

Meeting Report

South-East Asia and Western Pacific Bi-Regional Meeting of Malaria Drug Resistance Monitoring Networks



9–12 November 2015
Siem Reap, Cambodia

WORLD HEALTH ORGANIZATION
REGIONAL OFFICE FOR THE WESTERN PACIFIC

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MEETING REPORT

SOUTH-EAST ASIA AND WESTERN PACIFIC BI-REGIONAL MEETING OF MALARIA
DRUG RESISTANCE MONITORING NETWORKS

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WORLD HEALTH ORGANIZATION
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NOTE

The views expressed in this report are those of the participants of the South-East Asia and Western Pacific Bi-Regional Meeting of Malaria Drug Resistance Monitoring Networks and do not necessarily reflect the policies of the World Health Organization.

This report has been prepared by the World Health Organization Regional Office for the Western Pacific for those who participated in the Southeast Asia and Western Pacific Bi-Regional Meeting of Malaria Drug Resistance Monitoring Networks held in Siem Reap, Cambodia, 9–12 November 2015.

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Keywords:

Malaria / Drug resistance / Regional health planning / Communicable diseases

ABBREVIATIONS

ACPR	adequate clinical and parasitological response
ACT	artemisinin combination therapy
AL	Artemether-Lumefantrine (Coartem™)
AM	Artemether
API	Annual parasite incidence
AS	Artesunate
AS+Amo	Artesunate+Amodiaquine
AS+SP	Artesunate + Sulfadoxine-pyrimethamine
AS+MEF	Artesunate + Mefloquine
BBINS	Bangladesh, Bhutan, India, Nepal, Sri Lanka
CQ	chloroquine
DHA-PIP	dihydroartemisinin-piperaquine
Doxy	Doxycycline
ERAR	Emergency Response to Artemisinin Resistance
Global Fund	The Global Fund to Fight AIDS, Tuberculosis and Malaria
HF	Health Facility
IMR	Institute of Medical Research
K13	Kelch 13
LFU	loss to follow-up
LPF	late parasitological failure
MoD	Ministry of Defence
MoPH	Ministry of Public Health
NMPE	National Institute of Malariology, Parasitology and Entomology
NMCP	National Malaria Control Programme
PMI	President's Malaria Initiative
PQ	primaquine
RAI	Regional Artemisinin Initiative
RDT	rapid diagnostic test
TES	therapeutic efficacy studies
WHO	World Health Organization

SUMMARY

In the South-East Asia and Western Pacific regions, antimalarial drug resistance monitoring has been strengthened through the establishment of three drug-resistance monitoring networks: the Greater Mekong Subregion network, the Pacific network and the Bangladesh, Bhutan, India, Nepal and Sri Lanka (BBINS) network. The South-East Asia and Western Pacific Bi-Regional Meeting of Malaria Drug Resistance Monitoring Networks was co-organized by the WHO regional offices for South-East Asia and the Western Pacific, WHO headquarters and the Emergency Response to Artemisinin Resistance (ERAR) hub together with the WHO Representative Office in Cambodia. Sixty participants from 14 countries attended, including therapeutic efficacy studies (TES) investigators and malaria programme managers, along with technical consultants and representatives from key partner agencies.

At the end of the meeting, participants were expected to have:

- 1) reviewed the malaria drug resistance situation in the Greater Mekong Subregion, the Pacific and South Asian countries;
- 2) reviewed implementation of the WHO TES protocol;
- 3) discussed the role of K13, the molecular marker for tracking artemisinin resistance, and of other molecular markers for monitoring malaria drug resistance in the Region; and
- 4) developed work plans and budgets for the networks and the countries for TES monitoring in 2016–2017.

Technical presentations from WHO staff included an overview of the sentinel sites and activities in the three TES networks of the Greater Mekong Subregion, the BBINS and the Pacific, implementation/ monitoring and reporting issues using the standard protocol including requirements from ethics committee, updates on the K13 marker for artemisinin resistance, and the global antimalarial drug efficacy database. Much discussion centred on implementation and monitoring challenges encountered before, during and at end of the studies. The update on the *Strategy for Malaria Elimination in the Greater Mekong Subregion 2015–2030* and treatment policy change was also presented. All countries prepared a two-year work plans and budgets for TES (2016–2017).

Recommendations for Member States:

- 1) Countries are recommended to continue to strengthen high quality TES implementation using the standard WHO protocol.
- 2) Strengthening and sustaining capacity of national programmes to implement TES is critical. Supporting the strengthening of microscopy capacity (regular refresher training for TES microscopists) is critical as is training of those who collect slides.
- 3) Alternative ACT regimens need to be tested before deciding on drug policy change as soon as signs of declining efficacy manifest.
- 4) Countries are recommended to maintain regular monitoring visits to TES sites.
- 5) Countries are recommended to facilitate integration of monitoring of drug efficacy into routine surveillance systems in pre-elimination settings.

Recommendations for WHO:

- 1) Tasks for the networks focus on coordination, information sharing and technical support to the above activities with particular emphasis on strengthening cross-border information sharing and coordination.
- 2) WHO is recommended to share the finalized monitoring tools and reporting guidelines with in-country and external monitors.
- 3) WHO is recommended to provide support for countries moving into elimination as they adopt new approaches to monitoring and surveillance beyond TES.

1. INTRODUCTION

1.1 Background

The South-East Asia and Western Pacific Bi-Regional Meeting of Malaria Drug Resistance Monitoring Networks was convened in Siem Reap, Cambodia in November 2015 to review and plan therapeutic efficacy studies (TES). This was the first meeting to bring together participants from the Greater Mekong Subregion, the BBINS and the Pacific networks. The meeting was an opportunity for participants to share information and experiences in implementing TES at a time when many countries are taking steps towards pre-elimination or elimination while others still face t high malaria burdens and the increasing risk of artemisinin and multidrug resistance. The meeting was organized by the WHO regional offices for South-East Asia and the Western Pacific and the Global Malaria Programme in WHO headquarters in coordination with the WHO ERAR hub in Phnom Penh, Cambodia.

1.2 Objectives

At the end of the meeting, participants were expected to have:

- 1) reviewed the malaria drug resistance situation in the Greater Mekong Subregion, the Pacific and South Asian countries;
- 2) reviewed implementation of the WHO TES protocol;
- 3) discussed the role of K13, the molecular marker for tracking artemisinin resistance, and of other molecular markers for monitoring malaria drug resistance in the Region; and
- 4) developed work plans and budgets for the networks and the countries for TES monitoring in 2016–2017.

1.3 Opening session

Dr Eva Christophel, Malaria Regional Advisor for WHO Regional Office for South-East Asia delivered the opening remarks on behalf of Dr Shin Young-soo, WHO Regional Director for the Western Pacific. Many countries in the South-East Asia and Western Pacific regions have achieved the malaria targets of the Millennium Development Goals. With the sixty-eighth World Health Assembly's endorsement of the *Global Technical Strategy for Malaria 2016–2030*, countries are accelerating control efforts. Leaders of the East Asia Summit in 2014 also agreed to work towards an Asia Pacific free of malaria by 2030. Urgent challenges of multidrug resistance of falciparum malaria remain and increased efforts are needed to strengthen monitoring and improve coordination.

Dr Siv Sovannaroeth, Chief of Technical Bureau, National Center for Parasitology, Entomology and Malaria Control, Cambodia also welcomed the participants to Siem Reap and noted that while there has been great progress against malaria in Cambodia and the Greater Mekong Subregion, the malaria burden remained high along with the threat of multidrug resistance. Given that malaria's artemisinin combination therapies (ACTs) were failing, he reminded participants of the urgency to develop new alternative drugs.

