

Minutes of an Informal
Consultation on
Resource Mobilization for
the Containment of
Artemisinin Tolerant Malaria on
the Cambodia-Thailand Border



Phnom Penh, Cambodia
17-18 June 2008



Meeting Report

REPORT

**MINUTES OF AN INFORMAL CONSULTATION ON
RESOURCE MOBILIZATION FOR THE CONTAINMENT OF
ARTEMISININ TOLERANT MALARIA ON THE
CAMBODIA-THAILAND BORDER**

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The views expressed in this report are those of the participants in the Informal Consultation on Resource Mobilization for the Containment of Artemisinin Tolerant Malaria on the Cambodia-Thailand Border

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ABBREVIATIONS

ACD	Active case detection
ACT	Artemisinin-based combination treatment
AMT	Artemisinin monotherapy
ARC3	Artemisinin Resistance Confirmation, Characterization, Containment Project
BCC	Behaviour Change Communication
BMGF	Bill and Melinda Gates Foundation
CDC	Centers for Disease Control and Prevention
CMS	Central Medical Store
CNM	Center for Malariology, Parasitology and Entomology. Cambodia
DDF	Department of Drug and Food
DFID	Department for International Development, UK
EDAT	Early diagnosis and treatment
GF	Global Fund
IRS	Indoor Residual Spraying
LLIHN	Long-lasting insecticide-treated hammock net
LLIN	Long-lasting insecticide-treated net
LSHTM	London School of Hygiene and Tropical Medicine
MC	Malaria Consortium
MMP	Mekong Malaria Program
MMW	Mobile Malaria Worker
MMV	Mobile Malaria Volunteer
MSAT	Mass Screening and Treatment
NMCP	National Malaria Control Programme
PCR	Polymerase chain reaction
QA	Quality Assurance
RCC	Rolling Continuation Channel
RDT	Rapid diagnostic test
RGC	Royal Government of Cambodia
URC	University Research Center
USAID	United States Agency for International Development
VBDC	Vector Borne Disease Control
VHV	Village Health Volunteer
VMW	Village Malaria Worker
WHO	World Health Organization

1. OPENING REMARKS

Dr Eva Maria Christophel began the consultation with an overview of the problem and the purpose of the meeting:

- There is strong evidence of drug resistant parasites along the Thai-Cambodia border, which requires large-scale containment/elimination efforts that go far beyond current malaria control efforts.
- Strategies and budgets have been developed, and considerably more resources are needed than those currently available.
- During the two-day meeting, these plans would be presented including gaps, strategies, and implementation issues.
- The goal of the meeting is to build the partnerships and to begin to raise the additional funds that will be needed to sustain this endeavour.

Dr Duong Socheat gave opening remarks on behalf of the Government of Cambodia. He thanked the participants for their involvement and the WHO for providing technical and financial assistance.

Dr Richard Nesbit gave opening remarks on behalf of the WHO Regional Office for the Western Pacific. He thanked the Government of Cambodia for hosting this consultation.

2. SELF INTRODUCTIONS

The participants introduced themselves and the current or potential roles of their organizations in malaria in Cambodia or Thailand (Annex 1: List of Participants).

Ms. Nora Petty from the William J. Clinton Foundation gave a brief PowerPoint presentation on her organization's current global and country-level malaria activities.

3. PRESENTATIONS

The agenda of this informal consultation is attached as Annex 2. Ms Nora Petty and Dr Jo Lines were the Rapporteurs for the two-day consultation. The first session was co-chaired by Dr Duong Socheat and Dr Charles Delacollette.

3.1 Current Situation of Artemisinin Tolerance

Dr Pascal Ringwald presented current data on artemisinin tolerance. The key points of his presentation included:

- A review of data from 2001 to 2006 at the Thailand-Myanmar border showed a significant increase in the proportion of patients failing to clear their parasitaemia by day

2. Prior to 2001, 95.5% of patients became aparasitaemic within 48 hours compared to 77.9% between 2001 and 2005. A small but statistically significant decline in efficacy was observed over the years. Over the same period of time the proportion of infections attributed to parasites with two or more pfmdr1 copy number also increased.

- On the Cambodia side, the two-day and three-day parasite clearance times in all the sentinel sites using 2001-2007 therapeutic efficacy monitoring results of ACTs showed that 40%-60% of cases are still parasitemic on day 2 in south-west Cambodia, as compared to less than 10% in the north-east. On day 3, while 10% are still parasitemic in the south-west, all patients from the north-east would have cleared. Overall, approximately 10% treatment failures are observed in the south-west and less than 5% in the north-east.

A consensus statement from the ARC III meeting on 9 February 2008 was read by Dr Ringwald:

- While ACT treatment efficacy remains high in most studies, prolonged parasite clearance times following treatment with some ACTs and artemisinin monotherapy have been observed along the Thai/Cambodian border. This clinical and parasitological observation might reflect the emergence of *Plasmodium falciparum* tolerance to artemisinins, but other factors have not been ruled out.
- At present there is no clear evidence that bona fide artemisinin resistance has emerged and disseminated, but the evidence is worrying enough to justify intense investigation. WHO and partners are conducting collaborative public health and scientific investigations to confirm and characterize tolerance and/or resistance and measure its extent.
- Because of the potentially catastrophic consequences of failing to contain emerging tolerance and/or resistance, it is recommended that malaria elimination efforts in the South-East Asian region initially focus on this area.

