Report of the Greater Mekong Sub-Region

Malaria Operational Research Symposium

Apsara Angkor Hotel

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Acronyms, Abbreviations, and Technical Terms

3DF	Three Diseases Fund
ACT	Artemisinin-Based Combination Therapy
ARI	Acute Respiratory Infections
BCC	Behavior Change Communication
BVBD	Bureau of Vector-borne Diseases
CHV	Community Health Volunteer
CNM	National Center for Parasitology, Entomology, and Malaria Control
COMBI	Communication for Behavior Impact
D3+	Day Three Positive
EMG	Ethnic Minority Groups
EDAT	Early Diagnosis and Treatment
EWS	Early Warning System
FSAT	Focal Screening and Treatment
G6PD	*Glucose-6-Phosphate Dehydrogenase*
GFATM	Global Fund to Fight AIDS, Tuberculosis, and Malaria
GIS	Geographic Information System
GMS	Greater Mekong Sub-region
HCP	Health-Care Provider
HMIS	Health Management Information Systems
IEC	Information, Education, and Communication
INGO	International Non-Governmental Organization
IRS	Insecticide Residual Spraying
ITN	Insecticide-Treated Nets

IVM	Integrated Vector Management
LLIHN	Long-Lasting Insecticidal Hammock Nets
LLIN	Long-Lasting Insecticidal Net
KAP	Knowledge, Attitude, and Practice
MC	Malaria Consortium
M&E	Monitoring and Evaluation
MDA	Mass Drug Administration
MDG6	Millennium Development Goal 6
MIS	Malaria Indicator Survey
MSAT	Mass Screening and Treatment
NGO	Non-Governmental Organization
NIMPE	National Institute for Malariology, Parasitology, and Entomology
NMCP	National Malaria Control Program
NSP	National Strategic Plan
OR	Operational Research
pGAPDH	*Pf* Glyceraldehyde-3-Phosphate Dehydrogenase
PCD	Passive Case Detection
PCR	Polymerase Chain Reaction
PCT	Parasite Clearance Time
Pf	*Plasmodium falciparum*
PfMDR1	*Plasmodium falciparum* Multi-Drug Resistance Gene
Pv	*Plasmodiumvivax*
PQ	Primaquine
QA	Quality Assurance
QC	Quality Control

RCT	Randomized Control Trial
RDMA	Regional Development Mission – Asia
RDT	Rapid Diagnostic Test
SMS	Short Message Service
USAID	United States Agency for International Development
VBDU	Vector-Borne Disease Unit
VHV	Village Health Volunteer
VHW	Village Health Worker
WHO	World Health Organization

Executive Summary

Operational research (OR) encompasses a wide range of problem-solving techniques and methods to improve decision-making and efficiency in delivering malaria care and control. While it is an important component of most national malaria-control strategies, it is too often compromised by other competing priorities. Moreover, research agendas can be fragmented and/or donor-driven. This regional symposium was intended to facilitate the development of an operational research framework for malaria control and elimination in the Greater Mekong Subregion (GMS), by identifying common regional malaria research priorities, facilitating linkages across the region, and promoting greater coordination and sharing of findings.