Chair and co-chair appointments were made as follows: Dr Siv Sovannaroeth as Chair and Dr Abu Nayeem Mohammed Sohel as Co-Chair for day one; Dr Bouasy Hongvanthong as Chair and

Dr Sanchai Chasombat as Co-Chair for day two; and Mr Leo Sora Makita as Chair and Dr Rini Poespoprodjo as Co-Chair for day three.

The rapporteurs were Dr Leang Rithea for the Greater Mekong Subregion Network, Dr Fe Esperanza Caridad J. Espino for the Pacific Network and Dr Aniruddha Ghose for the BBINS network.

The meeting agenda is available at Annex 2 and the list of participants is available at Annex 3.

2. PROCEEDINGS

2.1 Therapeutic efficacy studies (TES): standard protocol

A review of the four assays for monitoring drug efficacy and resistance was presented, noting that TES remain the "gold standard" for monitoring the efficacy of a country's first- and second-line drugs and to guide national treatment policy. The key elements of the 2009 TES protocol include the importance of PCR analysis to differentiate recrudescence from reinfection and of day three positivity rate as parasitological marker for partial artemisinin tolerance. Ensuring necessary ethical approvals and registration for TES is critical. Ideally TES should be carried out during one transmission season. In terms of quality control, blood smears should be examined by two microscopists and a third independent microscopist in the case of discordant results. Parasite genotyping is necessary to distinguish between recrudescence and reinfection. Additional tools to monitor drug resistance were reviewed including variations in TES methodologies for different transmission settings.

2.2 Anti-malarial drug resistance monitoring in the Greater Mekong Subregion, BBINS and Pacific networks and implementation challenges

From 2008 to 2012, there were 10 areas of suspected resistance and three areas with confirmed resistance in the Greater Mekong Subregion. TES conducted in 2012 showed the presence of K13 in many parts of Cambodia, northwest and northeast Myanmar, Yunnan province in China, Viet Nam, and in the south of the Lao People's Democratic Republic. Given these results, additional sites (provinces) were added in 2015. In Myanmar, cure rates are still very good but Day 3 positivity is increasing in some sites. In the BBINS network, there are 11 active sentinel sites in central and northeast India and three active sentinel sites each in Nepal and Bangladesh. Bhutan and Sri Lanka are in the elimination phase and are engaged in active case surveillance and 28-day follow-up. K13 mutations have not yet been identified in the BBINS or the Pacific countries that conduct TES. Severe malaria and high density parasitaemia cases use the second-line treatment and the efficacy can also be monitored.

Implementation challenges across the networks included: insufficient time to complete studies; difficulties with selection of sites in a rapidly changing malaria landscape; lengthy processes required for ethical approval; training TES teams; and administrative/logistic delays. Problems emerged when the study protocol was not adhered to e.g. when consent for pregnancy tests was not gained for female minors or for storage and future use of unused samples. Other laboratory issues included poor quality slides, mixed infection, improper labelling and storage of filter paper blood spots, quality control in molecular procedures, validation of study data and completeness of the case recording and consent forms. Additional issues concerned non-TES activities where research institutes: validate microscopy by PCR leading to difficult interpretation; use molecular markers for vivax studies which are not yet validated; and add research questions which is an extra burden to the programmatic TES work.

Completing TES within the designated 12-month period was challenging given the delays associated with fund disbursements, achieving the required patient sample size and completion of technical and

financial reports. The K13 marker, while useful, also posed challenges, particularly mutations. Countries requested more guidance from WHO. The WHO Ethical Committee's proposal to exclude 9–18-year-old girls from TES in contexts where this may not be culturally appropriate was also discussed. The importance of high quality microscopy was also discussed, including the challenges of interpreting results compared with day 0 PCR results, and sub-patent mixed infection with microscopy for countries with high prevalence of both *P. falciparum* and *P. vivax* e.g. in the Pacific.

2.3 Presentations by principal investigators on TES results

2.2.1 Greater Mekong Subregion network

Cambodia

Despite some periods where case numbers appeared to be levelling out, the current trend is upwards with malaria remaining a serious public health challenge. The national drug policy introduced Quinine and tetracycline as the first-line treatment in 1992. In 2000, the combination therapy three-day mefloquine (MEF) (20mg/kg) plus artesunate (ASU) was introduced as the first-line treatment against *P. falciparum*. In 2008, dihydroartemisinin-piperaquine (DHA-PIP) was adopted as first-line treatment of both *P. falciparum* and *P. vivax* after high levels of treatment failure of AS+MEF were confirmed in 2007 in western Cambodia. Between 2008 and 2014, the efficacy of DHA-PIP declined and alternative treatments were tried. Differences in ACT efficacy in western and eastern Cambodia have been observed in the last 15 years. However, very recent results also show eastern Cambodia i.e. Siem Reap, Steung Treng and Mondulkiri with less than 90% efficacy of DHA-PIP in 2014 as well as presence of K13 mutations compared to previous years. Given the resistance situation in Cambodia, TES should be continued in sentinel sites and other areas.

China

From 2000 to 2006, China experienced an increase in cases followed by a rapid decline. By 2014, local cases had declined from 4262 in 2010 to 57 in 2014. In 2014, 3078 malaria cases were reported, a decrease of 25.4% from 2013. In 2014, most malaria cases in China were imported and *P. falciparum* malaria only occurs in border areas, with local transmission only in Tibet and Yunnan provinces, in nine counties along the China-Myanmar border. The national malaria treatment guidelines since 2009 include: Chloroquine and primaquine (ACTs may be used if these drugs fail) for *P. vivax* and DHA-PIP, artesunate+ amodiaquine, and artemisinin – naphthoquine for *P. falciparum*. DHA-PIP efficacy has remained above 95% in four border sentinel sites. For K13 marker, 12 types have been found, the majority of which were F446I (33%) and P574L.

The Lao People's Democratic Republic

Trends in malaria cases in the Lao People's Democratic Republic show a sharp decline from 2000 to 2010 with a subsequent rise in 2011 due to an outbreak in Attapeu province. The number of *P. falciparum* cases dropped from 23 756 in 2010 to 7301 in 2015, and the number of *P. vivax* cases more than halved. Malaria deaths declined from 350 in 2000 to two in 2015. Artemether + Lumefantrine is the first-line drug for uncomplicated *P. falciparum* and *P. vivax* malaria with oral Quinine+Doxy as second-line treatment. For vivax malaria, low-dose primaquine is recommended following a glucose-6-phosphate dehydrogenase (G6PD) test.

From 2005 to 2012, TES results showed ACTs were highly efficacious in the Lao People's Democratic Republic. In 2013, Artemether-Lumefantrine (AL) efficacy was at 90% with 22.2% day-three positives, and K13 assays confirmed artemisinin resistance in Champasak province (mainly C580Y, and R539T). In 2014, Sekong province results showed 86% adequate clinical and parasitological response (ACPR) and 20% day-three positives (pending K13 results).

Myanmar

Malaria morbidity and mortality declined from 1990 to 2013. Data as of 2013 shows that *P. falciparum* accounts for 73% of all malaria cases, *P. vivax* for 24% and 3% of cases are mixed species. Myanmar has three first-line ACTs against *P. falciparum*: AL, AS+MEF co-blister, and DHA-PIP followed by primaquine 0.75 mg/kg stat dose. For *P. vivax*, the treatment regime is chloroquine 25 mg/kg body weight over three days + primaquine 0.25 mg/kg per day for 14 days [except pregnancy, infants and G6PD deficiency]. The 2009–2013 TES tested DHA-PIP, AL, ASU+MEF for *P. falciparum* and chloroquine for *P. vivax*.

