risk of re-introduction in post-elimination (transmission-dynamics research); risk of resistance of anti-malaria drugs; and risk of resistance to insecticide.

**Discussion**

A comment was made on the importance of partners using common terminology, particularly in relation to artemisinin resistance and treatment failure. Currently, artemisinin resistance is defined as slow clearance time, however, slow clearance does not mean that the ACT is failing; this would also require a degree of partner drug resistance.

China’s response was that not all *P. falciparum* cases in China could be treated with artemisinin as between 1–3% of cases were not sensitive to artemisinin and the cause was unknown. It is possible that some isolate is not sensitive to artemisinin but there is no data to confirm this. As far back as 1983 evidence showed that some cases could not be treated by artemisinin derivatives. The second question concerned self-treatment with herbal medicines for those with fever. In China, self-treatment is virtually non-existent as antimalarial drugs are provided free of charge which has eliminated the need for self-treatment. Occasionally, returning migrant workers bring back antimalarial drugs from Africa and self-treat.

A final question concerned the criteria used by China to declare a county malaria-free. China noted that additional techniques and support are needed to determine how to deal with the challenge of false positives and how to clearly evaluate an area as malaria-free. Low parasitemia cases remain a concern because of the presence of fever but no identification of a parasite. Therefore, hospitals may not report cases where fever is present but no parasites are detected.

Regarding D3 and D7 investigation, China confirmed that classification was done by: (1) reporting; (2) classification cases as local or imported and investigating; and (3) D7 – foci investigation – country CDC confirms origin. Sometimes, communication with other provinces is necessary to identify the origin of the case. WHO uses a 14-day period because the period for transmission is limited; China uses a 7-day period because it is appropriate for country context.
2.1.1.3. The Lao People’s Democratic Republic

The Lao People’s Democratic Republic currently has one province in Tier 1, four provinces in Tier 2 and 13 provinces in Tier 3. From 2011, the country experienced a sharp rise in annual parasite incidence with a dip in 2013 and a subsequent rise in 2014. This rise is explained in part by the seasonal nature of malaria in the Lao People’s Democratic Republic and also the introduction of RDTs resulting in increased detection.

Despite the rise in cases, however, the number of deaths has continued to decline. Artemisinin resistance has been reported in the southern province of Champasak. Also of concern was a primary report of TES in Sekong province (Tier 2) with two cases presented positive at D3 (N=40). A research project on targeted artemisinin resistance is being considered in a Tier 2 province. An additional study is also being considered to assess the efficacy, safety, and tolerability of Triple ACTs compared to artemisinin-regular ACTs in uncomplicated falciparum malaria, and to map the geographical spread of artemisinin and partner drug resistance.

Key challenges include an insufficient number of staff in some provinces and districts, as well as low technical capacity especially at the district level. Skills development on data use and management as well as programme planning is required. This will be addressed through development of more simplified reporting and discussing alignment of key NMCP indicators into the DHIS2.

Another challenge is bottlenecks in disbursements due to the prescriptive nature of Global Fund budgets that limit the flexibility to respond. The CMPE is addressing this by improving coordination with principal recipients and the Global Fund.

Difficulties in delivering health messages for hard-to-reach populations have been addressed by piloting the interpersonal communication approach in village strata 3.

Finally, a major challenge is the pressure on NMCP management to respond to a diverse number of priorities by external partners and donors which are uncoordinated and often contradictory in nature.

Discussion

Clarification was sought on the reason for the number of *P. vivax* cases in 2014, which, although less than 2013, appeared to be higher during the wet and hot seasons. Part of the explanation could be that *P. vivax* is increasing in the northern part of the country, although more data is needed to confirm this. A follow-on question concerned the increase of *P. vivax* while *P. falciparum* declined and whether the use of primaquine could explain this. The response was that while primaquine was not used in previous years, it was being introduced as a cure for *P. falciparum* malaria. More data is needed on how to manage *P. vivax* cases.

2.1.1.4. Myanmar

Myanmar accounts for more than 70% of the malaria burden in the GMS with 284 of a total of 330 townships malaria endemic. However, malaria is declining, with a downward trend of morbidity and mortality. Increased use of RDTs and village-level volunteers in hard-to-reach areas will be supported by Millennium Development Goal 3. Drug resistance remains a problem with D3 parasitemia along the Thailand-Myanmar border at around 20%. Current malaria prevention and control activities cover 270 townships with support from the Global Fund and will expand to all 284 townships with additional Global Fund support. Under RAI, 52 townships are covered in Tiers 1 and 2.

Operational research includes a preliminary survey on repellents and impregnated clothes; a longitudinal entomological study; a community-based survey on malaria prevention and control; health facilities survey; FDA drug quality control; post-market surveillance; and MMP survey on treatment-seeking behaviour and utilization of bed nets.
Key challenges include inadequate human resources of Vector Borne Diseases Control staff at central, state/regional and township levels; weak coordination among donors/partners at all levels; limited communication infrastructure at all levels; disease surveillance system; delayed reporting from remote areas; detailed data not available for effective planning; large datasets difficult to manage and transfer due to limited IT infrastructure; lack of a centralized surveillance system that captures data from the private sector; and useful data on reactive case detection severely delayed or not submitted.

Discussion

Clarification was sought on the ban of oral artesunate monotherapies in Myanmar. Myanmar confirmed that new registration of oral artemisinin monotherapies has been banned since 2012 but acknowledged that stock remained in the market. In remote areas with no health facilities or health care workers, people used these as a supplement, and without providing alternatives, it would not have been wise to ban these outright. The last producing company's license will expire in 2014. Myanmar is now increasing availability of ACTs and promoting ACT use down to the village level. Artesunate monotherapy is no longer being legally imported.

The control of larva at community level was also raised as an issue. Myanmar piloted this approach in Kayah state but reported problems in implementation because of difficulties reaching forest and mountainous areas. More community-based surveys are being undertaken to assess the viability of other approaches. Although not all malaria is in forest areas, most malaria is transmitted from there or imported from other areas within the country, so village-level larva control is still not believed to be the optimal approach.

2.1.1.5. Viet Nam

Malaria stratification in Viet Nam involves five provinces in Tier 1, 20 provinces in Tier 2 and 38 provinces in Tier 3. Central Viet Nam has the highest endemicity. Morbidity and mortality has declined significantly with a case reduction of 90.5% and mortality reduction of 95.9%. An update on artemisinin resistance was provided. Treatment failure of \textit{P. falciparum} with artesunate was 14.6% in Binh Phuoc Province. Results of therapeutic efficacy studies (TES) between 2009 and 2013 identified four provinces in Tier 1 and 10 provinces in Tier 2. Updated results of TES in 2014 identified one additional province in Tier 1 and one in Tier 2.

Vector control activities have predominantly been the distribution of bed nets with limited use of indoor residual spray. Diagnosis is mostly done using microscopy. Case treatment is low compared to standby and presumptive treatment for the general population. In contrast, the military has a high percentage of case treatment due to the efficiency of the health system.

Major challenges for Viet Nam’s response to malaria remain and efforts to address these include maintaining high coverage of vector control interventions (providing LLIN, long lasting insecticidal hammock nets (LLIHN); improving the performance at peripheral levels (community health centres, village health workers) in case management; involving the private sector; supporting active case detection and focused screening and treatment; improving the access of MMPs to malaria control activities; strengthening surveillance system; operational researches on new tools; and enhancing cross-border collaboration.