3.2 Overview of the Strategy to Contain/Eliminate *Plasmodium falciparum* Parasites Tolerant to Artemisinins on the Cambodia-Thailand border

Dr Eva Maria Christophel provided an overview of the international response to the discovery of artemisinin tolerant parasites since January 2007:

- **January 2007, Phnom Penh:** WHO Informal Consultation on Containment of Malaria Multi-Drug Resistance on the Cambodia-Thailand Border
- **19 January 2008, Geneva:** WHO Meeting on Containment of Artemisinin Tolerance
- **9-10 February 2008, Bangkok:** ARC3 Clinical Trials Meeting
- **13-14 February 2008, Bangkok:** WHO MMP Informal consultation to define a strategy to contain/eliminate *Plasmodium falciparum* parasites with altered response to artemisinins
- **25 Feb.-1 March 2008, Phnom Penh:** National Stakeholder Planning Workshop to contain/eliminate *Plasmodium falciparum* parasites with altered response to artemisinins on the Cambodia-Thailand border

- **Since then:** Intense operational planning and budgeting in Cambodia and in Thailand

The overall goal is the “containment of artemisinin-tolerant *Plasmodium falciparum* parasites by removing selection pressure and reducing and ultimately eliminating falciparum malaria.”

Based on the available evidence and discussions during these consultations, the containment region is currently defined as:

Zone 1: Districts where both routine drug efficacy monitoring as well as research studies have found artemisinin tolerant parasites (index cases). This zone lies mainly along the Cambodia-Thailand border. Zone 1 includes eight Administrative Districts (AD) in Cambodia and three districts in Thailand.

Zone 2: Includes the areas surrounding Zone 1 where we do not yet have sufficient data, but where tolerant parasites may be expected to be spreading from Zone 1. Zone 2 includes nine provinces in Cambodia (excluding town areas) and risk areas (A1+A2+B1) in seven provinces in Thailand.

In Zone 1, an elimination strategy will be implemented (including mass screening, focal use of IRS, intense surveillance, active case detection); whereas in Zone 2 “an intensified/accelerated control strategy,” which goes beyond the current routine programmes of the two NMCPs, will be implemented.

Dr Christophel briefly outlined the seven objectives of the containment/elimination project, and the main activities related to each objective. The seven main objectives are as follows:

1. To **eliminate artemisinin tolerant parasites** by detecting all malaria cases in target areas and ensuring **effective treatment** and gametocyte clearance;
2. To decrease drug pressure for selection of artemisinin tolerant malaria parasites, through **preventing the use of artemisinin monotherapy** treatment (AMT), fake and substandard drugs and inappropriate treatment **in the private sector**;
3. To **prevent transmission** of artemisinin tolerant parasites by mosquito control and personal protection;
4. To limit the spread of artemisinin tolerant parasites by targeting **mobile populations**;
5. To support containment / elimination of artemisinin tolerant parasites through comprehensive **BCC, community mobilisation and advocacy**;
6. To undertake basic and operational research to fill knowledge gaps and ensure that strategies applied are **evidence-based**; and
7. To provide effective **management and coordination to enable rapid and high quality implementation of the** strategy.

The activities related to these objectives were presented in greater detail later in the meeting.

3.3 Cambodia Containment Project Strategy and Objectives (emergency/short/medium term)

Dr Socheat presented Cambodia's emergency, short-term, and medium-term plans for containment/elimination in Zone 1 and Zone 2:

Emergency (2008): The emergency action plan and budget was presented at a USAID meeting in April. The total amount of resources needed to start operations in Cambodia in 2008 is US\$ 4 944 924.

Short-term (Jan. 2009-June 2010): The Short-Term Plan for 2009 to mid-2010 is the main focus of this informal consultation. The total of the Cambodia portion of the project is US\$ 25 914 330 (including administrative and overhead costs). The Short-Term Plan is supposed to cover the gap until other longer-term sources of funding can be made available.

It was noted that the budget for the Short-Term Plan had been drawn up without taking into account the possibility that some of the budgeted commodities might be provided by the 2008 emergency plan or by the pending application for funding through the Global Fund (GF) Rolling Contingency Channel, if these were successful. If, during the coming months, USAID funds the 2008 emergency plan, or if the GF funds the RCC, then the items that are covered by these other sources will be subtracted from the Short-Term Plan budget. However, the overlap is not large. Most elements of the Short-Term Plan are new and go well beyond the previously-planned routine control activities, requiring new sources of funding.

Medium-term (June 2010-2014): Cambodia is in the process of developing a Global Fund Round 9 proposal, which would continue the successful containment activities in Zone 1 and Zone 2, and possibly scale-up to other areas based on the results from additional surveillance efforts. This medium to long-term strategy has not yet been fully costed.

3.4 Cambodia Containment Project: Description of Main Activities for Each Objective

Dr Kheng Sim presented Cambodia's main activities for each objective and total short-term cost of implementing these activities.

Objective 1: Detection and Treatment

Zone 1

- Mass Screening and Treatment (MSAT): By far the largest budget item under Objective 1 is mass screening and treatment, which is to take place in Zone 1 as a research activity. It is currently being proposed to use both rapid diagnostic tests (RDT) and PCR for screening, and positive cases are to be treated with atovaquone-proguanil. The exact role of PCR and RDTs remains to be defined, but it is agreed that evaluation of the mass-screening approach as an elimination tool will be an important output of this work.

Zones 1 & 2

- Expand Village Malaria Worker (VMW) network in Zone 1 and Zone 2 to provide greater access to high-quality early diagnosis and treatment. Introduce Mobile Malaria Workers (MMWs) for targeting of the mobile/migrant populations with Early Diagnosis and Treatment (EDAT), behaviour change communication (BCC), and free-of-charge personal protection methods.

- Additional capacity building/training will be needed to improve case management in the public sector. In addition, the VMW/MMW network will need to receive greater support and supervision.
- Investigation: A new intervention will include the active follow-up of an expected 1200 day 3 positive patients.