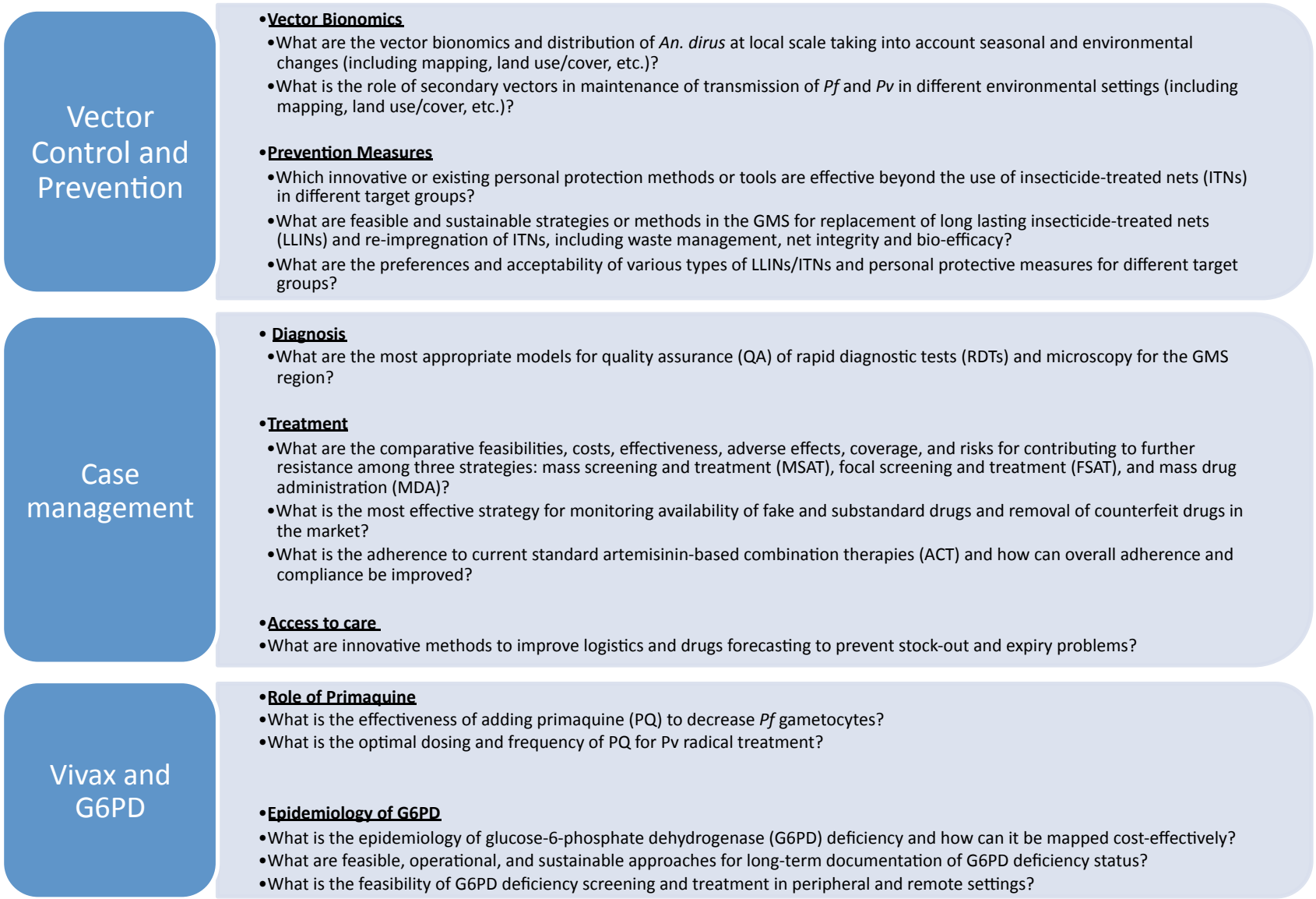
Enormous strides have been achieved in the reduction of malaria morbidity and mortality across the region, with some countries pursuing malaria elimination. However, in other areas malaria persists and those most at risk are the hardest to reach. They are characterized by those living in remote locations, poverty, ethnic minorities, and/or migrant or mobile status. The latter in particular are both difficult to reach and may have the greatest risk of spread of resistant parasites or re-introduction of malaria parasites to new locations. Drug resistance and the changing vector ecology of Anopheline mosquitoes triggered by development projects and climate change add further complexity to malaria control and elimination.

A Malaria Operational Research Framework for the Greater Mekong Sub-region was developed based on preliminary consultations with national malaria control programs to identify priority operational research areas, unmet needs and knowledge gaps. The most critical operational research questions to address in the GMS were formulated during this Regional Malaria OR symposium with inputs from National Malaria Control Programs (NMCPs), WHO, USAID, CDC, and other key stakeholders in the region. A series of lectures on technical subjects, including vector control, migrant/mobile populations, surveillance, case management, *Plasmodium vivax*/G6PD, and *Plasmodium falciparum* elimination were also part of the discussion. This document, which immediately follows the executive summary, represents the results of discussions and brainstorming sessions of national malaria programs and researchers of what they believed to be imperative needs for operational research to support the control and elimination of malaria in GMS. This broad framework encompasses vector control and prevention, case management, *Plasmodium vivax* and G6PD, vulnerable populations, monitoring and evaluation, surveillance, health systems, and the private sector.