Results from the 2013–2014 TES show delayed parasite clearance to AL in six of 28 cases in Mawthaung, Tanintharyi Region, and to DHA-PIP in three of 28 cases in Myawaddy, Kayin state (pending K13 results), both along the Thai-Myanmar border. No delayed clearance was found in Buthidaung, Rakhine state and K13 studies indicated no mutant samples although quality control analysis is ongoing. C580Y, N458Y, A481V, N537I, R539T were observed in Kyeikdon samples (Myanmar-Thai border area), but not on the western border of Myanmar.

Thailand

Malaria cases in Thailand have declined from 65 000 in 2010 to fewer than 40 000 in 2014. Case reports by species for 2015 show that vivax accounts for 66% of cases and falciparum 34%. The proportion of Migrant 1, Migrant 2 and refugee cases has declined since 2010 with Thais accounting for more than half of all cases in 2015. Most transmission occurs in villages along the Thailand/Myanmar and Thailand/Cambodia/Lao People's Democratic Republic borders. There are 10 TES provinces in Thailand, some testing AS+MEF in areas where it has never been tested; DHA-PIP in suspected areas of resistance and chloroquine for *P. vivax*. Results from the 2009–2012 TES showed declining ACPR in three provinces: Tak (90%), Kanchanaburi (93%) and Ranong (87%). In 2012, ACPR in Kanchanaburi was at 75%. The first-line regimen has been changed to DHA-PIP in May 2015, though it may be necessary to use AS+MEF where it remains efficacious. Preliminary results testing DHA-PIP in Kanchanaburi showed over 90% ACPR.

Viet Nam

Despite a declining trend in cases from 2000 to 2014, Viet Nam faces new challenges with the proportion of vivax cases steadily increasing since 2009. The treatment guidelines since 2013 recommend: first-line DHA-PIP for *P. falciparum* and chloroquine plus primaquine for *P. vivax*, and second-line: quinine + Doxy or Clindamycin. For complicated falciparum & vivax malaria, IV artesunate is followed by oral ACTs or intravenous quinine. In the 2012–2013 TES testing DHA-PIP, delayed parasite clearance was recorded in Binh Phuoc, Dak Nong and Gia Lai provinces. In 2013–2014 the proportion of day-three positives increased in Binh Phuoc and Gia Lai but not Dak Nong. Three additional sites, Khanh Hoa, Kon Tum and Quang Nam also showed a delay. TES for 2014–2015 is ongoing in Binh Phuoc, Gia Lai, Quang Tri, Ninh Thuan and Dak Lak provinces. DHA-PIP is still highly efficacious for falciparum malaria (97.4–100%) in all seven sentinel sites, despite the increasing day-three positivity rates of 14.3–36%, with confirmed K13 mutations in some sites.

2.2.2 BBINS network

Bangladesh

Malaria cases declined from 2000 to 2011 but have increased from 2012 to 2015. The majority of cases are *P. falciparum* with a slight increase in *P. vivax* cases. National Malaria Control Programme (NMCP) data shows a decline in malaria deaths from 478 in 2000 to 9 in 2015. Most cases are from

the southern part of the country bordering Myanmar and India and from the hill tracts in the south. The treatment guidelines are first-line is AL and primaquine (15 mg) against *P. falciparum* malaria, and chloroquine and primaquine for 14 days (15mg) or 0.3 mg/kg daily for children against *P. vivax*. TES results in 2013–2014 in Teknaf Upazila of Cox's Bazar district, Lama Upazila of Bandarban district and Kalmakanda Upazila of Netrakona district showed no evidence of drug resistance and no K13 mutations. However malaria remains a significant public health burden. Challenges include long ethical clearance, difficulties in patient recruitment for 28 days follow-up and rapid turnover of government staff necessitating constant retraining of TES teams.

Nepal

Malaria transmission in Nepal is concentrated in the southern and western parts of the country. There have been no malaria deaths since 2012. Approximately 80% of all cases are *P. vivax* and 20% are *P. falciparum*. Of 1700 cases reported in 2014, 40% were imported cases. Porous borders create challenges for malaria control with ongoing migration flows. Almost 70% of malaria is now concentrated in four districts and TES sentinel sites are located in these areas. Nepal uses AL and primaquine (0.25 mg/kg body weight) single dose against falciparum malaria and chloroquine (25 mg/kg bw) for three days + primaquine (0.25 mg/kg body weight per day) against vivax malaria. TES results 2013–2014 indicated only one late failure in Kailali province in 2013. K13 studies at Institute Pasteur Cambodia showed all the parasites from Nepal were of wild type.

2.2.3 Updates on the K13 marker for artemisinin resistance: working definition of artemisinin resistance

Prolonged treatment with artemisinin remains highly effective in South-East Asia with 7-day treatment still having 95% efficacy in Cambodia, China, Myanmar and Viet Nam, and 3-day artesunate + ACT showing 100% efficacy. Patients with a delayed parasite clearance response are still cured by ACTs, provided that the partner drug remains effective, even in areas of high prevalence of K13 mutations (China, the Lao People's Democratic Republic, Myanmar and Viet Nam). Mutations in the K13-propeller domain were shown to be associated with delayed parasite clearance *in vitro* and *in vivo*. Artemisinin resistance could become total resistance at any point. The selection of resistance to a partner drug is correlated with the half-life of the partner drugs. The implication of treatment of severe malaria in artemisinin resistance needs to be studied by a combination of artesunate and quinine which could be used to overcome the problem of delayed clearance. Of the 180 different mutations of K13, 150 still require validation. Systematically mapping K13 with clinical data is critical. TES results indicate resistance to piperaquine (DHA-PIP) in Cambodia, although treatment failure remains low despite delayed day-three clearance.

2.2.4 Global Antimalarial Drug Efficacy database and reporting tools

Dr Ringwald provided an overview of the various data sources that are fed into the TES database (raw data, publications and unpublished reports). Information from the global TES database is used in various ways to create summary tables and maps, for reports such as the global drug efficacy and drug resistance report and the World Malaria Report. The database supports the sharing of data between and for countries. Annual reporting using the template and developing maps by following the template methodology were both demonstrated.

2.2.5 Monitoring TES

The WHO definition of TES monitoring is "the act of overseeing the progress of the study, and of ensuring that it is conducted, recorded, and reported in accordance with the approved study protocol" Participants were reminded that the purpose of monitoring is to verify: that patient rights and well-being are protected; the reported TES data are accurate, complete and verifiable from source documents; and that the conduct of the trial complies with approved protocol/amendment(s) and good

clinical practice (GCP). The procedures for planning the first site visit were reviewed as well as the process for determining the frequency of site visits. The risks involved in TES were reviewed. Issues included fraud in data collection; serious errors in analysis and perceived coercion of subjects to enrol in research studies.

2.2.6 Pacific network

Indonesia

Over the past 20 years the NMCP successfully reduced the annual parasite incidence (API) in Indonesia from 4.68 cases per 1000 people in 1990 to 1.38 cases per 1000 in 2013. However, five provinces in eastern Indonesia (Papua, Papua Barat, Maluku, Maluku Utara and Nusa Tenggara Timur) are still highly endemic. In 2009, the Government launched a programme to eliminate malaria in the Indonesian archipelago by 2030. The 2010 national treatment guidelines recommend DHA-PIP for *P. falciparum* and *P. vivax*, + 0.75mg/kg bw primaquine single dose for falciparum cases and 0.25mg/kg/d for 14 days for vivax cases. The ongoing TES results in four sentinel sites revealed no prolonged day-three parasite clearance. DHA-PIP remains highly effective in Indonesia and there is no evidence of K13 mutations associated with artemisinin resistance. Key challenges include strengthening provincial/district capacities to conduct TES and longer duration for patient recruitment and study completion.