Objective 2: Reduce drug pressure in the private sector

Zones 1 & 2 (and beyond):

- The Ministry of Health is already in the process of instituting a nationwide ban on the sale of artemisinin monotherapies in the private sector, because these are believed to be an important source of selection pressure for resistance. Additional resources are needed to enforce the ban including:
 - o Training of health and drug inspectors;
 - o Face-to-face training and other incentives for private sector providers to adhere to the ban;
 - o Radio and TV campaigns to educate providers and consumers about the ban.

Objective 3: Personal Prevention

Zone 1

- Provide 147 000 long-lasting insecticide treated nets (LLIN) for all 268 000 people (regardless of distance from the forest) at a rate of two persons per net.
- Provide 53 000 long-lasting insecticide treated hammock nets (LLIHN) to all of the people at a rate of one net per family.

Zone 2

- Provide 501 000 LLINs to the 1.02 million population living <2km from the forest at a rate of two persons per one net.
- Provide one LLIHN to every family living <2km from the forest.

Zones 1 & 2:

- Re-treat all treatable nets in Z1 and in Z2 within 2km of forest; estimated numbers: 90 000 nets in Z1 and 330 000 in Z2 <2km. Focal Indoor Residual Spraying (IRS) of 50 houses around selected index cases (linked with case investigation in Objective 1).

Objective 4: Mobile / Migrant Populations

Zones 1 & 2

- It is recognized that there is limited knowledge about the mobile population in Cambodia. Therefore, the first step is to conduct a situation analysis.

- Other targeted interventions including BCC, and a newly-created cadre of “Mobile Malaria Volunteers”, will be specifically directed at mobile/migrant populations.
- It is hoped that the situation analysis will identify further opportunities for intervention.

Objective 5: Behaviour Change Communication (BCC)

Zones 1 & 2

- Development and dissemination of messages for MSAT, cross-border interventions, rational drug use, and personal protection methods.
- Mass media campaigns (radio and TV) for the containment project.
- Increased supervision and support to Village Health Volunteers (VHVs) who are responsible for distributing IEC/BCC materials and messages.

Objective 6: Operational Research (OR)

(To be covered in more detail by Dr Shunmay Yeung and Professor Nick White)

Objective 7: Management, surveillance, M&E

Zones 1 & 2

- The largest budget item is designing and managing a spatial database system for surveillance, MSAT, case follow-up, etc.
- Capacity building activities are focused at the peripheral levels: ten provinces, 27 Operational Districts (ODs) and 341 Health Centres (HCs) in the containment zones.

After the presentation it was clarified that if Cambodia’s receives funding for its Global Fund Rolling Continuation Channel (RCC) proposal or from USAID for the emergency plan, then the containment/elimination budget will need to be modified (see above section 3.3).

3.5 Thailand Containment/Elimination of Artemisinin Tolerant *P.f.* Parasites: Strategy & Action Plan

Dr Wichai Satimai presented key data from Thailand that shows reduced treatment efficacy of artesunate and mefloquine, especially in Trat province, which borders Cambodia. The proportion of positive cases at day 3 along the Cambodia-Thailand border is also comparatively high in 2006-2007.

Dr Wichai presented an overview of the action plan. Thailand already has some existing funding from GF Round 7 that can be used for implementing the containment/elimination strategy. However, in order to reach the stated goal of the project, there is still a short term gap of US\$ 8 263 181.

3.6 Thailand Containment/Elimination of Artemisinin Tolerant *P.f.* Parasites: Strategy and Action Plan (Continued)

Ms Saowanit Vijakadge outlined the containment activities on the Thailand side and the gap between existing and needed resources for implementing the short-term action plan.

Objective 1: Detection and Treatment

Zone 1

- Passive Case Detection: All *P.f.* cases in the public health facilities will be detected by microscopy and managed with atovaquone-proguanil. The new drug combination was chosen to decrease pressure on artesunate in this area.
- Active Case Detection: There will be fixed schedule malaria clinics with microscopy diagnosis during border market days.

Zone 2:

- PCD: Strengthen malaria control activities in health clinics (#53) and community malaria posts (#59) delivering EDAT by microscopy and RDT and treatment with ASU-M.

Zones 1 & 2

- Case investigation and follow-up with vector control operations on all *P.f.* cases (on days 1, 2, 3, 7, 14, 21, 28).

Objective 2: Prevention

Zone 1:

- Increase coverage by LLINs in Thai and non-Thai of M1 status (staying >6 months) to reach one net per person. Target population = 128 096.

Zones 1 & 2

- Re-impregnate 100% of existing nets with LL insecticide.
- Provision of one LLIN or LLIHN for each new migrant worker and for the mobile population.
- Promote the use of repellent among the mobile population, which is estimated at 5% of total population.
- Vector operations in active foci for mobile population.

Objective 3: Mobile/Migrant Populations

Zone 1

- As in Cambodia, there is still too little known about migration patterns, health-seeking behaviour, and magnitude of migrant/mobile population. Therefore, the Thai team will also conduct a situation analysis.

Zones 1 & 2

- Improve cooperation between private enterprise owners and provincial/district authorities to improve access to and use of malaria diagnosis and treatment by migrant workers.

- Technical meeting with Cambodian counterparts to articulate strategies, policies, and follow-up of cross border confirmed malaria cases.

Objective 4: BCC

Zones 1 &2

- Joint workshop with Cambodia counterparts to review existing IEC/BCC and to develop common materials.
- Train volunteers on new IEC/BCC.
- Malaria awareness campaign in 59 A1 (high transmission) villages.