Key recommendations to further promote collaboration and address knowledge gaps include the need to improve linkages with and capacity of universities, encourage annual research workshops in every GMS country, ensure that findings are translated into practice, and update and share existing databases and information clearinghouses. Symposium participants also emphasized the importance of career development for young researchers, strengthening GMS ethical review committees, and increased funding for operational research. There was considerable discussion about funding issues, including that research budgets are often vulnerable to budget cuts, how to fund regional studies, and the fact that

donor research priorities are not consistent with those of NMCPs. Great enthusiasm was expressed for **more collaboration** and **coordination** on OR for the GMS region.

Figure 1. Framework for Malaria Operational Research in the Greater Mekong Sub-region



Vulnerable Populations

- **Defining vulnerable populations**
  - Who are mobile and migrant populations and among them who are most at risk for malaria?
  - What are the social, spatial, and economic characteristics of mobile and migrant networks relevant for malaria control and elimination?
  - What are the care and treatment-seeking behaviors of mobile and migrant populations and how are they accessing malaria prevention and treatment resources?

- **Innovative interventions**
  - Which innovative malaria prevention and treatment measures are most accessible to mobile and migrant populations?
  - What is the feasibility and effectiveness of MDA in the context of adequate coverage of mobile and migrant populations?
  - What is the effectiveness and impact of behavior change communication (BCC) strategies targeting mobile and migrant populations?

Monitoring & Evaluation and Surveillance

- **Monitoring and Evaluation**
  - How can overall data quality and data collection be improved (e.g., linking drug quality and adherence to treatment outcomes)?

- **Surveillance**
  - What are operationally feasible approaches for implementation of Day 3 Positive (D3+) surveillance and response in the context of strengthening overall surveillance systems in the GMS?
  - How can innovative tools and technologies (e.g. SMS, mobile phones, internet, field application of PCR, pooled-PCR techniques) be piloted and scaled up to improve community-based surveillance and timely malaria reporting from remote areas?
  - What is the best approach for designing and implementing an early warning system (EWS) for epidemic forecasting, detection, and response as countries move towards lower malaria transmission and elimination?

Health Systems and Private Sector

- **Health Systems**
  - How can information and data from various operational research be best consolidated (e.g., comprehensive GIS-based database with multi-layers at each country and regional level) and used to inform policy and program implementation?
  - What is the cost-effectiveness and sustainability of using community networks and organizations as part of integrated disease programs within country specific contexts?
  - What is the feasibility and cost-effectiveness of integrating malaria into national disease surveillance and response systems?

- **Private Sector**
  - What are the barriers and incentives for sustainable engagement of the private sector in malaria control and elimination strategies?
  - What innovative strategies can be piloted and scaled up to engage the private sector (heath and non-healthcare related sectors) in malaria diagnosis and treatment, vector control, and information education and communication (IEC)?

Introduction and Overview

Opening Remarks by His Excellency Dr. Duong SOCHEAT (Director, Cambodian National Center for Parasitology, Entomology, and Malaria Control)

Symposium Objectives and Overview by Dr. David SINTASATH (Asia Technical Director, Malaria Consortium)

Operational research (OR) encompasses a wide range of problem-solving techniques and methods to improve decision-making and efficiency in delivering malaria care and control. While it is an important component of most national malaria-control strategies, it is too often compromised by other competing priorities. Moreover, research agendas can be fragmented and/or donor-driven. This regional symposium was intended to facilitate the development of an operational research framework for malaria control and elimination in the Greater Mekong Sub-region (GMS), by identifying common regional malaria research priorities, facilitating linkages across the region, and promoting greater coordination and sharing of findings.

The key objectives of the meeting were:

- To share/exchange information about malaria operational research activities recently conducted or planned by national programs
- To identify country priorities, needs, and gaps in conducting operational research towards strengthening malaria control and elimination
- To formulate a malaria operational research agenda for GMS with inputs from national programs, partners, research institutions, and other key stakeholders

The methodology used to develop the Malaria Operational Research Framework was initiated from the administration of a questionnaire to GMS National Malaria Control Programs (NMCPs), and then further developed during the symposium through discussion and structured small-group activities to identify the key knowledge gaps in operational research, to outline priority OR areas, to formulate answerable research questions, and to rank them via use of a scoring system designed to build consensus and identify priorities.