Discussion

The role of the military in assisting with the elimination agenda was discussed and it was noted that in Viet Nam the military already collaborates with the Ministry of Health and plays an important role in helping with malaria elimination particularly at the cross-border points. Clarification was sought on the use of prophylaxes in the country and it was confirmed that this treatment was only used for military personnel traveling from non-malaria to endemic areas.
2.1.1.6. Thailand

Currently, 50% of Thailand's population live in malaria-free provinces; 42% in areas of low transmission and the remaining 8% in areas of high transmission. In 2014, Thailand saw an overall case decline of 15.71%. The breakdown by species of all cases was P. vivax at 50.95% and P. falciparum at 39.03%. Diagnosis is performed using both RDTs and microscopy. Around 120,000 RDTs were disseminated in 2014 to malaria points and health promotion hospitals with support from GF.

A shortage of trained microscopy staff has become a significant challenge with proficiency testing at hospitals revealing 10% of staff need training. Drug quality control has emerged as a key issue to be addressed and new systems are being established to ensure routine quality control of medications. Investigation and treatment outcomes for financial year 2014 show a decline in follow up at D3 (directly observed treatment) of confirmed uncomplicated P. falciparum cases treated with ACT in target areas from 39.55% in 2013 to 19.48%. In addition, the percentage of confirmed P. vivax cases that received appropriate antimalarial treatment according to national guidelines also declined from 84.64% in 2013 to 72.13% in 2014.

Treatment efficacy studies (artesunate and mefloquine) indicate that some provinces are near the threshold, however artesunate and mefloquine are currently the only drugs approved for use by the Thailand Malaria Drug Policy committee. A key success has been the web-based reporting system developed by Mahidol University for tracking D3 follow-up and adverse drug reactions.

Looking forward, a National Programme Review is planned to include effective early warning indicator/response and a better surveillance system. Its other goals are to: increase access to existing diagnosis and treatment facilities; increase compliance to standard treatment guidelines; revise the National Diagnosis and Treatment Guidelines; strengthen treatment adherence; improve quality assurance for diagnosis and treatment; expand TES beyond Tier 1; and advocate for greater financial commitment.

Discussion

Clarification was sought on whether there were plans to change first line treatment in Thailand. Thailand responded that changing the composition of the drug policy committee to ensure better representation across agencies was the first step in facilitating access to greater options for relevant drugs for treatment. Regarding the increase in malaria cases in Rachathani province in 2014, investigations revealed that this was due to illegal border crossing for logging.

It was noted that now that the issues had been identified, a rapid decline in number of cases was predicted. The viability of cross-border screening points was raised in the context of migrants often avoiding screening points. It was argued that screening points remain important. Among 3000 cases screened in Kanchanaburi and Tak province 5% and 10%, respectively, were found to be asymptomatic cases. Therefore to achieve elimination, screening for asymptomatic infections would continue to be important at border crossing points to ensure that the parasite reservoir is identified and eliminated.

Regarding the proportion of confirmed cases treated, a question was raised about the decline in 2014. The response was that the data needs to be verified. The information came from malaria clinics in the vertical programme and not from public or private hospitals.

Dr Alonso, Director of WHO Global Malaria Programme, reminded country delegates that WHO was ready and willing to help countries adapt global guidelines to fit into their national policies and contexts and that the programme is not focused on simply issuing global guidelines but ensuring they can be adapted and used by all countries.
Regarding border crossings, Dr Alonso informed participants that it would be useful to capture country experiences as this would also help inform the adaptation of policies at the global level.

Future challenges

With only five or six endemic provinces in Thailand, it is often difficult to ensure malaria stays a priority at the national level. In the next 5 to 10 years most countries will have a small numbers of patients. This will make it difficult to retain expertise since most health staff will not have diagnosed or treated a malaria case. It will also be hard to keep this as a priority and to justify production of antimalarial drugs. Research centres are also asking how to maintain expertise. Success of the programme could result in difficulties in maintaining malaria as a country priority.

2.1.2. Partner and Donor updates

2.1.2.1. Asian Development Bank (ADB) Regional Malaria and Other Communicable Disease Threats Trust Fund

In December 2014, the Trust Fund was approved by the ADB Board and agreed on a start-up date of January 2015 with a US$ 18 million allocation. Other financial commitments include a UK Department for International Development (DFID) contribution of US$ 19.2 million and the Australian Government's US$ 16.3 million contribution through the Department of Foreign Affairs and Trade (DFAT). A Regional Workshop on Reinforcing Health Security in the GMS followed. Agreement was reached to focus on countries with artemisinin resistance as well as regional activities.

Malaria activities have been integrated into an on-going ADB CDC II programme in the GMS (US$ 14 million). Resources for Trust Fund Priorities are split equally between regional projects (leadership and financing; quality commodities; data improvements; and health impact assessments) and Country Rapid Responses building on existing ADB projects as well as building a CDC III project integrating malaria into other work.

ADB’s lending activities include the Health Security Project for 2017–2022, which supports International Health Regulations (2005), malaria and CDC, with potentially up to US$ 200 million combined loan and grants for all countries for five years. This includes loan and/or grant activities in Cambodia, the Lao People’s Democratic Republic and Viet Nam. It follows the successful IHR-targeted Communicable Disease Control Programs I and II (which is ending in 2016). Regional-based activities will include work to support the issue of migrant populations in Myanmar.

2.1.2.2. Asia Pacific Leaders Malaria Alliance (APLMA)

The Asia Pacific Leaders Malaria Alliance (APLMA) was formed at the 2013 East Asia Summit when an affiliation of heads of government formed to accelerate progress against malaria and to eliminate it in the region by 2030. APLMA is not an organization, a programme or a funding body. It does not involve membership.

At the East Asia Summit in 2014, leaders reiterated their commitment to the Declaration of the 7th East Asia Summit on Regional Responses to Malaria Control and Addressing Resistance to Anti-malaria Medicines. They welcomed the APLMA Task Force Progress Report 2014 and agreed to the goal of an Asia Pacific free of Malaria by 2030. They tasked the APLMA co-chairs to submit a plan for achieving this goal to the 10th East Asia Summit in Malaysia and to implement the recommendations of the APLMA Task Forces.
APLMA is in a strong position to assist NMCPs raise finances by reminding leaders of their commitment to elimination, of the resources needed to achieve it and the resource gaps countries are facing. APLMA aims to have the road map developed by June or July 2015 for endorsement at the 10th East Asia Summit in November 2015.

2.1.2.3. Bill & Melinda Gates Foundation (BMGF), “Accelerate to Zero”

The Global Health department of the BMGF has an annual budget of US$ 200 million for malaria. The strategy is based on three main priorities: (1) demonstrate an accelerated path to elimination; (2) invest in new interventions; and (3) mobilize support. The goal is to “bend the curve” away from resurgence and sustain progress to accelerating to zero transmission. This will be achieved by ensuring complete detection of all cases (both symptomatic and asymptomatic) and treatment of all cases and thereby the elimination of the human parasite reservoir and completely preventing transmission.

The GMS is one of three priority regions supported by BMGF. The goal of BMGF investments is that they are catalytic and will leverage additional funding from other sources. Significant resources are put into advocacy and engaging current partners to be effective. BMGF is shifting away from universal coverage to effective coverage to ensure that interventions are relevant to the geographical area and specific population. BMGF advocates for a country-led process with support from donors and other partners. Innovation is important for the development of effective tools to achieve complete eradication of malaria. All interventions must be evidence-based through operations research to inform effective policy.

2.1.2.4. Australian Government Department of Foreign Affairs and Trade (DFAT)

In 2013, AusAID was integrated into DFAT which was followed by a reformulation of Australia’s development policy. The country’s primary focus remains the Indo-Pacific region. Health and development remain key pillars of Australia’s aid programme, and the entry point is health security.

Important benchmarks within DFAT’s performance framework include private sector, gender, innovation and governance. The recent health portfolio review noted the importance of addressing malaria. A new health sector strategy is currently being developed which will focus on HSS and health security. There is optimism that the current engagement and commitment will remain in place for malaria elimination.