Objective 5: Operational Research

Zones 1 &2

- Detect the residual effect of LLIN/LLIHN against main malaria vectors in the field.
- Study on vector resistance by biochemical technique.

Objective 6: Management, surveillance, M&E

Zones 1 & 2

- As in Cambodia, a large budget item is the development and implementation of an improved spatial data management system. Thailand will collaborate with BIOPHIX, Mahidol University to develop a surveillance system.
- *In vivo* therapeutic efficacy studies and monitoring of *cytochrome b* marker for atovaquone resistance in three districts with a change in first line treatment.
- Collaborate with Pasteur Institute to conduct QA on RDTs.
- In order to run an effective containment programme, there needs to be more staff for project management and coordination at all levels, including salaries for full-time staff, allowances for part-time staff, and per diems for field staff.

After the presentation Dr Wichai made the point that when Thailand faced economic crisis ten years ago, many factories laid off workers. Jobless people went back to the forest to work and gather food, and there were an increasing number of malaria cases. Now that fuel and food prices are climbing, it is important that we prepare for a similar situation.

Dr Kanyok asked if and how Thailand had calculated the cost for containment beyond the first two years. He also wanted to know how Thailand expected to cover the expenses beyond the short-term period. Dr Wichai said that they have not yet costed a medium-term strategy, but that they hope other organizations, in particular GF and USAID, will support the programme in the long run.

There was also a short discussion about the proposed treatment for cases in Zone 1, and the possible advantages of adding artesunate to atovaquone-proguanil.

3.7 Measuring Achievements of Multi-Country Containment Interventions

Dr Delacollette stressed that the information he was presenting represented his personal views and had not been fully discussed within the WHO. In his presentation he suggested various process and outcome indicators tied to different objectives in the containment plan.

One of the first activities in the plan of action is to set-up a cross border meeting to define the indicators to be used and review the suggestions.

Dr Delacollette also emphasized that while most of the interventions in this short-term project are focused in Zone 1 and Zone 2 where there will be elimination and intensified control efforts, respectively, it is important not to forget about other zones which include the Mekong region and beyond. In these areas, monitoring of tolerant parasites is very important in order to determine the magnitude and spread of the problem.

There was a useful discussion about the technique(s) to be used to detect infection in the mass screening.

Dr Chansuda asked about experience with PCR, and questioned its cost-effectiveness versus investing in microscopy. Dr Delacollette said that PCR can detect two to four more cases than microscopy and it is becoming more cost-effective: the IPC (Institut Pasteur Cambodia) can conduct PCR testing for about US\$ 1 per person.

Dr Lines explained that mass-screening in whole populations has not previously been used as an elimination technique: the idea is new. The rationale is an extension from the method of Mass Drug Administration, which was occasionally used as a means of transmission control when malaria drugs were cheap and parasitological diagnosis was difficult. At that time, treating everyone presumptively on the spot was cheaper and easier than taking slides from everyone, and then trying to relocate the positive people in order to treat them hours or days later. Now, in this case, we wish to avoid mass-deployment of artemisinins, and the only available and effective drug without artemisinins is atovaquone-proguanil. This is so expensive that presumptive treatment of the entire population is out of the question. On the other hand, instant parasitological diagnosis using RDTs (rapid diagnostic tests) has become possible in recent years. In principle, therefore, a substantial proportion of infections can be detected with RDTs and treated in the field, and this is the rationale behind the proposal for mass-screening.

However, it seems unlikely that RDTs will detect a sufficiently large proportion of all infections. In order to be effective for transmission control, methods based on mass treatment of whole populations must as far as possible achieve complete coverage: every infection that is missed is important. The issue is not so much the fact that RDTs detect only 90% to 95% of the infections detected by conventional thick-film blood slides. Rather, it is the fact that there are many infections that are undetectable by either of these methods, because the parasitaemia is too scanty. This was only discovered in the last few years: we used to think that thick films were detecting 90% of more of all infections. Now, we have discovered that the number of infections detectable by PCR methods is three- to four-fold higher than the number detectable by conventional thick blood films. These very-low density infections are not clinically important, because they are too scanty to cause illness in most people, but they are important for transmission, because some of them are infective to mosquitos. This means that RDTs are probably detecting only a minority of all infections. For this reason, there are now suggestions that PCR could be used instead for the mass-screening. PCR would have the advantage of detecting more infections than any other method, but unlike RDTs it cannot give the immediate results that are one of the main justifications for the mass-screening approach. Using PCR for MSAT would pose huge logistic challenges in the field work – in particular it would mean going

back after (not less than) three days to find the positive people. This delay would not be a big problem in itself, but re-contacting the positives on such a large scale has never been attempted: it could consume a lot of time and transport resources, and finding 100% of them might be impossible.

Dr Christophel also pointed out that there is evidence that there are a very high number of asymptomatic cases in the border area. Dr Shunmay emphasized that there was consensus that operational research (OR) around the early stages of MSAT is critical because there is still limited existing knowledge. If designed well, OR will be able to inform future implementation of MSAT in Cambodia and perhaps in other countries as well. A draft proposal is being circulated on how to do this. According to Dr Shunmay, logistics are going to be very challenging in the field to avoid cross-contamination and to track down positive cases three days after testing. Mr Katz pointed out that they needed an indicator to identify drop-off rates due to logistical issues. Dr Kanyok inquired about whether it is effective to screen on one day and then treat on another. Dr Shunmay responded that this was an issue that was being discussed now, but that the assumption was that the person who tests positive will still have parasites three days later. Dr Kanyok expressed additional worries about whether or not the three day waiting period would create additional transmission. Dr Delacollette explained that there will also be community-based workers who will be able to provide treatment at any time. The PCR capacity of IPC, in terms of throughput of samples, is thought to be about 1000 samples per day. It is possible that they might not be able to turn around the results in the three days that have been promised, but the information still may be useful even later because these are thought to be stable infections, and we will be able to identify asymptomatic people who would not be picked up by other methods. It was agreed by all that there needs to be additional discussions around the design and logistical issues of mass screening and treatment using PCR. Dr Lines suggested running a formal experimental trial with three arms: 1) RDTs only 2) PCR (one day waiting period) and 3) no intervention.