Dr Socheat pointed out in his opening remarks about the need to look at the impact of climate change on malaria vectors. There is a great deal of concern about climate change, but there currently lacks a solid body of evidence with which to address this issue with policymakers. Other critical gaps include social/human behaviors especially of mobile and other vulnerable populations, as well as the need for increased budgets and greater technical capacity to build the evidence base required to strengthen malaria control and elimination in the GMS.

Country Situation Analyses, Operational Research Plans, and Discussion

A representative from each of the NMCPs presented their current national malaria goals and strategies, followed by outlining current and planned OR endeavors, as well as unmet needs and knowledge gaps. While several countries are approaching malaria elimination, foci of malaria – including drug-resistant strains and higher burden in hard-to-reach populations – persist and have the potential to undermine advances. These unmet OR needs and knowledge gaps are barriers to achieving the targets of the following national malaria strategies. More details from these presentations can be found in Appendix 3.

Cambodia.Cambodia's strategy for the current period through 2015 is to consolidate and scale up interventions in order to achieve universal coverage and contain artemisinin resistance, while moving towards pre-elimination. The national program hopes to sustain control and achieve pre-elimination by 2020, and in the long-term, focus on phased elimination of malaria in the country (2021-2030). The NMCP's objectives include:

- Improving access to early diagnosis and treatment with emphasis on detection of all malaria cases,
- Decrease drug pressure for selection of artemesinin-resistant malaria parasites by improving access to appropriate treatment and preventing use of monotherapies and substandard drugs in both public and private sectors;
- Improve access to preventive measures and specifically prevent transmission of artemisinin-resistant malaria parasites among target populations;
- Increase community awareness and behavior change among the population at risk and support the containment of artemisinin-resistant parasites through comprehensive behavior change communication (BCC), community mobilization, and advocacy; and
- Provide effective management and coordination to enable rapid and high-quality implementation of the strategy.

In recent years, the Cambodia malaria program has conducted a large number of studies, focused on anti malarial drug efficacy, vector control, artemisinin and insecticide resistance and containment, G6PD deficiency screening, behavior change communication and anthropological studies. However, significant gaps in information to base implementation of activities still remain. Knowledge gaps include access and reaching migrant and mobile populations, development of effective referral systems, integrated vector management, and studies on the environmental change impact on vectors, amongst others. CNM reports that there is a lack of recruitment and long-term capacity development of young scientists, and that there should be efforts to sustain such capacity in country.

*Discussion.*Strengthening the country programs is contingent on improving the capacities of the individuals and institutions involved. Young scientists need not just training, but an attractive career path and professional support. While there are efforts underway to strengthen links with Cambodian universities, a comprehensive effort is needed especially given the shortcomings of the Cambodian education system. Meanwhile, dozens of studies are underway, but there is no central clearinghouse even within one country to collaborate and share information. There have been efforts to create this,

but they have not been regularly updated or utilized, much less linked to those in other countries. There was broad agreement that improved access to bibliographies, reference materials, and raw data (especially GIS) would be very beneficial, especially if it could serve the entire region. Collaboration needs to be improved, and researchers from outside the region should ensure that they coordinate, share, and disseminate their findings within Cambodia and GMS. One strategy might be to strengthen research ethics committees, and require that all proposals need to be vetted *and* findings shared.

Innovative strategies of interest include the use of short message service (SMS) mobile telephone reporting by VHWs, engaging the private sector for rational drug use, and appropriate treatment of non-malarial fevers at the village level. There is also a strong demand for better village-level data and research about the effectiveness of intervention strategies, especially behavioral ones, because it is not known whether or how research findings are actually being applied in the field.

China.The country's NMCP has set as its priority to stop indigenous transmission nationally, except for the border areas in Yunnan province by the end of 2015. Its ultimate goal is to achieve no local transmission of malaria in the whole country by 2020. This goal would be achieved through the following objectives:

- Ensure access to early, accurate diagnosis, and prompt, effective, safe treatment through public and private sectors;
- Ensure full coverage of the population at risk with appropriate vector control measures;
- Strengthen malaria health education, promotion, and community mobilization efforts and change behavior to maximize utilization of malaria control and elimination services;
- Ensure comprehensive coverage of vulnerable, poor, and marginalized populations at high risk of malaria with appropriate interventions;
- Strengthen the malaria surveillance system by improving case reporting, passive and active case detection, entomological and anti-malarials resistance monitoring, and ensuring adequate outbreak response capability; and
- Provide effective program management, based on firm leadership commitment, to enable high quality implementation of strategies from malaria control to elimination.