Malaysia

Malaria trends for 2001–2014 showed a decline in case numbers from 12 780 in 2001 to 3923 in 2014. Indigenous cases reduced from 8808 to 606 in the same period. Malaria deaths have also declined. Most cases are in the east of the country in Sabah and Sarawak plus some pockets in rural areas. The 2000 national treatment guidelines recommend AL (3 days) + single dose primaquine 0.75mg/kg (max 45mg) for *P. falciparum* malaria, and Chloroquine 25mg base/kg over three days + primaquine 30mg daily for 14 days for *P. vivax* malaria. Results from the national anti-malaria drug response surveillance programme 2003–2006 in 18 sites in seven endemic states in Sabah showed 31% failures to chloroquine and 6% failures to chloroquine +SP.

In 2014, hospital-based national surveillance of drug responses against malaria parasites started using an online surveillance reporting system (VEKPRO) which captures all malaria cases at hospital/field levels. In 2014, it reported 99% ACPR to AL in 140 of 141 *P. falciparum* cases that completed 28-day follow-up and 100% in January–October 2015 in 111 enrolled cases from 15 states nationwide.

The Philippines

From 2000 to 2014, malaria cases have declined, largely attributable to improved vector control, highly effective drugs and aggressive advocacy. *P. falciparum* is decreasing in proportion with vivax, with 36 596 cases in 2000 and 4972 in 2014. Approximately 75% of the caseload is concentrated in Palawan province, where infection by five plasmodium species has been reported. Since 2009, the Philippines has been using AL as first-line treatment + Primaquine on day four against *P. falciparum*, and chloroquine (25 mg/kg) over three days + primaquine (0.25 mg/kg/day) for 14 days against *P. vivax*. Palawan province has been a TES sentinel site since 2009, for both falciparum and vivax cases: in 2013–2014: AL vs *P. falciparum*; chloroquine vs. *P. vivax* and in 2015 - AL vs *P. falciparum*. For all TES, no treatment failures were observed with the exception of one day 21 failure in the 2013 TES. In 2015, the 28-day ACPR was 100% in 71 *P. falciparum* cases, with one recurrence seen at day 41. Analysis of K13 on TES 2013 *P. falciparum* samples collected in Palawan (n=84) showed no mutations (Menard et al, submitted). Problems observed in TES implementation included lost to follow-up especially on vivax due to long follow ups and confounding PCR results on day 0 mixed species identification.

Papua New Guinea

The highest malaria burden is in provinces located in the northwest and north east of Papua New Guinea. National treatment guidelines recommend AL as a first-line drug against uncomplicated *P.falciparum* and *P.vivax* malaria, and DHA-PIP as second-line. TES is not carried out by the programme as part of routine surveillance and remains an ongoing challenge due to limited capacity in logistics, health infrastructure/diagnostic facilities and human resources. From 2011 to 2014, TES was implemented by the Institute of Medical Research (IMR) with external support. TES was carried out in the following sites: Mugil, Madang; Alexishafen, Madang; Maprik, East Sepik; and Alotau, Milne Bay. It assessed the efficacy of AL vs. AS-naphthoquine against uncomplicated *P.falciparum* and *P.vivax* infections; the efficacy of AL vs. DHA-PIP against *P.falciparum* and *P.vivax* mono-infections; and primaquine dose escalation study for *P.vivax*. Results in 2014 showed no evidence of day-three positives and an APCR above 95% in all sites. For K13, results from a 2012–2014 study show no evidence of K13 mutations and no evidence of slow parasite clearance at day-three in 55 samples from eight provinces in Papua New Guinea. Another major challenge is the high proportion of *P.vivax* malaria mostly among children under age 10.

Solomon Islands

Data on malaria incidence trends between 2000 and 2014 showed 75% decline. Mortality trends showed periodic decline and increase, reportedly due to social factors. Overall *P.falciparum* dominates the malaria burden except in 2015 data (January–July). The 2009 national malaria treatment guidelines recommend first-line AL for all species; and second-line quinine. TES conducted in 2009–2010 for the sentinel site in Tetere, Guadalcanal province showed 100% ACPR for *P.falciparum* and 94.9% (uncorrected) APCR for *P.vivax*.

For K13, 2009 data is being published (data with the principal investigator at Walter Eliza Hall Institute (WEHI) of Medical Research, Melbourne). The Pacific Network facilitated improved collaborative efforts within and between partner countries. However the changing malaria epidemiology has affected recruitment rates at sentinel sites, in particular for the *falciparum* arm. Challenges include inadequate human resources and financial support for drug resistance surveillance, and difficulties for coordination of data quality in island-setting sentinel sites.

Vanuatu

Malaria trends from 2000 to 2015 show a decline in all species. The 2014 API is 3.8 with an annual blood examination rate of 14% and test positivity rate at 3%. The pre-elimination zones are Torba and the elimination zone is Tafea. The 2009 national treatment policy recommends AL + primaquine 0.25/kg single dose for uncomplicated *P.falciparum* malaria; and AL + primaquine 0.25/kg x14 days for *P.vivax* malaria. Results of TES studies for 2011–2012 testing AL against *P.vivax* in Vaemali, Epi island and Shefa province showed 98.8% APCR. The TES in 2013 in Santo Island, Sanma province showed four of 35 relapsing cases. Challenges include too few *P.falciparum* cases to conduct TES. Operational research is ongoing on *P.vivax* relapses against primaquine in Solomon Islands and Vanuatu by WEHI, with three months follow-up; three arms: control, 0.25 and 0.5 mg/kg for 14 days, on non-deficient G6PD individuals (tested by rapid diagnostic test (RDT)).

2.2.7 Efforts to eliminate malaria in the Greater Mekong Subregion

WHO launched the *Strategy for Malaria Elimination in the Greater Mekong Subregion* in May 2015 with the goals of eliminating malaria by 2030 in all Greater Mekong Subregion countries; maintaining malaria-free status and preventing the reintroduction of malaria. Regional priorities include: interruption of transmission in areas with multidrug resistance in border areas between Cambodia and Thailand; reduction of transmission in high transmission areas in Myanmar; and control of malaria in areas of resurgence. Country-level priorities include: elimination of malaria in areas of multidrug

resistance and flattening of the epidemiological landscape by reducing transmission in areas of high transmission.

Interventions are focused on case detection and management; and prevention, case and entomological surveillance. Supporting elements for implementation includes innovation and research, and working towards an enabling environment, including multisectoral engagement and governance. A preliminary budget of US\$ 700 million has been prepared for regional malaria elimination. An overview of artemisinin resistance and treatment failure in the Region followed, including guidelines for changing drug treatment policy. If the proportion of day-three parasitaemia is under 10%, policy change is not necessary. If over 10% at day-three, it is an indication that artemisinins are failing, and if treatment failures are over 10%, it is an indication that the partner drug is also failing. In areas where DHA-PIP failures are over 10%, AS+MEF should be reintroduced.