3.8 Operational Research

Professor White reminded the participants that approximately ten million children in Africa have died because of parasite genes that have emerged from this region. Artemisinin resistance is truly a global threat, and therefore we need to act even in the absence of complete information. Because of this, OR will be essential for informing future elimination efforts. Professor White summarized some of the outstanding questions related to this project:

Outstanding questions:

Epidemiology: Professor White questioned whether artemisinin resistance had spread already. He believes that it is likely that artemisinin tolerance has spread throughout Cambodia. Viet Nam could be figured out by gathering data from malarious regions near the Cambodia border. And what happens in Tak, Thailand, will be a good guide to what is happening in Myanmar. Drug resistance has traditionally spread westwards from Cambodia, through South Asia to Africa. In this case, once resistance has migrated across Thailand to Myanmar, it will be virtually unstoppable. For this reason, mapping the extent and spread of artemisinin tolerance is critical for identifying the full problem and where to intervene, and then evaluating the effectiveness of the containment interventions. There are many different existing data sources that can be used to inform this kind of mapping exercise, but more robust data will be needed. Dr Shunmay addressed some of the gaps in the current data sources.

Biology: We still do not know the underlying biochemical and genetic mechanisms of resistance.

Interventions: There is still a lot of uncertainty about what are going to be the most effective approaches to containment/elimination, what drugs should be used, etc.

Dr Shunmay discussed some of the potential OR proposed for short/medium term in Cambodia and Thailand related to specific interventions:

OR related to EDAT (Objective 1):

Thailand will monitor resistance to atovaquone (a new drug in Thailand) only used in Zone 1.

Cambodia will conduct a qualitative and quantitative evaluation of the expanded VMW project, implementation research on focal screening, treatment, and targeted control, *in vivo* studies on drug resistance, and collection of day three PCR samples, sensitivity and specificity of new *Pf/Pv* RDT.

OR related to mass screening and treatment (Objective 1):

- **Cambodia:** As discussed above, it will be essential to design methods to measure whether MSAT is effective for malaria elimination and for the containment of resistance. Is it acceptable and feasible? What are the differences in the effectiveness of RDTs only versus RDTs + PCR?
At the moment the plan is to use atovaquone-proguanil +/- primaquine for treatment in Zone 1 during MSAT. There is scant data on the use of primaquine with atovaquone-proguanil. Should we conduct a clinical trial first?
If we use atovaquone-proguanil, will it select for atovaquone resistance?

It was suggested that the London School of Hygiene and Tropical Medicine (LSHTM) and the US Centers for Disease Control and Prevention (CDC) could help to design the MSAT study. OR will be needed to evaluate the costs (financial and human) of PCR.

OR on the private sector:

The private sector in Cambodia is a crucial part of the elimination/containment strategy, because it is very important to reduce the availability of artemisinin monotherapies (AMT), which are thought to be an important source of selection for resistance. The private sector approach is still a “work in progress.”

The Royal Government of Cambodia (RGC) has decided to ban the sale of all antimalarials in Zone 1 in the private sector. Therefore, in this zone, OR will focus on incentivizing and supporting private sector providers to refer patients to the public sector. In Zone 2, where nationally-approved first-line ACTs will still be allowed but artemisinin monotherapies will be banned, OR will include face-to-face training of providers, incentives to get providers to prescribe ACTs, greater data collection and monitoring.

In Tanzania, the Clinton Foundation has piloted a successful subsidy on ACTs in the private sector, which has drastically increased the uptake of ACTs in the intervention area.

There is no planned OR in Thailand on the private sector.

OR on vector control:

Both Thailand and Cambodia will monitor the residual effect of LLIN/LLIHN. In addition, Cambodia plans to evaluate the acceptability of different LLINs /LLIHNs and conduct an entomological study on forest vectors in areas of changing ecology.

OR on mobile and migrant populations:

As mentioned earlier, both countries will conduct a rapid situational analysis to gather additional information on the mobile/migrant population.

After the presentation, it was discussed that the OR needed to be prioritized for the short-term plan to ensure it addressed the most critical questions immediately. Professor White said that, considering the global implications, research priorities should focus on stopping the spread of the resistant parasites. Dr Kanyok asked if the focus should be on a larger Mekong elimination strategy because of the possible spread of resistance. Professor White said that the geopolitical realities make a Mekong elimination strategy unlikely. If the parasites have already reached Myanmar then there is nothing than stop them from getting to India and then beyond there. It was decided that OR priorities needed to be discussed at a later time and that a steering committee needed to be established at the national level to agree on and prioritize IR/OR in Cambodia.

3.9 Capacity in Relation to Large Scale Operation, Implementation Structure

Dr Socheat presented on the current human capacity, expected GF-supported staff, and projected gap at different levels in order to manage and implement the containment plan.

At all levels of the health system, there are human resource constraints in terms of numbers and capacity.

Community-level constraints: VMWs are integral to improving access to EDAT in remote areas. There are currently 400 VMWs in 200 villages in Cambodia.