DFAT currently contributes to the ADB regional malaria trust fund and is fully engaged in APLMA. DFAT also supports the malaria agenda through bilateral support to Cambodia and Myanmar (through the Global Fund) and through a programme that will seek funding approval to address the issue of substandard medicines. This programme will work with the Australian Therapeutic Goods Association and build partnerships with Thailand and Viet Nam regulatory authorities, as well as with the Lao People’s Democratic Republic and Myanmar to build capacity on drug quality. Although the programme will address all essential medicines, there is an expected focus on malaria.

Plans are currently underway for an independent review of the first 18 months of the ERAR Hub scheduled between March and April 2015. Key stakeholders will be invited to contribute to the review. This is an opportunity to consider the effectiveness and sustainability of the ERAR mechanism and the future in the changed context of elimination, as well as governance of the entire response to malaria. A key focus is ensuring that all political, technical and financial resources are used as effectively as possible for the best possible outcomes. As a lead technical agency WHO has a key role in this process.
2.1.2.5. Japan International Cooperation Agency (JICA)

JICA first provided support for malaria control in Myanmar in 2003. This support had a focus on MMPs who live mostly in mountainous areas. The programme was developed around the training of volunteers and worked to avoid overlap with the Ministry of Health. For the 2015 financial year, technical assistance will be given with the key goals of: (1) strengthening technical and management capability of vector-borne disease control; (2) strengthening management capabilities at the township level; and (3) developing the model to reduce transmission intensity in different epidemiological settings. (targeting interventions in areas with *An. dirus* malaria).

The key message from JICA is that sustaining control is not enough, as resurgence will occur. The time has come for a paradigm shift and more focus on innovation of new and more effective tools.

2.1.2.6. USAID/President’s Malaria Initiative (PMI)

The *President’s Malaria Initiative Strategy (2015–2020)* aims to (1) reduce malaria mortality by one-third from 2015 levels in PMI focus countries, achieving a greater than 80% reduction from PMI’s original baseline levels; (2) reduce malaria morbidity in PMI countries by 40% from 2015 levels; (3) assist at least five PMI focus countries to meet the WHO criteria for national or subnational pre-elimination. Areas of strategic focus include scaling up of proven interventions; adapting to new epidemiology and incorporating new tools; improving country capacity to collect and use information; mitigating risks against the current malaria control gains; and building capacity and strengthening health systems.

PMI’s planning process involves the development of a national Malaria Operational Plan for all countries. The Malaria Operational Plan is developed a year and a half to two years in advance of implementation. PMI’s focus is to balance the implementation of proven interventions with the need for new tools and to ensure efficient coordination with ERAR and NMCPs.

2.1.2.7. Global Fund Regional Artemisinin Initiative (GF-RAI)

The Global Fund grant of US$ 100 million over three years (2014–2016) involves country components in five GMS countries at US$ 85 million and an intercountry component of US$ 15 million. The UN Office for Special Projects (UNOPS) Myanmar was selected as Regional Principal Recipient by the Regional Steering Committee (RSC) in 2013 and the grant agreement was signed in February 2014. All Country Coordinating Mechanisms selected their current in-country PRs to be UNOPS’ partner for RAI country components (UNOPS for Cambodia, Myanmar and the Lao People’s Democratic Republic and co-PR for Thailand and Viet Nam).

The overall objective of RAI is to contribute to the elimination of *P. falciparum* malaria in the GMS, and to prevent the emergence or spread of artemisinin resistance to new areas. The goal is for grant implementation to be flexible, performance- and impact-based and adaptable to new challenges and evidence.

The intercountry component primarily focuses on cross-border activities targeting MMPs in border areas. The country components are designed to complement existing Global Fund financing, targeting specific areas of resistance (Tiers 1 and 2). RAI and WHO work in close collaboration, with WHO policy documents being essential for guidance. Both WHO country offices and ERAR provide assistance to national programmes and PRs regarding RAI implementation; WHO ERAR stakeholder meeting results are also taken forward into RAI funded activities. An example of this is the activities defined in the 2014 meetings on MMPs that were taken forward in the reprogramming.

**Discussion**

Concerning financial support for drug regulatory initiatives, Cambodia commented that although WHO had spoken of the root cause of artemisin resistance being related to the irrational use of
ACTs, donors were not focusing on drug regulatory initiatives in their budgets, which should be a priority. Cambodia proposed that donors consider funding activities related to drug regulatory authorities as few resources are currently available for this. The Chair (Dr Satimai) noted that DFAT is considering supporting drug regulatory initiatives through an ASEAN subcommittee or establishing a new committee to manage commodities and regulatory authorities.

DFAT responded that initial discussions took place with the Lao People’s Democratic Republic, Myanmar, Thailand and Viet Nam, however DFAT would still be happy to also discuss with Cambodia and include it as part of the initiative. The focus would be on working with national medicine regulatory authorities to look at tools, instruments, regulations and in-country capacity to improve and carry out in-country regulation. However it would also be important to build upon regional initiatives. The plan was to engage with ASEAN on this and to have the Australian Therapeutic Goods Association be the key manager of the initiative.

WHO China noted that there is a gap between programmes and national regulatory authorities in many countries which must be addressed. High-level advocacy is required to engage other stakeholders who play important roles in ensuring the quality of medicines in each country. Additionally, this aspect of work is not taken into consideration when developing proposals for malaria elimination. This needs to happen within the country and those in the regulatory positions and organizations need to be empowered. WHO is working with national drug authorities and has established a set of related priority activities that vary between countries. This is a good start but it needs to be scaled up. Malaria funding is available but it will be important to continue to make the case.

Regarding the issue of donor coordination and limited resources, an nongovernmental organization requested further information on the current coordinating mechanisms that donors use to ensure effective coordination.

The response from APLMA was that many of these issues at national and regional level require attention from regional leaders. Partners need to think about engaging heads of governments about donor coordination. DFAT supported this statement, underlining the importance of leadership of supra-national bodies to provide the framework within which donors mobilize resources.

While WHO is pivotal in providing the overarching technical strategy and framework within which all stakeholders operate, another effective mechanism is also required to ensure that financial resources are mobilized in the most effective way, and this may or may not be through WHO. Leaders of each country should play more active roles in this. Mechanisms are needed to ensure that as traditional donors’ resources are dropping and new donors are appearing, new coordination challenges can be effectively managed.

Thailand FDA explained that Thailand is a partner for capacity building of regulatory activities through the ASEAN Harmonization Initiative and its Pharmaceutical Product Working Group in ASEAN countries. This forum is still active with the next meeting scheduled in Vientiane, Lao People’s Democratic Republic, in March 2015. It will be very useful to have these networks for co-assessment of new malaria drugs within the region. Countries will want to know how to access donor funds for programmes on hard-to-reach populations and for operational research.

The Global Fund noted the importance of specifically targeting where transmission is occurring and where there is intelligence of the transmission dynamics. Political leaders of the region need to tackle the governance structure and financing and policy in the region. It is a challenge for all partners to work together to develop a workable solution. High-level political leadership and better policy guidance is needed to ensure that all donors will spend their resources wisely.
2.2. Review of Day One

Dr Mulombo recapped what had been achieved during the previous day’s discussions. Countries had provided an overview of what was happening at country level, and information had been shared between different stakeholders and donors supporting interventions. Key issues include the need to strengthen coordination, address human resources needs, respond to the request for flexible funding and the issue of stakeholder coordination at country level.

Other issues raised were the need for advocacy at high levels, of which participants had discussed possible options on the way forward. Dr Mulombo informed participants that WHO ERAR was in the process of finalizing the Regional Elimination Strategy and that inputs received during the two-day informal meeting with partners would be incorporated into the next draft. He concluded his remarks by reminding partners of the focus of day two, which would be on discussing the governance structure.