2.2.8 Strengthening quality assurance system for malaria microscopy

The Asian Collaborating Training Network for Malaria (ACTMalaria)'s work on quality assurance systems from 2004 to 2015 was reviewed. The first external competency assessment in 2004 revealed many problems with microscopy. In 2005, an external competency assessment of microscopists was established. By 2009 all countries were assessed with the exception of Nepal which joined in 2012. An overview of the key elements of quality assurance systems for malaria microscopy was provided followed by a review of the implementation challenges related to malaria microscopy. A functional quality assurance systems for malaria microscopy must include: (1) standard operating procedures developed, disseminated, with supervised application monitored/evaluated and updated as needed; (2) all providers of malaria microscopy services trained according to the standard operating procedures using a standardized set of training materials, including reference slides; (3) assured and maintained competency of microscopists, external competency assessment, national competency assessment (NCA), proficiency testing and refresher training. A status update of the external competency assessment from 2010 to 2015 for all countries was provided. One of the biggest challenges related to microscopy is that poor quality slides cannot be examined/are not readable and consequently produce discordant results in PCR.

2.2.9 Country TES plans 2016–2017

The country TES plans are available at Annex 1.

Bangladesh

In 2016 Bangladesh will conduct the studies in two sites (Ramgarh Subdistrict, Khagrachari and Nykhonchori Subdistrict, Bandarban) bordering India and Myanmar.

In 2017, a TES on chloroquine-primaquine for the treatment of *Plasmodium vivax* malaria will be conducted also in the above two sites. The studies will be funded by WHO, the Global Fund to Fight AIDS, Tuberculosis and Malaria, NMCP and academic institutions. The TES implementers will be NMCP and the Department of Medicine, Chittagong Medical College. Strengthening the core of expert microscopists will be important since there are only two level 2 microscopists.

Cambodia

In 2016 Cambodia TES are planned for: Preah Vihear – AS+MEF; Ratanakiri - DHAPIP (first line) and quinine + tetracycline (second-line); Oddor Mean Chey – DHA-PIP; Battambang – AS+MEF or AS+Amo; Kg. Thom – DHA-PIP. In 2017, the sites will be: Kratie – AS+MEF; Siem Reap – AS+MEF (first line) and quinine +tetracycline (second -line); Stung Treng – DHA-PIP or AS+MEF; Kg. Speu – AS+MEF; Pursat- AS+MEF.

TES will be funded by WHO and other partners. To ensure accurate diagnosis, quality of both microscopy and RDTs must be assured at all levels of the health sector. The national quality assurance/control guidelines for malaria along with standard operating procedures for laboratory diagnosis will be finalized and disseminated to all provincial and operational district staff and service providers, including staff training at National Center for Parasitology, Entomology and Malaria Control central laboratory, provincial and OD laboratories. For external quality control, microscopy will be assessed through the submission of samples by expert microscopist at the National Center for Parasitology, Entomology and Malaria Control. All laboratories will participate in the WHO accredited external competency assessment. A slide bank is being developed to support quality assurance and training on malaria diagnosis, as quality microscopy is essential to detecting treatment failure.

Sites were selected on the basis of sufficient cases, border areas, new sites with no known status of efficacy of current drugs, old sentinel site, and transmission from all sites between May and October 2015, with the concurrence of WHO experts. For the study of AS-Amodiaquine and quinine + tetracycline (second-line), the rationale is that these drugs have never been evaluated in Cambodia and all ACTs available are becoming less effective.

Cambodia plans to look at new sites and may need to look at new foci. The areas using first-line treatment are being monitored every two years. These are WHO-funded sites and did not include the regional artemisinin initiative or Global Fund. Global Fund resources cannot be used in Cambodia to conduct TES.

China

In 2016, China will focus on DHA-PIP for *P. falciparum* malaria and chloroquine for *P. vivax* malaria in Yunnan province. The study will include seven sentinel sites in 2016 and seven sentinel sites in 2017. TES will be funded by WHO and implemented by the National Institute of Parasitic Diseases (NIPD), the Yunnan Institute of Parasitic Diseases (YIPD) and county CDCs. China has two level 1 WHO-certified microscopists available for TES.

Discussion included that about half the sites will conduct TES with the remaining areas to use routine case surveillance, due to China's size. Monitoring would be conducted by County CDC teams, and hospitals for active case detection would be responsible. Most cases are amongst mobile migrants so the focus will be counties in the border areas targeting Pf and *P. vivax* patients.

Indonesia

TES will assess the efficacy of DHA-PIP in five sites in 2016 and two in 2017. The sites for 2016 are: Timika, Papua province; Jayapura/Jayapura district, Papua province; Manokwari, West Papua; Molucca, Central Sulawesi and Jamba. The justification for sites includes high endemicity and anecdotal reports of day three positives from a clinical practice in Manokwari. An extension for the current TES is being sought until December 2015, with a proposal to move one study site (East Kalimantan) as only one case was found there. The capacity to perform TES is not available in many locations in Indonesia. WHO will be the sole financial support for TES in Molucca, Central Sulawesi and Jambi, and the TES will be implemented by Eijkman Institute. In Timika, joint funding will be provided by WHO and Menzies School of Health Research and implemented by Timika Research Facility. In Jayapura, WHO and the Ministry of Health will provide funding, to be implemented by Eijkman Institute. In Manokwari, funders will be WHO and Ministry of Health, and implementers, Timika Research Facility and Eijkman Institute. Indonesia has a strong core of WHO-certified level 1 microscopists.

The Lao People's Democratic Republic

In 2016, the Lao People's Democratic Republic chose four sites: Champasak to test an alternative ACT, DHA-PPQ, and Attapeu, Sekong and Salavanh to test AL. In 2017, DHA-PIP will be tested in Champasak, Salavanah and Sekong: while Attapeu will test AL. The justification for site selection includes strategic location, malaria prevalence, validation of previous year's results, or establish baseline data with alternative ACTs. TES will potentially be funded by WHO or the Global Fund's New Funding Model. Implementers will be CMPE/PHO. The number of level 1 expert microscopists is sufficient.

Discussion included that given that AL is starting to fail, the Lao People's Democratic Republic should include a national treatment guideline workshop for 2016 to be ready to address the situation. From preliminary results in Sekong province, there was a suggestion for TES to be repeated in 2016 to validate the results. Sites have been identified in the southern part of the country, but depending on results in current studies, they need to be more flexible for site selection. Coordination with provincial and military hospitals is important. Regional artemisinin imitative projects doing case detection in villages should refer cases to district or provincial hospitals where TES is ongoing. The Lao People's Democratic Republic was also commended for significant improvements in microscopy quality.

Malaysia

Malaysia will test AL and chloroquine in five districts in 2016 in the Central, Northern, Eastern, Southern and Borneo regions, and again in the same sites in 2017. The TES Monitor will be the State Vector Officer and the monitoring and supervision will be provided by the National Malaria Elimination Programme. The implementers of TES will be the National Public Health Laboratory and the Institute for Medical Research. Funding will be drawn from the Ministry of Health Operational Budget.

Myanmar

Myanmar plans to conduct TES in seven sentinel sites in 2016 and three in 2017, to test AL in *P. falciparum* and *P. vivax*, chloroquine against *P. vivax*, and DHA-PIP against *P. falciparum*. Justification of site selection is based on the following:

- Tabaikkyin township, Mandalay Region - located in the heart of Myanmar with pockets of transmission and many gold mine workers;
- Tamu, Sagaing Region – Myanmar-India border, with migrant workers;
- Bee Linn, Mon State – close to Myanmar-Thailand border, with gold mine and rubber plantation workers;
- Thandaung, Kayin State - bordering Kayah State and Thai-Myanmar border, with pockets of transmission around natural lake;
- Buthidaung, Rakhine State – located at western part of Myanmar, bordering Bangladesh (Cox-Bazar) with moderate malaria transmission;
- Kawthaung, Tanintharyi Region – southern Myanmar, bordering Thailand - known artemisinin resistance;
- Bamaw, located in Kachin State – located at northern Myanmar, bordering China;
- Loikaw, Kayah State – close to Myanmar-Thailand border.