China's recent OR studies have focused on control strategies for outbreaks in Yellow and Huaihe river areas as well as Tibet, and surveillance of drug resistance in the Yunnan province (border areas). Current and planned OR includes studies on radical treatment for *Plasmodium vivax*(Pv), developing new tools for rapid diagnosis of malaria, molecular markers for artemisinin resistance, and G6PD detection.

The NMCP has identified knowledge gaps in the epidemiology and treatment of *Pv*; improved diagnostic tools for low density parasites, early warning systems, vector studies, economic evaluations for control strategies as well as indicators for elimination of malaria. There is a need for OR financing and human resources, as well as technical assistance in vector control, *in vitro* culture of *Pv*and surveillance.

*Discussion.*As China moves towards elimination, it is imperative to address malaria in bordering countries, as well as target the private sector. Malaria may well be under-reported because private doctors do not necessarily report cases. In terms of village-level treatment, there is an excellent VHW system, but the management needs to be improved and better coordinated. Meanwhile, attractive

career paths for young scientists are essential; the training is there, but many promising candidates choose other pursuits.

Lao PDR. By the year 2015, the NMCP will intensify malaria control efforts, targeting remaining endemic communities and key risk groups, to progressively roll out malaria elimination in selected provinces. The strategies outlined to achieve this goal include:

- Strengthen program management;
- Maximize access to effective vector control and personal protection measures;
- Improve access to early, effective diagnosis for malaria;
- Support routine malaria case management;
- Strengthen routine Malaria Information System;
- Maintain malaria epidemic preparedness and response capabilities;
- Progressively roll out malaria elimination in selected provinces; and
- Maximize utilization of malaria services through BCC and strengthening community mobilization efforts.

Along with surveys for malaria prevalence, malaria indicator survey, bednet survey, passive case detection survey, and ethnic minority group survey, the NMCP has also conducted studies to evaluate village health volunteer performance with diagnosis (RDT) and treatment (ACT), as well as evaluations of IEC tools and a study of LLIN acceptance. Further research is needed on integration of surveillance, response and community volunteers' work with other diseases in the health system, as well as mapping of G6PD deficiency and clinical trials for a safe regimen of primaquine, supply chain management system improvements and communication, impact of development projects (infrastructure) on malaria, and feasibility studies for suitable prevention methods to vulnerable populations such as forest goers.

*Discussion.*One critical advocacy area to strengthen the National Institute of Malariology, Parasitology and Entomology (NMPE) of Lao PDR is regular workshops with all partners, and development of a simple surveillance protocol that can be regularly replicated in-country. Currently, Lao PDR is dependent on intermittent national surveys, but lacks funds for routine monitoring. Such monitoring is especially important because development projects (roads, mines, dams, rubber plantations, etc.) and deforestation are radically altering the landscape and are associated with local population displacement and an influx of migrant workers. All this is altering the vectors, but without routine surveillance it is impossible to adapt control efforts.

Myanmar.The NMCP's goal by 2010 is to reduce malaria morbidity and mortality by 50% of the year 2000 level, with the ultimate goal to achieve the Millenium Development Goal (MDG) 6 by 2015. The following strategy areas have been identified as key to achieve these goals:

- Information, Education, Communication (IEC) at the grassroots level;
- Prevention through personal protection and environmental measures;
- Prevention, early detection, and control of epidemics;
- Early diagnosis and appropriate treatment;
- Intersectoral collaboration;
- Community involvement;

- Capability strengthening of health staff; and
- Operational research

Recent OR studies in Myanmar have focused on monitoring the efficacy and quality of drugs as well as the stability of combination tests and effectiveness of coolboxes in different geographical areas. Planned and current OR includes these topics, while adding G6PD deficiency studies at the community level and efficacy of LLINs over time. However, information is still needed on the stability of ACTs, mapping of artemisinin resistance and G6PD deficiency, effectiveness and rationale of primaquine and other gametocytocidal drugs, evaluation of side effects of ACTs and patient compliance to regimens, evaluation of BCC inputs impact, and research on health care providers' adherence to national drug policies. Myanmar will require funding, capable human resources especially at the community level and technical assistance in order to conduct the necessary OR to bridge information gaps.