2.3. Update on the WHO Global Technical Strategy for Malaria (2016–2030)

Tremendous progress has been achieved globally over the past 15 years. Key achievements include the following:

- Global malaria incidence has declined by 30%;
- Malaria mortality rate has reduced by 47%;
- Under-five malaria mortality rate in Africa has declined by 58%;
- Over 4 million malaria deaths averted since 2000;
- 49% of the at-risk population in Africa has had access to an ITN in recent years – compared to 3% in 2004;
- 392 million courses of ACTs procured in 2013 – up from 11 million in 2005; and
- 319 million RDTs delivered to countries in 2013 – up from 46 million in 2008.

Most of these successes have been due to the scaling up of successful interventions. However, huge challenges remain. Around 3.2 billion people globally are still at risk of malaria. Malaria deaths are still unacceptably high. Most countries are still far from achieving universal coverage of at-risk populations with core interventions. Perhaps the biggest problem is that around 60 million cases are still undiagnosed and untreated. In addition, drug and insecticide resistance present serious challenges. All of these factors led to the need for a new global strategy.

The new WHO Global Technical Strategy for Malaria 2016–2030 is based on three pillars:

1. ensuring universal access to malaria prevention, diagnosis and treatment;
2. accelerating efforts towards elimination and attainment of malaria-free status; and
3. transforming malaria surveillance into a core intervention.

The three pillars are underpinned by two supporting elements: harnessing innovation and expanding research, and strengthening the enabling environment. To implement the strategy a total of US$ 105 billion is required for the period 2016–2030 with an additional US$ 0.7 billion per year required for research and development. WHO is confident that these goals are very achievable and that countries will play the lead role in the global malaria response.

Discussion

The Chair invited country representatives to comment on the Global Malaria Strategy in the context of the GMS, noting that the current forum provided a rare opportunity for NMCP managers to come
together for discussion. He also noted that the plans will be executed by NMCPs, therefore the concerns of various countries about insufficient human resources must be addressed. The elimination workforce needs to be bolstered while national policy-makers need to be convinced to maintain malaria experts and programmes.

**Thailand** saw the goals as realistic within the context of three approaches.

1. Advocacy is important to get policy-makers to commit to supporting elimination.

2. A sound technical approach that outlines how to address transmission among MMPs (which will increase rapidly with the ASEAN Economic Community as well as improved transport systems between countries). The issue of conflict and insurgency is also of concern. However, Thailand was encouraged by the innovative approach to tool development as insecticide resistance is a real concern.

3. Financial: as Global Fund support will soon come to an end for many countries in the region, financial solutions to support initiatives to prevent reintroduction will be critical. Targeted advocacy for allocation of resources will be important at both national and subnational levels. Thailand will advocate for an internal certification process at provincial level to certify malaria-free zones and to continue with financing to prevent reintroduction.

**Cambodia** expressed that the strategy needs to be locally adapted. Flexible funding will be required and motivation incentives need to continue after elimination.

**Myanmar** noted that every country has its own context and social norms and that ongoing technical and other support will be required. As case numbers decline, policy-makers will lose interested, hence more effort to target malaria in remote areas will be necessary. Advocacy for ongoing political and financial support will be critical post-elimination. Developing approaches to help national malaria staff remain engaged and motivated will also be a priority.

**China**’s elimination goal of 2020 has been reached, however, concern remains over transmission at the China-Myanmar border. Although artemisinin resistance has not occurred in China, drug resistance for ACTs remains. Further research is required to confirm this. China supports Thailand’s suggestion for more research on ACT resistance and artemisinin/artesunate resistance in the GMS. China would like to see more joint activities in the region through the network on drug monitoring supervision and inspection.

**The Lao People’s Democratic Republic** noted the importance of clear, operational guidelines to convince the national government that elimination is achievable, particularly in a context where some provinces are highly endemic and others are close to pre-elimination. The malaria situation in the Lao People’s Democratic Republic is dynamic with a lot of migration flows in and out of the country. The country will require a lot of technical and financial support to achieve its 2030 milestone. Despite successes, the challenge of addressing malaria among MMPs remains significant. The current level of financial resources is insufficient to implement current activities. There is also a need for a clear strategy for MMPs. Currently there are recommendations but there are no clear strategies. Adopting Thailand’s approach and obtaining provincial level elimination certification may be one way of convincing the government.

**DFAT** raised the ongoing need for advocacy in the GMS to gain high-level political commitment for malaria elimination. DFAT further inquired how the Global Malaria Strategy would help convince politicians, financiers and community leaders of the need to engage and the feasibility of achieving the strategy’s goals. The response was that the “what, where, when and how” still needs to be developed, however the key issue is how to keep the commitment. The Global Malaria Action Plan tool is currently being developed which will deal with the above issues. The regional consultations
also had a back-to-back discussion on the Global Malaria Action Plan. In terms of the targets, information was triangulated to ensure that the goals were not just aspirational but fully achievable.

**BMGF** noted that all partners aim for aspirational goals. NMCPS are concerned about how to mobilize human and financial resources. The critical question that needs to be answered is the structure of community health care forces that will be left in place once malaria is eliminated. BMGF reiterated that the foundation is listening to NMCPS on how they will structure their elimination programmes and what they will do to ensure that health systems are strengthened and malaria expertise remains.

### 2.4. Update on artemisinin definition

Dr Ringwald noted that it is critical that all partners speak the same language when it comes to drug resistance and treatment failure. He provided a review of previous and current definitions of resistance and treatment failure. The working definition of partial artemisinin resistance was developed based on observations from routine therapeutic efficacy studies of ACTs, clinical trials of artesunate monotherapy, and K13 sequencing.

**Suspected endemic artemisinin resistance** is currently defined as:

- \[\geq 5\%\] of patients carrying K13 resistance-associated mutations; or
- \[\geq 10\%\] of patients with persistent parasitemia by microscopy on day 3 after treatment with ACT or artesunate monotherapy; or
- \[\geq 10\%\] of patients with a parasite clearance half-life of \(\geq\) five hours after treatment with ACT or artesunate monotherapy.

**Confirmed endemic artemisinin resistance** is defined as:

- \[\geq 5\%\] of patients carrying K13 resistance-associated mutations, all of whom have been found, after treatment with ACT or artesunate monotherapy, to have either persistent parasitaemia by microscopy on day 3, or a parasite clearance half-life of \(\geq\) five hours.

The fact that ACT treatment failure is not equal to artemisinin resistance was underlined. Treatment failure can overcome delayed resistance if treatment is prolonged, for example, from three to seven days enabling the partner drug to complete the job of clearance. In addition it was noted that remarkable progress has been made with the identification of the K13 molecular marker for artemisinin resistance. The K13 mutation is associated with four other mutants, though it is not yet known what they represent. This is all under investigation but indicates a multigenial/genetic mutation that leads to artemisinin resistance.

**Discussion**

BMGF noted that how to tackle elimination in the context of drug resistance remains a key question. Countries will continue to look to WHO for clear guidance on how to proceed. WHO responded that the target of elimination will not be met without a good first line treatment in all GMS countries.

Thailand commented that there were four ways to manage drug resistance. The first was a change of regimen; the second was to keep the first line drug but to focus on adherence and compliance; the third was to extend the time of treatment; and the fourth was to increase dosage. WHO commented that these options are valid but slightly contradictory. Maintaining treatment adherence is difficult if the treatment period is extended. Consideration of safety and toxicity issues must also be taken into
account when increasing dosage. Although this could be an option, simply increasing the dosage may not work because the parasite will adapt.