Funding will be provided by WHO and implementers will be the Department of Medical Research (DMR) headquarters, Pyin Oo Lwin) and the Defense Services Medical Research Center (DSMRC).

Discussion included that for border regions, results are valuable when looking at resistance because the focus is on treating where the disease was acquired. TES results will show the response parasites are having to the drugs based on the areas where cases were found. For TES sites in border areas, countries should strengthen cross-border information exchange including the types of drugs used and the results. WHO's rationale in bringing the three networks together was for policy-making decisions to be influenced by TES findings on the other side of the border in neighbouring countries.

Nepal

In 2016, Nepal planned to test AL for *P. falciparum* malaria, and again in 2017, together with chloroquine against *P. vivax*. The studies will be implemented by KIST Medical College in coordination with the Ministry of Health and Population and the Epidemiology and Disease Control division. The TES monitors will be the Ministry of Health and Population, the Epidemiology and Disease Control division and WHO. Six visits are planned per year. The TES will be funded by WHO. The Microscopist 1 and Microscopist 2 slide readers will be at sentinel sites and Microscopist 3 reader will be at the Epidemiology and Disease Control division and the Vector-Borne Disease Research and Training Centre for microscopy quality assurance/control. An assessment of current level 1 experts is proposed for 2016.

Papua New Guinea

Papua New Guinea's TES planned for 2016–2017 will involve two sites: Mugil on the north coast and Lemakot in the islands. Restricting to two sites will allow capacity to be built to conduct TES in the future. Site selection was based on the high incidence of malaria and presence of infrastructure. Drugs to be tested are AL and DHA-PIP, with an estimated budget of US\$ 60 000 per site per annum. The Department of Health and Central Public Health Laboratory will lead the study, with one medical officer (supervisor). The Australian Army Medical Institute will assist with molecular work and trainings will be required for microscopy and GCP.

The Philippines

TES sites for 2016 include Rizal, Bataraza, Brooke's Point and Puerto Princessa all in Palawan province and another in Tawi Tawi. Drugs to be tested for *P. vivax* malaria are chloroquine and primaquine 15 mg vs 30 mg if adequate numbers of eligible vivax patients are recruited. The proposed budget is US\$ 108 695.

In 2017 the TES will focus on testing the efficacy of AL and quinine plus in Rizal, Brooke's Point, Bataraza and Puerto Princessa in Palawan province. Funding will be provided by the Government of Philippines and implementers will be the Research Institute for Tropical Medicine and the Department of Health.

Solomon Islands

In 2016, the TES site will be at Tetere, Guadalcanal Province covering five health facilities (one hospital and four rural health centres). In 2017 the TES site will be Auki, Malaita province covering four health facilities (one hospital and three rural health centres). The target is to recruit 60 *P. falciparum* and 60 *P. vivax* cases. The third reserve site will be in Makira province. The estimated budget is US\$ 75 000 with funding from WHO. There is also a budget for molecular markers and K13 analysis which will be under the Australian Army Medical Institute. Two level one certified microscopists are available. TES will be implemented by the Ministry of Health and Medical Services.

Thailand

For 2016–2017, Thailand plans to conduct TES in 11 sentinel sites, two on the eastern border with Cambodia and nine on the western border with Myanmar. The drugs to be tested on the eastern border are DHA-PIP and AS+MEF for *P. falciparum* and chloroquine for *P. vivax* malaria. On the western border, AS+MEF will be tested in six sites in the south (Yala, Songkhla, Surat Thani, Chumporn and Prachuap Khirikhan), while DHA-PIP will be tested in Ranong. In Kanchanaburi, DHA-PIP against *P. falciparum* and chloroquine against *P. vivax* will be tested. Site selection was based on areas showing resistance or at risk of developing resistance as well as having adequate case numbers and functioning facilities.

For 2017, three sites were proposed on the western border and one on the eastern border. In Kanchanaburi, Artesunate – Pyronaridine (Pyramax™) will be tested, while DHA-PIP will be tested in Ratchaburi and Songkhla and chloroquine in Songkhla and Ubon Ratchathani. With only one level one WHO-certified microscopist available from the programme, there is a need to strengthen the core of expert microscopists to serve as qualified TES validators.

Vanuatu

In 2016, Vanuatu proposes three sites: Malekula, Ambyrum Maewo and Santo. Technical assistance is required to help complete the TES plan and other needs include microscopy training and clinician TES implementation training to assist monitoring and supervision. WHO will fund the TES. Implementation will be led by Esau and NMVB in Malekula and the Ministry of Health for the other sites. There is a need for skills strengthening of microscopy experts.

Viet Nam

In 2016, Viet Nam plans to test the efficacy of DHA-PIP in five sites: Bin Phuoc, Dak Lak, Khanh Hoa, Quang Tri and Kon Tum, as well as chloroquine in Bin Phuoc and Khanh Hoa. In 2017, the efficacy of DHA-PPQ will be monitored in Bin Phuoc, Gia Lai, Ninh Thuan and Dak Nong. Chloroquine will also be monitored in Gia Lai and Dak Nong. Viet Nam has a strong core of level 1 microscopists but strengthening of the quality control/assurance system in microscopy for TES is required as well as training on K13 analysis for laboratory staff. Refresher training for microscopists, TES staff and of GCPs for all staff in charge of TES (two years certificate validity, Ministry of Health rule) is also required.

Discussion included Viet Nam's plan to test pyronaridine-artesunate (Pyramax™) as a possible option for the future and asked whether DHA-PIP could be replaced with pyronaridine-artesunate in one site. Viet Nam conducted this test with the army in 2010/2011 and there is a publication showing very high efficacy. Regarding testing efficacy of Pyramax, this was a costly process requiring at least US\$ 100 000 and must be carried out like clinical research. Viet Nam submitted a proposal for such a study. The data presented in this workshop is for routines TES.

Network plans

The key priority areas identified by the three networks were:

- Improve cross-border coordination and on-site drug selection
 - TES sentinel sites, results/mutual selection
 - Treatment used near border;
 - Epidemiological information;
 - Annual review meetings (three networks)

- Establish web-based data management and early warning system
- Training/mentoring for TES; GCP/Good Laboratory Practice; manuscript writing for publication
- Strengthen molecular laboratory work (genotyping, e.g. K13)
- Build quality assurance and control systems on a yearly basis to strengthen microscopy capacity – external quality assurance programme (EQAP)
 - Identify reference laboratory
 - WHO microscopy QA Manual; country standard operating procedures
 - Establish national core of trainers to conduct basic and refresher microscopy training annually
 - Provide technical assistance to set-up national slide bank
 - External competency assessment of malaria microscopists will be done by WHO

3. CONCLUSIONS AND RECOMMENDATIONS

3.1 Conclusions

- All countries had a significant decrease in malaria cases in recent years.
- For falciparum malaria, overall results show that while artemether-lumefantrine (AL) and dihydroartemisinin-piperaquine (DHA-PIP) are still highly effective in most of the countries (except Cambodia), slow parasite clearance is increasing in Viet Nam and in the south of the Lao People's Democratic Republic. K13 mutations are present in all countries of the Greater Mekong Subregion, and none from the Pacific and South Asian countries. Two main mutants are emerging in the east and west Greater Mekong Subregion.
- Mapping of K13 mutations need to be correlated with clinical data.
- For vivax malaria, chloroquine is still effective in countries using this drug. Early relapse with ACTs has been observed in Pacific island countries (Chesson strain). Monitoring primaquine efficacy is operationally difficult, and molecular markers for relapsing vivax need to be further defined.
- Alternative ACT regimens need to be tested before deciding for drug policy change as soon as signs of declining efficacy become manifest
- The issue of including/excluding girls 9–18 years needs further discussion. This also depends upon cultural contexts and national ethics committee approvals.
- Regular monitoring visits to TES sites very useful in addition to internal supervision
- Funding to continue TES is available from several partners.