Discussion. A question was raised on Myanmar's treatment regimens, particularly the existence of *three*recommended treatments in the national guidelines. Concern was expressed that this could lead to coordination and resistance problems. However, given that there have been very few efficacy studies, various international non-governmental organizations (INGOs) have their own guidelines, and that field-level application and compliance are serious problems. The NMCP maintains one primary treatment protocol, and two secondary ones.

Thailand. The Thai NMCP's goal is to achieve 80% of the country free of malaria transmission by 2020, through:

- Minimizing active malaria transmission areas and limit transmission only to restricted areas
- Ensuring that malaria patients have access to diagnosis and treatment according to national standards
- Reducing multi-drug resistant malaria and preventing its transmission
- Ensuring that high-risk populations including those in border areas receive appropriate healthcare
- Supporting research and development for malaria control

Thailand has recently implemented a variety of operational research that includes studies on the susceptibility of *An. Maculatus* and *An. minimus* to synthetic pyrethroids, a costing evaluation of QA for microscopy, effectiveness of social marketing for personal protection products in agriculturists, residual effects of impregnated bednets against specific vectors, as well as the efficacy of a 3-day regimen of artesunate-mefloquine along the Thai Cambodian border, amongst others. However, knowledge gaps persist, especially in case management, surveillance, prevention and control measures, BCC of public and private providers, and consumers, and strengthening of health systems in general.

*Discussion.*As Thailand embarks on development of its elimination strategy, the critical risk groups are ethnic minorities and migrants from neighboring countries. Existing BCC and information/education IEC programs do not fit the health behaviors and beliefs of these groups. The critical research gap for Thailand would be to develop BCC/IEC for them specifically, not just translate materials that are effective with Thais.

Vietnam. The NMCP's objective is to continue to roll back malaria in the high endemic areas and the high risk groups, while developing and strengthening sustainable factors for malaria control. Specifically, Vietnam's NMCP aims to reduce morbidity to <1.5/1,000 people and reduce mortality to <.03/100,000 people, as well as not having any major malaria outbreaks.

Recent OR studies in the country have been undertaken to re-examine the malaria epidemiology, efficacy of malaria treatment regimens, G6PD deficiency among ethnic groups in Vietnam, Pv resistance to chloroquine, as well as research on vector control measures (insecticides' residual effects and resistance) IEC strategies for ethnic groups and mobile populations, malaria treatment efficacy of new drugs, and the influence of natural and artificial environment in malaria. More research is needed, though, especially in the areas of monitoring and case management in containment and elimination areas, use of primaquine and IEC strategies for seasonal migrants. The NMCP strongly feels that there is a need to train young staff on operational research design, methodology, proposal and results writing; as well as financial support and international technical assistance for research institutions and international organizations.

Discussion. Questions focused on BCC/IEC for ethnic minorities, particularly in central Vietnam. This is a gap in research and expertise. There is, on the other hand, an excellent PhD program and in-country expertise in parasitology. However, the academic department should be better linked into field research and monitoring.

Regional Operational Research Priority Areas

Draft Operational Research Plan of Action in Infectious Diseases of Poverty 2011-2015 by Dr. Jun NAKAGAWA and Dr. Bayo FATUNMBI (Technical Officers, World Health Organization)

While there has been significant progress toward meeting the targets of the Millennium Development Goal #6 (MDG6) in combating malaria and other diseases of poverty, critical gaps remain, which highlight the need for coordinated research and action. WHO has thus made operational research a priority, in particular research that targets programmatic gaps, addresses bottlenecks, and provides tools and strategies for implementation. The overall goal is "to reduce the burden of ill health due to communicable diseases and eliminate those diseases where feasible based on evidence from research, thus contributing to the achievement of MDGs," with a regional research objective "to harness science, technology, and broader knowledge in order to produce research-based evidence and tools to reduce the burden of, and eliminate where feasible infectious diseases of poverty in the Western Pacific Region." There are four objectives that specifically apply to malaria, concerning vector control, early diagnosis and treatment, comprehensive coverage of high-risk vulnerable populations, and acceleration of malaria-elimination efforts. To this end, WHO is supporting small-scale grants and training opportunities, and also promoting collaboration and proposal development on multi-sectoral interventions.