Current Bottlenecks	Proposed Solutions
VMWs are mostly concentrated in the eastern part of the country.	Expand VMW network in Zone 1 and 2.
Community-based volunteers, including VMWS, are only paid US\$ 2 incentive each month.	Increase monthly incentive of VMWs in Zone 1 and 2 who will take on additional responsibilities.
The CNM is responsible for supply management to VMWs.	Establish de-centralized system to ensure sufficient supply of RDTs, drugs, and support to the VMW/MMWs that will make expansion possible.
Mobile population is not currently targeted.	Select Mobile Malaria Workers (MMWs) to target mobile population.
Long-term sustainability of community-based volunteers.	Expand role of VMW/MMW to include treatment of ARIs and diarrhoeal disease.

Public Health System:

Current Bottlenecks	Proposed Solutions
Not enough staff at all levels.	Recruit new support staff to meet new needs.
Inadequate salary of existing staff.	Provide performance-based salary support to existing staff.
Insufficient capacity (e.g., management skills).	Conduct trainings and more supportive supervision.
Supply chain problems.	Strengthen supply management system.

Intersectoral: Good collaboration between Department of Drug and Food (DDF) and CNM.

Current Bottlenecks	Proposed Solutions
Limited interaction with other health programmes, and need support to address the private sector, mass screening, and the mobile population.	Establish country-level intersectoral task force. Hold intersectoral meetings at central and provincial levels.
Cross-border issues.	Hold cross-border meetings at national and provincial levels.

The GF Round 6 will support additional staff at all levels until 2012.

Dr Socheat then presented the number of additional people needed at all levels in order to successfully implement the containment project.

Following the presentation, Dr Kanyok asked about what would happen to the people recruited for the short-term project after it finished. Dr Socheat said that the CNM had already spoken with the Ministry of Health about how to absorb new hires into the health system. A few people expressed concern about the strain on the system, especially the supply chain, with the planned increase in number of VMWs. Dr Chea Ngoun, the head of the VMW unit, explained that the CNM was already collaborating with the Central Medical Store (CMS) and URC (an NGO partner which supports four provinces along the border, including VMW villages). URC has already piloted a different distribution system for the VMWs, which can inform the containment project.

Dr Wichai asked for greater clarification about the role of the private sector in Zone 1 and Zone 2 in Cambodia. In Zone 1, Dr Sim explained that the private sector will not be allowed to sell any antimalarial drugs. The DDF will help to supervise and train the private sector in this area. Outside of Zone 1 there will be a general ban on AMT, but PSI will continue to social market Malarine⁷ in the private sector through funds from GF Round 6. Dr Wichai asked if that will mean that private providers will lose all of the AMTs and ACTs in Zone 1 that they have in their shops without compensation. Dr Soheat said that they could not compensate each private provider, and Dr Chea Ngoun said that many of the private providers in Zone 1 are not even registered. Ms Petty suggested that they find a way of incentivizing the providers to give up their ACTs in Zone 1, especially if they were selling the nationally-approved Malarine⁷.

3.10 Capacity in Thailand

Dr Wichai presented on the capacity in Thailand to implement the containment project.

In Thailand, every village has one VHV for every ten households that are not paid but receive other non-monetary incentives. If a VHV works for a long time, they receive official recognition from the King. Also their children are offered the opportunity to go to a two-year public health college. A few of the best volunteers are selected to be village malaria workers (VMW), which can provide diagnosis and medication according to the national protocol. These workers are paid US\$ 60 on a monthly basis. In Zone 1, they currently have 59 villages with VMWs funded by GF. From experience, however, it was decided that they needed two workers per A1 “high-transmission” village. An additional 59 workers will be needed to cover Zone 1.

Provincial and district level staff need to be better trained on how to contain malaria (trying to move away from vertical system).

At the health centre level, the current staff is already over-burdened with responsibilities to take care of both physical and mental health of patients, which means that they will not have any time to take on the additional responsibilities related to the containment of malaria. There will need to be extra personnel at the HC level to help coordinate VMW.

The existing system for Active Case Detection (ACD), which includes providing health education and re-dipping nets, needs to be strengthened.

3.11 External Support

Dr Delacollette presented on the potential architecture of the containment project. He emphasized that this structure is not definitive, but still under discussion.

In order to address some of the challenges related to implementing the containment project, Dr Delacollette suggested establishing several levels of support.

On the international level, he proposed establishing an international containment task force, possibly chaired by the WHO, which would be in coordination with regional offices (Western Pacific Regional Office/South-East Asia Regional Office). The task force would be vice chaired by the NMCP managers for Cambodia and Thailand. Key funding and implementing partners would be included as well.

At the national level, Dr Delacollette said that it is vital to establish national task forces for both Thailand and Cambodia with high-ranking officials to back the project. Again, funding and

implementing partners at the national level should be included. Especially in Cambodia there are a number of government and non-governmental partners who should contribute at this level.

There is already a WHO Malaria Mekong Program (MMP), funded by USAID, with an office in Bangkok. The MMP currently helps to coordinate some activities between the two national programmes. It was suggested that the MMP could play a coordination role and provide technical assistance to the national programmes and other implementing partners.

As a part of the Bangkok meeting it was also suggested to have other technical committees because there are still many pending technical issues. Potential technical committees include:

- Case management
- Private-public mix
- Vector control and personal protection
- Mobile population/migrants
- Health sector strengthening
- M&E
- Information/passive and active surveillance
- Cross-border information for actions
- Operational/Implementation research
- Resource mobilization, publication, advocacy

Dr Delacollette said that technical assistance is also needed. Initial estimates of the TA needs are listed below. The estimated costs are more than US \$3 million (around 600 000 to 700 000 is currently available) for the first 18 months of the containment project (see table below).