- Noteworthy are countries such as Malaysia and the Philippines with national government budget allocation to conduct the TES, and Malaysia integrating TES into the routine surveillance system.

3.2 Recommendations

3.2.1 Recommendations for Member States

- 1) Countries are recommended to continue to strengthen high quality TES implementation using the standard WHO protocol.
- 2) Strengthening and sustaining capacity of national programmes to implement TES is critical. Supporting the strengthening of microscopy capacity (regular refresher training for TES microscopists) is critical as is training of those who collect slides.
- 3) Alternative ACT regimens need to be tested before deciding on drug policy change as soon as signs of declining efficacy manifest.
- 4) Countries are recommended to maintain regular monitoring visits to TES sites.
- 5) Countries are recommended to facilitate integration of monitoring of drug efficacy into routine surveillance systems in pre-elimination settings.

3.2.2 Recommendations for WHO

- 1) Tasks for the networks focus on coordination, information sharing and technical support to the above activities with particular emphasis on strengthening cross-border information sharing and coordination.
- 2) WHO is recommended to share the finalized monitoring tools and reporting guidelines with in-country and external monitors.
- 3) WHO is recommended to provide support for countries moving into elimination as they adopt new approaches to monitoring and surveillance beyond TES.

ANNEXES

Annex 1. TES country plans 2016 – 2017

2016	Drugs to Test	Proposed Budget (US\$)	2017	Drugs to Test	Proposed Budget (US\$)	Refresher Microscopy training	Monitoring and supervision	Other needs/gaps
Name of Site			Name of site					
Bangladesh								
Naiykhanchhari	AL for Pf	48,000	Naiykhanchhari	CQ-PQ for Pv	48,000	Planned Dec 2015 by NMCP	NMCP; Local civil surgeon office	Refresher training for microscopists/ health personnel training needed; funding constraints; stakeholders/donors involvement required
Ragmar	AL for Pf		Ragmar	CQ-PQ for Pv				
Cambodia								
Preah Vihear	ASMQ	38,000	Kratie	ASMQ	38,000	Needed	3-4 times	Refresher training for laboratory staffs & clinician
Ratanakiri	DP (first line), quinine +T (second line)	70,000	Siem Reap	ASMQ (First line)	70,000	Needed	3-4 times	
Oddor Mean Chey	DP	38,000	Stung Treng	Q+T (second line)	38,000	Needed	3-4 times	
Battambang	ASMQ or AS-Amo	38,000	Kg. Speu	DP or ASMQ	38,000	Needed	3-4 times	
Kg. Thom	DP	38,000	Pursat	ASMQ	38,000	Needed	3-4 times	
China								
Tengchong, Baoshan	DHA-PIP CQ	30,000	Tengchong	DHA-PIP, CQ	40,000	2	NIPD, YIPD 2 times/yr.	K13 test and analysis and QC; TES refresher training
Yingjiang,	DHA-PIP	60,000	Yingjiang	DHA-	60,000	4	NIPD,	

Dehong	CQ			PIP, CQ			YIPD 2 times/yr.	
Ruili, Dehong	DHA-PIP CQ	20,000	Ruili	DHA- PIP, CQ	20,000	2	NIPD, YIPD 2 times/yr.	K13 test and analysis and QC; TES refresher training
Menglian, Puer	DHA-PIP CQ	30,000	Menglian	DHA- PIP, CQ	30,000	1	NIPD, YIPD 2 times/yr.	
Longyang, Baoshan	DHA-PIP CQ	30,000	Longyang	DHA- PIP, CQ	30,000	1	NIPD, YIPD 2 times/yr.	
Lincang, Baoshan	DHA-PIP CQ	30,000	Lincang	DHA- PIP, CQ	30,000	1	NIPD, YIPD 2 times/yr.	
Longling, Baoshan	DHA-PIP CQ	30,000	Longling	DHA- PIP, CQ	30,000	1	NIPD, YIPD 2 times/yr.	
Indonesia								
2016 thru 2017			2017					
Timika, Papua Province (January-February 2016)	DHA-PIP	7,805	Continuation from 2016: Jayapura District, Papua Province - Manokwari, West Papua - Molucca - Central Sulawesi - Jambi	DHA- PIP		To be conducted January 2016 in Timika		Trained MD and microscopists for TES
Jayapura/Jayapura District, Papua Province	DHA-PIP	Planned for second half of 2016						
Manokwari, West Papua	DHA-PIP	thru						
Molucca	DHA-PIP	2017:						
Central Sulawesi	DHA-PIP							
Jambi	DHA-PIP	\$166,67 1						
						To be conducted Q1 2016 in Molucca		

Lao People's Democratic Republic								
Champasack	DHA-PIP	50,156	Champasack	DHA-PIP	50,156	1/year	4/year	1. TES refresher training for microscopists and provincial and District staff. 2. Coordination with local officials, companies and development owners. 3. Procure 1 motorbike for district/site
Attapeu	AL	50,156	Attapeu	AL	50,156	1/year	4/year	
Salavanh	AL	45,924	Salavanh	DHA-PIP & CQ	62,516	1/year	4/year	
Sekong			Sekong	DHA-PIP	50,156	1/year	4/year	
Malaysia								
Central Region	AL & CQ	373,020	Central Region	AL & CQ	373,020	3x/year	National MEP	
Northern Region	AL & CQ	671,220	Northern Region	AL & CQ	671,220	3x/year	National MEP	
Eastern Region	AL & CQ	696,080	Eastern Region	AL & CQ	696,080	3x/year	National MEP	
Southern Region	AL & CQ	497,200	Southern Region	AL & CQ	497,200	3x/year	National MEP	
Borneo Region	AL & CQ	1,367,240	Borneo Region	AL & CQ	1,367,240	3x/year	National MEP	
Myanmar								
Tabeikkyin, Mandalay Region	AL (Pf), CQ (Pv)	24000 (field) + 10,000 (molecular)	Myitkyinar	AL (Pf), CQ (Pv)	24000 (field) + 10,000 (molecular)	Yes (first quarter of 2016)	Moe Kyaw Myint	Regular refresher microscopy training Revalidation of certified microscopists
Tamu, Sagaing Region	DHA-PIP (Pf), CQ(Pv)	24000 (field) + 10,000						Capacity strengthening to have L1 expert