2.5. Draft strategy to move from malaria control to elimination in the Greater Mekong Subregion 2015–2030

As most GMS countries are considering, or have already committed to elimination, the development of a GMS strategy is timely. The overall goal of the strategy is to interrupt the transmission of malaria and eliminate the disease, in a sustainable way, within all affected countries of the GMS by 2030. The key regional priorities include interrupting transmission and eliminating multidrug resistance (including artemisinin resistance); reducing transmission in areas of high transmission; and controlling the resurgence of malaria. The prioritization does not mean that efforts to eliminate malaria in low transmission areas should be put on hold.

Success will depend upon the effective translation of the strategy into national elimination programmes and plans of action, wherein notification on each case of malaria is mandatory; adequate case-based malaria surveillance is established and fully functional across the entire territory; the planning of elimination measures is based on epidemiological investigation and classification of each malaria case and focus; universal coverage of disease management achieved; a strict total coverage of all active foci by effective vector control measures; national malaria elimination database established and operational; and a national monitoring elimination committee is set up.

In addition, investments in operational research to develop innovative and effective tools will be critical, as well as investment in human resources, strengthening leadership/management and defining the administrative policy and legislation. A costing exercise will be carried out in collaboration with the national malaria programmes in each GMS country in 2015.

2.6. Suggested timeline for the development of the GMS Elimination Strategy and planning process

Attention was drawn to the fact that the development of the GMS Elimination Strategy was a highly participatory process. The timeline was presented as follows:

<table>
<thead>
<tr>
<th>Milestone</th>
<th>Target date</th>
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</thead>
<tbody>
<tr>
<td>Produce 4th draft based on Partners Forum inputs.</td>
<td>19 February</td>
</tr>
<tr>
<td>Put 4th draft on the web for open web consultation.</td>
<td>20–28 February</td>
</tr>
<tr>
<td>Produce 5th draft and present to MPAC.</td>
<td>5–7 March</td>
</tr>
<tr>
<td>Establish Steering Committee for technical review.</td>
<td></td>
</tr>
<tr>
<td>Organize in-country workshop for updating national malaria strategic plans and national action plans, and provide inputs for a regional/cross-border component, based on the most recent version of the Strategy.</td>
<td>Mid-March to June</td>
</tr>
<tr>
<td>Include further inputs into the Strategy and produce final version of the GMS Malaria Elimination Strategy.</td>
<td>March–May</td>
</tr>
<tr>
<td>Launch the Strategy during the World Health Assembly side event on the Global Malaria Technical Strategy (2016–2030), Geneva.</td>
<td>18–26 May</td>
</tr>
<tr>
<td>Well-coordinated rollout/implementation of the GMS plan, including resource mobilization.</td>
<td>From mid-2015</td>
</tr>
</tbody>
</table>
2.7 Plenary discussions and feedback from donors and other stakeholders on the GMS Malaria Elimination Strategy

The Chair opened the discussion by noting that countries must focus on preparing their own strategy at country level. Certification of malaria-free provinces would be a good starting point. Countries can no longer rely on previous strategies but must look at current challenges as they work towards achieving the regional goal and agree to a timeline to reach the goal.

**The Lao People’s Democratic Republic** agreed in principle with the timeline, as it was in line with the targets set by the Prime Minister to eliminate *P. falciparum* malaria in 2020 and complete malaria elimination by 2025. However, lack of human and financial resources remains a significant concern for the country particularly in the context of drug resistance, MMPs and cross-border coordination.

At a meeting to improve the regional strategy held in November in Cambodia, discussions focused on the importance of each country continuing to address elimination at national level and ensuring that national plans were aligned to this target. The Lao People’s Democratic Republic is currently revising the national strategic plan which ends in 2015. This needs to consider if elimination is achievable in the current context where the focus is still on control in the southern provinces. Classification of provinces into elimination and control provinces is one way forward.

**Thailand** has set 2024 as the year to declare elimination, whereby elimination must be achieved by 2021, as the WHO certification process can take three years. Thailand has broken down its targets by earmarking 2015 as the year for policy sensitization, advocacy and development of detailed work plans, and 2016 to focus on large-scale implementation.

A national consultation in February 2015 revealed the following issues that must be resolved before Thailand can accelerate to elimination: the management body in the country needs to be strengthened, which cannot be done by a regular bureau. Also, the certification process must be included in the strategy as a tool for programme managers and policy-makers.

Dealing with elimination also means focusing on certification, not just elimination. This requires a mind shift from control to elimination. The definition of elimination by certification is also important. For instance, eliminating malaria among highly mobile populations is difficult; countries can be prone to putting the burden on each other when classifying cases as imported or indigenous. Having clear definitions early on would help this process. Regarding the target population, most attention is on MMPs but it is critical to detect all cases, cure all cases, think beyond mobile and hard-to-reach populations and ensure that long-term financial commitment needs are included in the strategy.

Drug resistance is also a big concern and Thailand’s systems are not sufficient to determine information such as the number of patients on ACTs returning on D3. In addition, the different patterns of resistance along the borders require innovative approaches. An example cited was a request from the Health Minister to issue certification to provinces to promote tourism. The certification process takes two to three years. Further, data sensitivity, especially on military records, needs to be addressed because certification cannot be issued without it. This requires political commitment.

With a high number of imported cases, **China** focuses on addressing malaria among MMPs. At the recent meeting in Shanghai on MMPs, discussion focused on the “1 Zone principle” (one buffer zone) for targeting malaria using one monitoring and evaluation (M&E) performance framework. This approach could be appropriate for combatting malaria on the China-Myanmar border. A Memorandum of Agreement between the two countries on health cooperation is a key focus, as dealing with imported cases is a high priority for China, particularly with the move to elimination.

**Myanmar** has borders with multiple countries which requires effective strategies to improve relations and intercountry collaboration.
**Bangladesh** has an updated strategic plan and has targeted malaria elimination by 2020. However, the target for elimination may be re-calibrated to 2025 following an outbreak detected in 2014 in areas bordering Myanmar and India. Further, case investigation takes place in low endemic areas but the priority regions are hilly areas bordering Mizoram and India. It is important that the same kind of management systems are put in place in border areas across GMS countries. In the 1960s, Bangladesh dedicated malaria personnel in all districts but health staff are now fewer and overburdened.

There are nongovernmental organizations currently working under the Global Fund but many issues are expected to arise once funding has concluded. Of the Global Fund's tranche of US $15 million that the government received, US$ 13.5 million went to long-lasting insecticidal nets, which are costly and not always effective. This underlines the need to focus on alternative interventions which requires political commitment.

**Comments from Donors**

WHO noted that all countries aiming for elimination are concerned about the importation of cases so it is important to focus on this as a regional issue.

Further, a strategy for resource mobilization is necessary. Experience can also be gained from looking at other disease eradication programmes. WHO could support NMCPs in having these conversations with senior officials at the country level.

RAI noted the importance of a regional plan for elimination. The challenge is to translate it into an action plan wherein WHO plays a key role in guiding this process. Existing resources can be used to help put this plan into action.

BMGF outlined a number of observations and suggestions to improve the current document.

- Putting control against elimination is a false dichotomy. Elimination is clearly defined. Control is the action taken. In the Elimination Strategy, there seemingly is a distinction between activities permitted under control and those that can be done to achieve elimination. This may be holding back some countries that are willing to be more aggressive in their approach.
- The Strategy would benefit from elaboration on a technical assessment for malaria to help define what needs to be done, i.e. malaria needs to be eliminated because of drug resistance but it cannot be eliminated without an effective drug. The conclusion might be that it is necessary to wait until there is a new molecule. However the document needs to outline more clearly how to be more aggressive with the tools currently available. Operationally, a more clearly defined level of rigor and precision will be demanded from all stakeholders. While financial resources are important, the approach must also be clearly defined in terms of testing, treatment and tracking. An example would be detecting the number of infections and treating them to impact the parasite. In addition, moving from universal to effective coverage is important in terms of vector control interventions and assessing what will have the biggest impact on transmission.
- Regional accountability through a common set of indicators on surveillance is still missing.
- Robust financial assessment and gap analysis are still required.