Technical assistance	Cambodia		Thailand		Bi-lateral	
	Available	Needed	Available	Needed	Available	Needed
Mekong Malaria Coordinator P5					X (USAID)	
Containment coordinator P4						X
Cambodia Containment coordinator P5	X (Japan)					
Cambodia medical officer P4	X (USAID)					

Thailand containment epidemiologist P4				X		
Cambodia Logistician P3		X				
Epidemiologist / statistician P.4		X				
Community mobilizer / Social scientist P.4		XX				
Mapping specialist P4		X				
Data manager P4		X				
Research coordinator P4		XX				
Provincial/district TA P4 (36 months)		X				
STC (mapping -6 months- ,anthropologist - 3 months- , health economist -2 months- , situation analysis appraisal - 4 months-, statistician - 6 months- , migrants - 6 months-, modelling 6 months ...)		XX				
National Programme Officer		X		X		

Dr Kanyok interjected to ask about how they planned to hire the large number of personnel so quickly, and what would happen to these people after the end of the 18 months.

Dr Delacollette said that it would be crucial to receive high-level WHO Headquarters support in order to get this project running as soon as possible.

It was then proposed that the Malaria Consortium (MC) play the role of funds manager for the containment project.

After the completion of the presentation, Dr Wichai expressed his concerns that Thailand might be managed by a non-governmental organization that is not the WHO. Dr Delacollette tried to emphasize that the MC would not be managing the VBDC, only the movement of the

grant monies from the donor to the countries. Dr Kanyok said that as a potential funder he takes Dr Wichai's comments extremely seriously. He strongly suggested greater discussion on this issue.

3.12 Grant Management and Implementation: Possible Role of Malaria Consortium

Dr Kolaczinski presented on the potential role of the MC as the grant manager of the containment project. He spoke about the MC's capacity to manage a grant of this size, emphasizing their previous experience managing large grants, history of working closely with governments, and high-level staff members who can provide technical assistance.

He said that it has been established in the two days that something needs to happen very quickly in both Cambodia and Thailand. This will require rapid procurement of essential commodities, channelling of funds for different partners, TAs to partners, extensive M&E to document impact, and ensuring accountability to the funders. He believes that the MC could collaborate with the Ministry of Health programmes, WHO, and other partners to ensure that this happened by:

- Disbursing funds to partners
- Procuring and delivery commodities
- Managing subcontracts
- Reporting on funds and performance of the partners to the donors
- Ensuring that activities planned are undertaken on time
- Providing technical input
- Supporting a transition to the next phase of the containment project.

In order to provide this type of support, the MC proposed to recruit a small team to work from both Bangkok and Phnom Penh offices.

After the presentation, Dr Kanyok asked about whether or not the WHO was interested in playing this type of grant management role instead of MC because it sounded like this would be a red-line issue for the national programmes.

Dr Nesbit said that WHO would not normally be keen to take on very large grant management exercises like this, but the circumstances are exceptional. Thus, if unsatisfactory alternatives were not available, and if the countries were keen on the idea, then the WHO would be prepared to take on this role.

Dr Kolaczinski clarified that the MC did not have any intention of dictating. He said that if the consensus was that the MC should not take on this role, then they would not take it forward. However, he emphasized that he thought that action needed to occur immediately and money needed to flow quickly. This should be a huge consideration in terms of selecting an organization that can disburse funds to the partners very quickly. He pointed out that WHO could be quite slow and bureaucratic in its disbursement procedures.

Dr Nesbit asked if the BMGF only gives through non-governmental organizations or if it was possible for the countries to act as the PRs. Dr Kanyok said that he would have to check on

this issue. He said that the BMGF would prefer to have one PR for this project, but that they were open in terms of what organization was chosen for this role. He would need to talk internally about whether a government organization could be funded directly.

It was decided that the issue of grant management could not be decided at the meeting. High-level internal discussions are needed.

3.13 Funding, Available Funding, Funding Gaps, Resource Mobilization, Partner Commitment

Dr Delacollette presented on the available funding and funding gaps for the containment project.

At the last USAID meeting in Bangkok in April, there was a request to present to the programme headquarters in Washington what is considered an emergency plan of action for 2008. The total request from Cambodia and Thailand was US\$ 6 million. Since there has not been a response on this emergency funding plan, the short-term 18 month budget for 2009 to mid-2010 includes some goods that are also budgeted in the 2008 emergency plan of action, and that will be covered by USAID funding if that proposal is successful. The time period for the short-term plan was chosen to take into consideration the earliest possible date that the two countries could apply for additional funding from the GF.

The donors were then asked to comment on their organization's ability to provide funding for the containment project.

Dr Kanyok from the BMGF said that while there is no guarantee that the Foundation will fund the containment project because in the past they have funded projects related to innovative technology, he will be very excited to receive a Letter of Intent for the project presented at the meeting, by whichever organization is chosen to manage the grant.

Dr Chansuda from USAID said that there is interest in funding, but there would have to be coordination among other donors at the higher level to ensure that there is no duplicate funding.

Dr Aitken, who was representing DFID, said that there isn't an opportunity to open up a new funding channel at this time for the DFID bilateral programme. Under the current HSSP, there is about US\$ 1.2 million from the World Bank which is programmed for malaria. If the NMCP requested reallocation, that would be considered, but probably not in time to cover emergency plans in 2008.

Mr Peter from AusAID said that the majority of funds are also going through the HSSPII process, but it is possible that there may some additional money for project support. If there was an appropriate mechanism to deliver services, AusAID would consider contributing funds in 2009.