Bee Linn, Mon state	AL (Pf), CQ	24000 + 10,000	Kawthaung, Tanintharyi Region	AL (Pf)	24000 + 10,000	Yes (first quarter of 2016)	Hnin Wai Lwin	microscopists for NMCP, DMR and all TES sites
Thandaung, Kayin State	AL (Pf), CQ (Pv)	24000 + 10,000					Kay Thwe Han	
Buthidaung, Rakhine state	AL, DHA-PIP (Pf), AL (Pv)	49500 + 20000 (molecular)					Kay Thwe Han	
Kawthaung, Tanintharyi Region	AL (Pv)	15,000					Myat Phone Kyaw	
Bamaw, Kachin State	DHA-PIP (Pf) CQ (Pv)	24000 + 10,000	Loikaw, Kayah State	DHA-PIP, CQ	24000 + 10,000	Yes (first quarter of 2016)	Khin Phyu Pyar	
Nepal								
Kailali (Dhangadi)	AL for Pf	12,780		AL in Pf	19,171	Refresher training to laboratory personnel at EDCD/VBDRTC * /sentinel sites (~7 staff/each site)	6/year	Funding and technical support needed *Molecular test not available * VBDRTC could be molecular test site if capacity enhanced (2017)
Dhanusha (Janakpur)		12,094		CQ in Pv	18,141		6/year	
Jhapa (Bhadrapur)		12,799			19,199		6/year	
Central Level		16,541			24,812		6/year	
Papua New Guinea								
2016 to 2017								
Mugil	AL and DHA-PIP	\$60,000				Needed	Medical officer	AMMI assist for molecular work
Lemakot								
Philippines								
Rizal	CQ; PQ 15 mg vs. 30 mg	\$108,695	Rizal	AL for Pf; quinin	108,695.65	Annual, before commencement	Dr. Antonio Bautista	EQAS for PCR
Bataraza			Bataraza					

Brooke's Point	if adequate # of eligible patients		Brooke's Point	e + for Pf			(GF)	Dr. Faith Alberto (Regional Office)
Puerto Princesa			Puerto Princesa					
Tawi-Tawi								
Solomon Islands								
Tetere	AL: Pf & PV	\$75,000 for both sites				Needed	VBDCP	Laboratory Support (Australian Army Medical Institute) & Report writing
			Auki	AL: Pf Pv		Needed		
Thailand								
Tak	PYR/AS-Pf	US\$ 100,000	Ratchaburi	DHA-PPQ-Pf	US\$ 100,000			Microscopy quality assurance Biomarkers/Molecular diagnosis facilities Drug level monitoring
Kanchanaburi	CQ-Pv / DHA-PIP		Kanchanaburi	AS-PYR - Pf				
Prachuap Khiri Khan	AS+MEF		Songkhla	DHA-PIP-Pf / CQ-Pv				
Chumporn	AS+MEF		Ubon Ratchathani	CQ-Pv				
Surat Thani	AS+MEF							
Songkhla	AS+MEF							
Ranong	DHA-PIP							
Yala	AS+MEF							
Srisaket	AS+MEF-Pf; CQ-Pv							
Ubon Ratchathani	DHA-PIP							
Vanuatu								

Malekula	AL					Needed	Esau & P Clinician	TA to complete TES plan microscopy training Clinician /implementer training to assist monitoring and Supervision
Ambyrum								
Maewo								
Santo								
Viet Nam								
Binh Phuoc	DHA-PIP; CQ	140,000	Binh Phuoc	DHA- PIP	120,000	Yes		- Training on K13 analysis - WHO support to get certificate of standard K13 analysis as reference lab; - Refresher training for microscopist and TES staff; - Refresher training of GCPs for all staff in charge of TES (2 years certificate validity, MoH rule); - WHO provide for half-life clearance time (t1/2) calculate software; - Strengthening of QA/QC in microscopy for TES; - Prolong study duration in order to get minimum required sample (long dry season in some sites)
Khanh Hoa	DHA-PIP; CQ		Gia Lai	DHA- PIP; CQ		Yes		
Dak Lak	DHA-PIP		Ninh Thuan	DHA- PIP; CQ		Yes		
Quang Tri	DHA-PIP		Dak Nong	DHA- PIP		Yes		
Kon Tum	DHA-PIP					Yes		

AGENDA

DAY 1 (10 Nov 2015)

Time	Schedule	Presenters
08:30	Registration of participants	
09:00	Welcome remarks	<i>Siv Sovannaroth, Ministry of Health, Cambodia Eva Christophel, SEARO Rabi Abeyasinghe, WPRO</i>
09:20	Self-introduction Review of the objectives and expected outcomes Nomination of Chair, Vice chair	<i>Maria Dorina Bustos</i>
10:00	<i>Group photo / coffee break</i>	
10:30	TES standard protocol and discussion	<i>Marian Warsame</i>
11:00	Anti-malarial drug resistance monitoring in the Greater Mekong Subregion, BBINS and Pacific Networks and implementation Plenary discussion on above topics	<i>Maria Dorina Bustos</i>
12:00	Lunch	
13:00	Greater Mekong Subregion (Greater Mekong Subregion) Network: Presentations by Principal Investigators on TES results of the last 2 years (15 min. presentation/country, followed by discussion) Cambodia China	<i>Leang Rithea Tang Linhua</i>
15:00	<i>Coffee / tea break</i>	
15:30	Greater Mekong Subregion Network presentations continued Thailand Viet Nam	<i>Sanchai Chasombat Bui Quang Phuc, Hyunh Quang</i>
16:30	BBINS Network: Presentations by Principal Investigators on TES results of the last 2 years (15 min. presentation/country, followed by discussion) Bangladesh Nepal	<i>Abu Nayeem Mohammad</i>
17:30	Closure of Day 1	
18:00	Reception at the Apsara Terrace	

Day 2 (11 Nov 2015)

Time	Schedule	Present
8:30	Updates on the Kelch 13 marker for artemisinin resistance; working definition of artemisinin resistance	<i>Pascal Ringwald</i>
8:50	Global antimalarial drug efficacy database and reporting tools	<i>Pascal Ringwald</i>
9:15	TES standard protocol and TES monitoring	<i>Marian Warsame</i>
9:45	Plenary discussion on above updates	
10:15	<i>Coffee / tea break</i>	
10:45	<p>Pacific Network: Presentations by Principal Investigators on TES results of the last 2 years (15 min. presentation/country, followed by discussion)</p> <p>Indonesia Malaysia Philippine s</p>	<p><i>Din Syafruddin / Jeane Rini Poespoprodjo Mohd Hafizi / Zulhainan Hamzah / Effie Espino</i></p>
12.15	Lunch	
13:15	<p>Pacific Network presentations continued</p> <p>Papua New Guinea Solomon Islands</p> <p>Vanuatu</p>	<p><i>Leo Makita / Moses Laman Albino Bobogare / Hulston Adam Fafale Esau Naket / Auguste Manwo</i></p>
15.00	<i>Coffee/tea break</i>	
15:30	Update on the Strategy for malaria elimination in the Greater Mekong Subregion (2015-2030) and treatment policy change	<i>Walter Kazadi</i>
16:00	Summary of country results and discussions	<i>Pascal Ringwald</i>
16:30	Introduction to group work	<i>Maria Dorina Bustos</i>
17:00	Closure of Day 2	

Day 3 (12 Nov 2015)

Time	Schedule	Present
8:30-12:00	Working Groups to prepare/update 2016-17 country TES plans / budgets and define tasks of the networks	<i>Facilitators: WHO staff</i>
10:00	<i>Coffee / tea break</i>	
12:00	Lunch	
13:00	Plenary presentation and discussion of country plans / budgets and network plans (5-10 mins / country) Greater Mekong Subregion Network <ul style="list-style-type: none"> - Cambodia - China - Lao People's Democratic Republic - Myanmar - Thailand - Viet Nam 	
14:15	BBINS Network <ul style="list-style-type: none"> - Bangladesh - Bhutan - India - Nepal 	
15:15	<i>Coffee/tea break</i>	
15:30	Pacific Network <ul style="list-style-type: none"> - Indonesia - Malaysia - Philippines - Papua New Guinea - Solomon Islands - Timor Leste - Vanuatu 	
17:00	Partners' comments	<i>ACTMalaria, DFAT, GFATM, UNOPS,</i>
17:15	Conclusions Recommendations and next steps	<i>Maria Dorina Bustos</i>
17:30	Closing remarks	<i>WHO</i>

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