DFAT underlined the importance of political commitment and backing from the government and stated that the current strategy should more clearly delineate key messages around the global, regional and national public good of addressing elimination as well as key messages around feasibility. Mobilization of resources would then logically follow. The reality is that current bilateral donors will not be the ones providing resources in 15 years. The argument needs to be explicitly addressed for other innovative financing mechanisms such as development bonds.
In addition, other untapped financial resources should be explored. A governance mechanism is needed that brings in a wider group of players. The focus of information sharing should not only be on reporting and surveillance but about Management Information Systems that work in real time, which should be more explicit. At the community level, appropriate strategies to engage communities need to consider the differences in languages, ethnicities, cultural practices and health-seeking behaviours of target populations, who may either have low levels of literacy or be illiterate.

WHO reinforced that the purpose of the session was to hear from all stakeholders and to incorporate their feedback into the Strategy for further improvement. In terms of the Strategy’s intended audience, WHO viewed the document as primarily a technical one and recognized that an accompanying document may be necessary for advocacy on political commitment and financial resource mobilization. Although the current Strategy is regional in focus, there should be clearer links with the Global technical strategy for malaria 2016-2030.

In addition, the terms “control” and “elimination” have been avoided in the GTS and the approach has been presented as a continuum so that countries can move towards elimination, whatever stage they are at. The Strategy should also incorporate the priority for innovation for smarter activities towards elimination. In terms of a sense of urgency, the GTS talks on accelerating elimination require a change in mind-set to embracing elimination. Some of the issues in the region include reaching MMPs as well as cross-border challenges, which remain significant and need to be addressed. However, drug resistance is not a problem in terms of elimination. Drug-based and vector control approaches can be implemented in a short space of time. Translation of the Strategy into a work plan at national level needs to be done quickly.

2.8. Options for governance/coordination of the Strategy to move from malaria control to elimination in the Greater Mekong Subregion, 2015–2030

Existing governance mechanisms include:

- WHO, including the ERAR Hub and its working groups, which provides technical coordination;
- Global Fund RAI Regional Steering Committee (RAI RSC) which provides oversight of the RAI grant;
- APLMA (and its topic-specific task forces) that advocates for high-level political support and in specific areas (e.g. finance, drug regulation);
- APMEN and its Advisory Board; and
- ASEAN and its expert/working groups.

There is a consensus that improved coordination and governance is required:

- to avoid duplication, inefficiency, fragmentation and high transaction costs for countries;
- to be more efficient and effective; and
- to ensure that nongovernmental partners empowered by their donors do not act independently without consultation.

Key areas that would benefit from strengthening coordination include strategic planning, research, data sharing, resource mobilization, review mechanisms, communications and advocacy, division of labour and private sector engagement.

Additional governance at country and regional levels would ensure engagement and buy-in of appropriate partners; shared oversight of implementation of the agreed strategy; optimal use of available resources – prioritization tracking of achievements and identification of bottlenecks and “failures”; and regular joint review of a common set of milestones/indicators and reallocation of resources if necessary.
Six options were presented for a governance/coordinating body for malaria elimination in the GMS:

- A task force/working group under APLMA;
- An expansion of the role of the ERAR hub;
- A sub-committee/working group under APMEN;
- Expanding the role of the RAI RSC;
- Taking advantage of the RAI RSC meetings to convene a back-to-back broader governance group;
- Locating the governance function with an appropriate ASEAN group.

These options could be considered as well as an independent monitoring group. An additional option was to build upon the success of the RSC by developing a model of an "RSC PLUS" co-chaired by a Regional Representative with WHO and APLMA to ensure strong links between the three groups. RSC PLUS membership should have the right balance between country government representation and other stakeholders/constituencies.

Discussion

The Lao People's Democratic Republic supported the idea of AMPLA taking on the role of governance because it would build on the multisectoral nature of the malaria fight. Supreme government mechanisms can be engaged through APLMA and the Elimination Scorecard is also an opportunity to have a combined group of indicators to hold countries accountable to their commitments. APLMA was formed because of the understanding that malaria has to be addressed in a multisectoral way and that it has to engage senior policy-makers across a range of ministries beyond the ministry of health.

In addition, the Lao People’s Democratic Republic also supported the idea of ACTMalaria playing a role because it brings together NMCPs and is a good platform for moving towards malaria elimination. The benefits of collaborating with ACTMalaria include the training provided, such as the quality of microscopy, which is very important in elimination.

WHO stated that it was important to consider governance both nationally and regionally. The governance body must have legitimacy and the GMS countries will determine this. One potential way to frame it would be to consider three key components: technical; financing and resources; and advocacy and communications.

Ideally, the governance mechanism should be fairly small to maximize effectiveness and comprised of senior members to give it legitimacy. It would need adequate resources to make it meaningful and also have a secretariat function to make work progress.

The governance body would ultimately report to leaders (i.e. at East Asian Summit). WHO affirmed that there is considerable value in building on existing structures and the Organization must not be too risk averse.

Cambodia expressed a preference for options 1 and 2 (outlined in the previous section) or a combination of these.

Thailand, through Mahidol University, affirmed that a coordinating office at the national level to link with the regional level governance body could be very effective.

RAI noted that defining which constituencies would be represented in the governance mechanism was important to avoid duplication of existing work. Much would depend on the individuals who constitute the governance body. It was also noted that it can take up a year for a committee to become effective. The current RSC could potentially work with APLMA for political advocacy.

BMGF noted a preference for option 4 which made sense in terms of managing financial streams and technical expertise; APLMA could then help push the agenda. Country representation would be critical with effective technical steering groups at country level that would meet every one or two
months. WHO could play an important role in leading the process with national governments with meeting every one to two months. The mechanism should also be seen as an opportunity to reduce the administrative burden on governments.

Dr Tulloch summed up the discussion by noting that the ERAR HUB would have the role of technical coordination; APLMA would advocate among high-level leaders and mobilize resources, while the RSC Plus would function as an expanded version of the RSC.

The governance mechanism needs the right balance in membership to ensure countries are adequately represented. The RSC review in 2015 will consider how to improve this but also perhaps to expand it to include other relevant players such as ministries of finance, for example.

2.9. Operational Research into additional tools for malaria elimination: TCE/TME/TME

Conventional methods to detect parasites such as RDT and microscopy are not sufficient to detect asymptomatic cases, even in areas of low transmission. Another approach to addressing asymptomatic reservoirs is to consider mass drug administration (MDA). Targeted MDA is one approach that has been used for about 30 years. Thirty-eight such studies previously undertaken yielded mixed results.

A study along the Thailand–Myanmar border involving four villages (high prevalence by qPCR) commenced in 2014. It required a great deal of work to get community buy-in and achieving 100% coverage was not possible.

The methodology covered willingness to participate; randomized to MDA or control and cross-over; all villages received LLINs and equipped with a malaria post; MDA: three rounds of DP+P at M0 M1 and M2; exhaustive surveys every three months by ultra-sensitive qPCR; entomology; and mapping.

Preliminary results showed that even in control villages where a village malaria worker was assigned and only LLINs were handed out, there was still a decrease in transmission. The results were positive with a parasite reduction of 100% where three rounds was achieved. Although the results were positive, this was a small-scale trial and needs to be scaled up. Regarding the falciparum parasite, after MDA, parasites disappeared completely but this was not the case with P. vivax (due to relapse infection).

The research community, governments and other stakeholders all have to work together to move forward.