Mr. Katz from the Clinton Foundation said that its current support for the malaria programme was through Technical Assistance, including a full-time person located at the NMCP. The Foundation is also planning to provide help with improving the procurement and supply management system. He said that they are a bit flexible, but do not have the funding ability that is required in this situation.

3.14 Closing Remarks: Summary of Consultation

Dr Kamini Mendis provided an overview of the consultation and recommendations for future action.

Conclusions

1. Proven artemisinin tolerant *P. falciparum* at the Thai-Cambodia border represents a threat of the utmost gravity to the future of malaria control nationally, regionally, and globally; it needs to be dealt with as a matter of great urgency.
2. Both countries have sound and evidence-based strategies and costed national plans which are ready to be rolled-out. The capacity to implement these plans exists or can be rapidly developed within the two countries with adequate financial and technical support. Willing partners exist for executing these plans.
3. Initiatives have been founded on sound evidence from well-planned research, and research is an integral component of the containment effort. Funding is a matter of great urgency. We have two plans; a start-up plan for 2008 (around US\$ 6 million), and a short-term plan for 2009 to mid-2010 (around US\$ 38 million). Thereafter funding will be sought from the GF. Potential donor interest has been expressed and must be followed-up with applications.

Recommendations

1. Applications for funding the immediate and short-term plans need to be prepared immediately.
2. Issues need to be resolved around grant management.
3. Intercountry and cross-border coordination frameworks and mechanisms exist. Coordination of technical containment activities between the two countries and partners at regional and global level needs to be established.
4. Other issues include linking national containment efforts with existing national malaria control efforts and related programmes, and plans for taking pre-emptive action at the Thai-Myanmar border also need to be considered.

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PROGRAMME OF ACTIVITIES

Tuesday, 17 June 2008

- 08:00 Registration
- 08:30 Opening remarks – *Dr Duong Socheat, Dr Richard Nesbit*
- 09:00 Self introductions (informal or formal with Powerpoint presentation):
areas of interest, policies, current engagements, perspective in this context
–
All partners present:
- ADB
 - Australia
 - Clinton Foundation
 - Cambodia CNM
 - DFID
 - Bill and Melinda Gates Foundation
 - Japan
 - Mahidol-Oxford University Research Collaboration
 - Malaria Consortium
 - RBM Partnership
 - Thailand VBDC
 - WHO
 - USAID
- 09:45 Group photograph and coffee/tea break
- Session 1: Situation analysis, strategy, action plans, knowledge gaps**
Chairs: Dr Duong Socheat, Dr Charles Delacollette
- 10:15 Situation of artemisinin tolerance, practical implications of current situation
for global malaria elimination, and update on ARC3 project - *Dr Pascal
Ringwald*
- 10:35 *Clarifications and discussion*
- 10:45 Overview of strategy to contain/eliminate artemisinin tolerant malaria on
the Cambodia-Thailand border and in Greater Mekong Subregion,
short/medium/long term - *Dr Eva Maria Christophel*
- 11:00 *Clarifications and discussion*
- 11:10 CAMBODIA:
Containment project operational plan (emergency 2008, short term)

January 2009 - June 2010, and long term), including summary budgets by objective and operational research needs -

Dr Duong Socheat

- 11:30 Description of main activities for each objective - ***Dr Kheng Sim***
- 11:45 *Clarifications and discussion*
- 12:15 Lunch
- 13:30 THAILAND:
Containment project operational plan (emergency 2008, short term January 2009 - June 2010, and long term), including summary budgets by objective and operational research needs -
Dr Wichai Satimai
- 13:50 Description of main activities for each objective - ***Dr Saowanit Vijaykadga***
- 14:05 *Clarifications and discussion*
- 14:35 Measuring achievements - ***Dr Charles Delacollette***
Clarifications and discussion
- 15:00 Coffee/tea break
- 15:30 KNOWLEDGE GAPS:
Summary of operational research needs in Cambodia and Thailand and at regional level, and gap between ARC3 basic research and operations research -
Dr Shunmay Yeung, Prof. Nicholas White
Clarifications and discussion
- 16:15 ***Discussion:***
Reaching a consensus on the most urgent elements of the containment plan in the short term (2008 and Jan. 2009 – June 2010) and on a prioritized research agenda
- 18:00 Reception at the Hotel Himawari

Wednesday, 18 June 2008

Session 2: From planning to action – how to make it work, issues to be addressed (containment operations and research)

Chairs: Dr Wichai Satimai, Dr Kamini Mendis

- 08:30 Capacity at all levels to implement such large scale operation, implementation structure, and what's needed:
CAMBODIA - ***Dr Duong Socheat***
Clarifications and discussion
- 09:00 THAILAND - ***Dr Wichai Satimai***
Clarifications and discussion
- 10:00 Coffee/tea break
- 10:30 Technical assistance and Coordination framework - ***Dr Charles Delacollette, Dr Kamini Mendis***
Clarifications and discussion
- 11:00 Grant management, possible role of Malaria Consortium - ***Dr Jan Kolaczinski***
Clarifications and discussion
- 11:20 Research implementation, coordination, partners, ownership
– ***plenary discussion***
- 12:00 Lunch

Session 3: Funding: available funding, funding gaps, resource mobilization, partner commitment

Chair: Dr Richard Nesbit

- 13:30 Available funding and funding gaps: emergency 2008, short term January 2009 - June 2010 and long term - ***Dr Charles Delacollette***
Clarifications
- 14:00 ***Discussion among all partners:***
Possible roles of different partners in their area of interest, how to ensure component ownership and credit, coordination, donor requirements, resource mobilization plan (short- and long term), consensus
- Recommendations

CLOSING - *Dr Duong Socheat, Dr Wichai Satimai, Dr Richard Nesbit*