Presentation of Operational Research Questionnaire Results by Diana PICÓN, Malaria Consortium

Ms. Picón reported on the findings of a questionnaire developed by Malaria Consortium, which was distributed to the GMS National Malaria Control Programs prior to the conference. The objective of the questionnaire was to identify common gaps and needs and duplications; facilitate sharing of efforts and outcomes; and support development of an operational research framework for the region. Areas with identified knowledge gaps include health systems; prevention and control; case management; BCC; M&E and surveillance; vulnerable populations; and private health care providers. There were numerous specific topics under each of these areas.

Breakout Groups: Identification of OR Priority Areas and Knowledge Gaps

Symposium participants were divided into groups and asked to identify the OR priority areas and knowledge gaps that they felt were most pertinent for their country or organization. Priority areas were identified under each of the following headings: health system strengthening; vector control and prevention; diagnosis, treatment, and case management; BCC/IEC; drug resistance; surveillance; elimination; vulnerable populations (especially migrants and mobile populations); monitoring & evaluation; and G6PD deficiency. These priority areas were used to formulate the key OR questions in the subsequent session on identifying and prioritizing OR questions.

Vector Control and Prevention	Case Management	Elimination	Drug Resistance	Surveillance and M&E
• Vector Bionomics • Secondary vectors and molecular characterization • Acceptability of LLINs • Cost-effectiveness of LLINs • Management of LLINs • Insecticide resistance monitoring	• QA/QC of RDTs and microscopy • Non-malaria fevers • Management of severe malaria • Drug compliance/ adherence	• Indicators for elimination • Use of molecular diagnosis • Drug protocol and policy	• Genetic marker for artemisinin resistance, mapping, and surveillance • New drug development or combinations • New tools to monitor drug resistance	• Mapping of burden of disease • Asymptomatic parasite detection • Use of new tools for community-level surveillance • Surveillance in non-health sectors • Harmonization of indicators and reporting

P vivax	G6PD and PQ	Vulnerable Populations	BCC	Health Systems and Private Sector
• CQ efficacy • Alternative drugs for Pv • Distinguishing relapse vs re-infection • Programmatic shifting of focus to Pv	• Epidemiology of G6PD • Improved point of care diagnosis of G6PD • PQ clinical trials and adverse effects	• Characterizing vulnerable populations • Access to care and treatment • Integrated approach (eco-bio-social) • Innovative personal protection measures	• Measuring effectiveness of BCC approaches • New BCC tools	• Data and information systems flow • Capacity-building and sustainability • Integrated disease surveillance • Human resource gaps • Strategies for private sector engagement • Intersectoral collaboration

Plenary Discussion

Operational Research into the sensitivity and effectiveness of RDTs was a point of considerable discussion. Even if an RDT is recommended by WHO, we do not know whether it is reliable on-site. Sensitivity is especially critical in areas where transmission levels are low. Quality control of the RDTs must be implemented at every point of the supply chain as well. Cold chains, storage conditions, and expiration of RDTs must all be adhered to, but frequently are not. Every step from manufacturing of the RDT to its actual use needs to be monitored. An associated problem is that many people do not even get a parasitological diagnosis, health providers especially in the private sector skip straight to treatment. These cases are not often reported in the health management information systems (HMIS). Rapid and accurate diagnosis in the field is essential if malaria cases are to be treated and reported correctly. Fortunately, there has been solid research already about which kits work best in the region, so the main challenge is using and storing them correctly. Existing RDTs will identify almost all symptomatic malaria cases. The real diagnostic challenge is surveillance of asymptomatic cases where RDTs and standard microscopy may fail to detect very low parasitaemias. Research into strategies to improve public-private coordination across all aspects of malaria, not just diagnosis and treatment, would be most welcome.

The main points of concern regarding treatment were use of monotherapies and uncontrolled drug sales in the private sector. While there is global resolution to curtail the use of monotherapies,in some cases that may be the sole available treatment. Cambodia effectively banned the use of monotherapies by progressive steps, using both "carrots" and "sticks." It first banned the import of monotherapies, and then only later the sale of them. Meanwhile, the price of combination therapies was subsidized so that they would also be cheaper. There was also discussion about comparing the efficacy and effectiveness for various treatment, and identifying drug-resistant strains, especially primaquine.