Discussion

WHO noted that the asymptomatic reservoir is very important and is probably linked to recent past history of intense transmission. It is likely there will be a reasonably high prevalence of asymptomatic cases so it is good to see it quantified. The question of how drugs can be used beyond case management is important. In the regional Elimination Strategy, language was noted about needing to explore drugs for prophylaxis to accelerate towards elimination beyond case management of sick individuals. In this context MDA is very useful. An Expert Review Group will meet in Geneva in May 2015 to look at evidence from this and other studies globally, to summarize evidence and provide guidance to countries and regions on the use of MDA approaches. MDA can be used for reducing biomass and also providing a prophylactic effect and may even have a role in the absence of a significant number of asymptomatic carriers. MDA could become a mass drug prophylaxis combined with insecticide control to interrupt transmission. Coverage and learning how to bring it up to scale are key issues.
The Chair echoed the importance of scale, giving the example of MDA in the Lao People’s Democratic Republic where it has been used since 1970. Targeted MDA is also used for outbreaks and the results depend upon coverage. Low coverage does not equate with good results. A key issue with MDA is defining the purpose of its use depending upon the setting. For example, during outbreaks it can quickly reduce morbidity and mortality. For the purpose of control or elimination, more thought is needed on the utility of MDA and how to position this intervention in the context of different transmission settings or types of migration patterns.

A question was raised on the selection of villages for the trial; a related question concerned the key challenges of the MDA trial over three months. The response was that it was challenging to ensure full coverage over the three rounds and different approaches must be tried. From an ethical perspective, giving drugs to people who are not ill means that no side effects can be tolerated – but the argument is that by protecting the village from malaria, there is a motivation for individuals to take part. However, people must be given the opportunity to opt out of the study.

Myanmar stated that it was important to consult with the Ministry of Health and the ethical committee about such research, particularly if it is going to be published. Senior Ministry of Health staff questioned why three doses were given, when in reality, only one dose was to be given. Determining if infections are recrudescent will be difficult when three doses are administered. Myanmar is concerned about resistance. In terms of community input pertaining to the Karen ethnic group, backpack health workers have conducted surveys in the past on nutrition, water and sanitation and malaria. A malaria control programme has been implemented since 2003. A resistance problem surfaced after discussions with local community health workers, internally displaced persons and Shoklo Malaria Research Unit (technical support). Further community research was planned.

Mahidol University Research Unit noted that the political context is quite complicated and the three rounds of treatment was based on the mathematical models showing the largest impact when three rounds of treatment were given. However, it was noted that due to the threat of selecting for drug resistant parasites by using MDA, it is important to do this only in the context of artemisinin resistance. Patients were followed up and those that remained positive were those that had either not received full MDA or had had secondary infection.

Determining the optimal level with which to conduct the study depends on a range of factors and needs further thought. The level of resistance is very important. In western Cambodia where failure rates range from 30–40%, more consideration of the appropriate drug is needed. It appears that with low parasitemia it is still good enough to clear; however the context is within the threat of untreatable malaria if rapid response is not carried out.

BMGF noted that the control villages show the benefits of providing treatment to people and access to diagnosis. There should not be too much concern on the delivery mechanisms but rather a focus on getting the treatment out. Around 70–80% reduction is very positive. Defining vulnerability and receptivity helps to define the best intervention mix for a given area. Measuring vulnerability to reinfection from outside is very important to consider. This should be reflected in the new guidance.

It is also important to look at new interventions in the region and the goal of MDA, which could be used for seasonal malaria given the chemo-prophylactic impact. As this approach is refined, it would be optimal to provide a core of test, treat and track services, even potentially in areas of low transmission or in high risk areas with MMPs. It is encouraging to see that even if there is “failure” it remains an important step. The question is if the cut off will be at three months or more. The acceptability to the community might be that it actually reduces the risk.

WHO noted that the ethical question is an important one and that MDA can be framed around two things: emergency context and prophylactic benefits, which will ameliorate many of the ethical issues around MDA.
The Chair opened the floor for final comments.

Mahidol University, Thailand, noted that artemisinin resistance and malaria elimination are long-term challenges. The meeting had been a good opportunity for very productive discussions and was very useful for NMCPs. Maintaining a workforce is very important and bringing in new tools also very important. Once a regional governance body is in place, a strong secretariat is needed to maintain close connection with NMCPs. If this path is followed, a significant change could be expected approximately five years from now.

The Global Fund noted that implementation issues and political components remain very important. From a Global Fund perspective, there was no funding at all against resistance just over two years ago. Now, it has established implementation of regional funding and coordination with NMCPs. The Global Fund has also established a governance structure (RSC) bringing all regional stakeholders together. This is an effective governance tool and one for analysing all information and adapting it to implementation. RSC was noted as a real success.

Looking forward, programmes are now halfway through the implementation of the US$ 100 million grant. It will be important to start working on the extension of the RAI programme. ADB has also established a trust fund of US$ 40 million that should become operational immediately and additional funding will be made available. The hope is that APLMA and ASEAN countries will come up with ideas to raise additional funds for the regional ART initiative.

BMGF expressed how encouraging it was to hear the conversation on the governance structure and how to expand this above and beyond what individual countries are doing, as resistance is a regional problem.
3. CONCLUSIONS AND RECOMMENDATIONS

3.1. Conclusions and recommendations

The informal consultation with partners, on the emergency response to artemisinin resistance in the Greater Mekong Subregion was an important forum for all Partners and stakeholders engaged in implementation of the ERAR Regional Framework of actions 2013–2015. Participants included a broad range of constituencies and acknowledged achievements by GMS countries and their partners in leading the fight against malaria and combating malaria drug resistance. As a result of worsening drug resistance, national programmes are now revising their malaria strategies from containment to the goal of elimination.

Eliminating malaria is a global responsibility that must be led by national governments and supported by all stakeholders. The huge financial burden of eliminating malaria requires a firm commitment by all partners to ensure that available resources are used as effectively as possible. Resources for innovation of new tools to combat malaria will be critical to the success of achieving the goal of elimination.

In addition, maintaining high-level political support at national, regional and international levels is another important factor for success. In the GMS, the presence of malaria drug resistance, including ACT resistance in several areas of the GMS, poses a significant challenge for all stakeholders, particularly when combined with large-scale migrant and mobile population movements that facilitate transmission across borders. In addition, the geography of the GMS results in many populations being hard to reach and requires additional efforts and innovative approaches to address this challenge. In this context it is critical that all partners redouble their efforts to engage in more effective communication both at national and regional levels.

For countries

- Countries have the key responsibility to lead the process of eliminating malaria and should continue to advocate for the necessary support to enable them to do this.

- The country response requires collaboration with a range of government ministries, beyond the Ministry of Health to ensure that the response is wide-reaching and well supported. Ongoing and pro-active cross-border collaboration is also critical for an effective response in a region characterized by large-scale migrant and mobile population movements.

For Donors

- Focus on harmonizing reporting tools to reduce the reporting burden on countries.

- Ensure that donor strategies are complementary to avoid duplication and provide optimal support for the national strategy.

- Develop flexible funding mechanisms that enable implementing partners to respond more effectively to the dynamic nature of malaria transmission in the GMS.

- Support national programmes to build and strengthen capacity of national health staff.

- Increase support to countries to improve their disease surveillance systems.

- Support operational research and innovation for new tools and recognize that traditional tools such as LLINs and insecticide-treated clothing are not appropriate in all contexts.
• WHO must assist countries to adapt global strategies and make them suitable for the local context.

**For other stakeholders**

• Recognize the leadership of the national governments and ensure that programmes are designed to provide support within existing national frameworks.

• Ensure improved coordination amongst partners, donors and national programmes.

• All country partners need to ensure their alignment to the national plan.

• Consider more proactive engagement with the Private Sector to maximize efforts and resources.

### 3.2 Closing Comments

Dr Jacobs thanked all participants for the detailed, useful discussions on a range of areas. He reviewed the key items discussed including the latest draft of the Elimination Strategy; interesting discussions on governance and the idea of the “3 1s”, which he found particularly encouraging. He stated more thinking is required on how to take the “3 1s” forward. In addition, discussion about the ERAR Hub and future directions have taken place. Dr Jacobs also noted that partners and stakeholders seem to be on the same page towards elimination, which is an opportunity that all should take advantage of.

Dr Alonso noted that broad agreement on the purpose and utility of the regional strategic plan was achieved and this will be taken forward and further revised. Broad agreement was also reached on what a governance structure could look like. He further confirmed that countries are at the centre and that they own and must run the process, and that all other stakeholders must provide support.

WHO has been entrusted with providing leadership, guidance and coordination for malaria programmes in 97 countries. While the focus has traditionally been in Sub-Saharan Africa and will continue to be so, it is also WHO’s intention that the GMP will pay more attention to the GMS and provide the necessary support to ensure that the elimination effort in the region is a success. Regional success in achieving elimination is also important globally. What happens in this region will be important for all global malaria work. Dr Alonso expressed his thanks to Thailand for hosting the informal consultation, to all the countries, donors and stakeholders and to Dr Mulombo and his regional team.
ANNEXES

Annex 1

Informal Consultation with Partners
on the Emergency Response to Artemisinin Resistance in the GMS
Bangkok, Thailand, 11–12 February 2015

AGENDA

Objectives:

- To review progress, share lessons learnt and identify solutions to challenges in the implementation of ERAR framework 2013–2015;
- To secure consensus on ERAR key activities to be implemented in 2015;
- To provide a forum for discussion and refinement of the GMS malaria elimination strategy
- To discuss implementation arrangements, including roles and responsibilities, for malaria elimination in the GMS by 2030.

DAY 1 (Wednesday 11 February 2015)

<table>
<thead>
<tr>
<th>Time</th>
<th>Activity</th>
<th>Presenter/Location</th>
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<tbody>
<tr>
<td>08:00 – 08:30</td>
<td>Registration</td>
<td>Meeting Secretariat</td>
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<tr>
<td>08:30 – 08:45</td>
<td>Welcome address</td>
<td>WR Thailand/CDS SEARO/DCD WPRO/GMP HQ</td>
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<tr>
<td>08:45 – 09:00</td>
<td>Key note address</td>
<td>DG Ministry of Public Health Thailand</td>
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<tr>
<td>09:00 – 09:30</td>
<td>Self-introduction and nomination of Chairing Committee</td>
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<tr>
<td>09:30 – 10:00</td>
<td>Group photo and coffee break</td>
<td>Secretariat</td>
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<tr>
<td>10:00 – 10:15</td>
<td>Objectives of the workshop</td>
<td>Walter Kazadi (ERAR Regional Hub)</td>
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<tr>
<td>10:15 – 10:45</td>
<td>Cambodia presentation</td>
<td>CNM Director (Cambodia)</td>
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<td>10:45 - 11:15</td>
<td>China presentation</td>
<td>NIPD Director (China)</td>
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<td>11:15 - 11:45</td>
<td>Lao PDR presentation</td>
<td>CMPE Director (Lao PDR)</td>
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<td>11:45 - 12:15</td>
<td>Myanmar presentation</td>
<td>Deputy Director/Program Manager, National Malaria Control Program Central VBDC (Myanmar)</td>
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<tr>
<td>12:15 – 13:15</td>
<td>Lunch and poster set up</td>
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<td>13:15 – 14:15</td>
<td>Poster viewing (work of ERAR stakeholders supporting ERAR Framework and malaria elimination in 2014)</td>
<td>All</td>
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<tr>
<td>14:15 – 14:45</td>
<td>Viet Nam presentation</td>
<td>NIMPE Director (Viet Nam)</td>
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<tr>
<td>14:45 - 15:15</td>
<td>Thailand presentation (20 minutes presentation plus 10 minutes discussions)</td>
<td>BVBD Director (Thailand)</td>
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<td>15:15 – 15:30</td>
<td>Coffee break</td>
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<tr>
<td>15:30 – 16:00</td>
<td>Coordination of the response to Artemisinin Resistance in the GMS: Lessons from the first year of full implementation (15 minutes presentation plus 5 minutes discussions)</td>
<td>Walter Kazadi (ERAR Regional Hub)</td>
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<tr>
<td>16:00 – 17:30</td>
<td>Partners and Donors’ updates (10 minutes presentations followed by 5 minutes discussions)</td>
<td>Chair</td>
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<td>• USAID/President’s Malaria Initiative</td>
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<tr>
<td>17:30</td>
<td>Meeting adjourns</td>
<td>Chair</td>
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<tr>
<td>18:30</td>
<td>Welcome reception</td>
<td>ERAR Regional Hub</td>
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**DAY 2 (Thursday 12 February 2015)**

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<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Presenter</th>
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<tbody>
<tr>
<td>08:30 – 09:00</td>
<td>Highlights from day 1</td>
<td>Meeting rapporteurs</td>
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<tr>
<td>09:00 – 09:20</td>
<td>Updates on artemisinin resistance and malaria drug policy situation in the GMS</td>
<td>Pascal Ringwald (GMP HQ)</td>
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<tr>
<td>09:20 – 09:40</td>
<td>Updates on road map for the development of GMS malaria elimination strategy and country planning processes</td>
<td>Eva Christophel (WHO WPRO)/Leonard Ortega (WHO SEARO)</td>
</tr>
<tr>
<td>09:40 – 10:00</td>
<td>Operational Research into new/additional tools for malaria elimination: Planned and ongoing trials in the GMS, and preliminary findings</td>
<td>Professor Arjen Dondorp (MORU)</td>
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<tr>
<td>10:00 – 10:15</td>
<td>Q&amp;A</td>
<td>Chair</td>
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<td>10:00 – 10:30</td>
<td>Coffee break</td>
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<tr>
<td>10:30 – 11:00</td>
<td>Updates on the Global Malaria Technical Strategy and implications for the GMS</td>
<td>Pedro Alonso (Director GMP)</td>
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<tr>
<td>11:00 – 11:30</td>
<td>Presentation of the revised GMS malaria elimination strategy</td>
<td>Mikhail Ejov (WHO consultant)</td>
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<tr>
<td>11:30 – 12.30</td>
<td>Plenary discussions and feedback from Donors and other Stakeholders on the GMS Malaria elimination strategy</td>
<td>Chair</td>
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<td>Time</td>
<td>Session</td>
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<td>12:30 – 13:30</td>
<td>Lunch</td>
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<tr>
<td>13:30 – 14:00</td>
<td>Brainstorming on options for governance of malaria elimination in the GMS</td>
<td>Jim Tulloch (WHO Consultant)</td>
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<tr>
<td>14:00 – 14:30</td>
<td>General discussions and feedback on options for Governance</td>
<td>Chair</td>
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<tr>
<td>14:30 – 14:45</td>
<td>Introduction to group work</td>
<td>Walter Kazadi</td>
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<tr>
<td>14:45 – 15:45</td>
<td>Group work by constituencies: how to move the strategy forward (country and regional action plans: what, where, when, how and by whom, including governance mechanisms)</td>
<td>Chair</td>
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<tr>
<td>15:45 – 16:00</td>
<td>Coffee break</td>
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<tr>
<td>16:00 – 17:00</td>
<td>Plenary presentations and discussions</td>
<td>Chair</td>
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<tr>
<td>17:00 – 17:30</td>
<td>Conclusions and recommendations</td>
<td>Eva Christophel and Leonard Ortega</td>
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<tr>
<td>17:30</td>
<td>Closing</td>
<td>MOPH Thailand</td>
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<tr>
<td>18:00</td>
<td>Meeting of the ERAR Technical Working Group on SME (for members only)</td>
<td>ERAR Hub</td>
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Annex 2

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