There was broad consensus that more social/behavioral as well as biological science research is needed to identify high-risk groups and the risk factors associated with them. Monitoring and identifying cases in low-level transmission areas is a key challenge, as are migrant communities who may re-introduce malaria into an area. The feasibility of such research was discussed – community-based research is a gap, as is how to partner with the private sector especially in the preventative aspects of malaria control, such as bednets and insecticides. Another research gap described was to find a better way of prioritizing between innovative research and high-quality routine surveillance systems.

Current OR Advances in a Changing Malaria Epidemiology and Resistance Containment Environment

The Malaria Vectors by Dr. Marc COOSEMANS (Professor of Parasitology, Institute of Tropical Medicine - Antwerp)

Dr. Coosemans discussed the high biodiversity of anopheles mosquitoes, highlighting how effective vector control must intercept breeding sites, resting behavior, and contact with humans. Anopheles' biting rhythms and differential behaviors inside houses, villages, and forest plots were presented, as was

the need for improved personal protection measures among mobile populations and forest workers. In terms of entomology operational research, key areas are the changing ecology and behaviors of vectors; innovative strategies for personal protection; monitoring insecticide resistance; regional databases and mapping; mosquito-collecting methods; and assessing the severity of infection. In sum, widespread distribution of LLINs is necessary but insufficient for effective vector control, because 30-50% of biting occurs before sleeping time, and forest workers and mobile populations tend not to use bednets. Better understanding of vector behavior is needed, as are tools to promote bednet use among these high-risk populations.

There was broad agreement that the entomological perspective on malaria control is underrepresented, and funding gaps reflect this. While there is research funding for malaria entomology in Africa, there is almost none for Asia "despite the fact that Asian mosquito issues are far more interesting and complex." Within GMS, research into mosquito vectors in Myanmar is particularly lacking.

The efficacy of mosquito traps, screening in houses, and insecticide-treated houses was discussed. However, in Southeast Asia most transmission does not take place in homes, but in junkyards and forest plots so these measures are unlikely to have substantial impact. Mosquito traps capture *all* species, not just the ones that carry malaria, people do not like screened houses, and large-scale insecticide spraying campaigns are not feasible – how can you spray an entire forest? Some participants questioned whether these home- and village-based measures might be cumulatively effective, but the available evidence indicates otherwise.

Migrant Populations in the Greater Mekong Sub-Region by Dr. Sylvia MEEK, (Technical Director, Malaria Consortium International)

Dr. Meek explained how migrant/mobile populations are not only high-risk for contracting malaria, but in spreading artemisinin-resistant parasites within countries and across borders including to areas where the disease had previously been eliminated. There is a large information gap about migrant/mobile populations, especially undocumented persons affected by extreme poverty and violence. They are also disproportionately important for malaria-control strategies. Dr. Meek discussed the characteristics of migration in each of the GMS countries, their risk factors, the challenges of accessing them, and possible approaches to malaria control. Asymptomatic carriers are of particular concern, and a recent study in Myanmar indicates that there is a "massive reservoir of untreated individuals." She summarized recent, ongoing, and planned studies to define mobile populations and methods of accessing them, and outlined further research needs, including novel approaches to BCC/IEC.

There was lengthy discussion and debate following this presentation. Participants spoke about the very different migration patterns among different GMS populations. For example, migrants from Myanmar tend to become long-term residents whereas Khmers are highly mobile, typically for short periods of time. There is particular concern that in Cambodia and perhaps elsewhere, these workers may reintroduce malaria into previously malaria-free areas, and spread drug-resistant strains. Patterns of migration are also changing rapidly – Pailin still attracts large numbers of migrants, but now they are agricultural workers rather than gem miners. Some participants indicated that there are already a lot of

innovative BCC/IEC, personal protection, and vector-control strategies underway, for example giving plantation owners/large landowners bednets to loan to migrant farm workers, which can be annually re-impregnated and re-loaned. One unmet area for programming is partnering with the private sector to extend the reach in providing malaria services to mobile populations. Concern was also expressed about how to instill a sense of duty to engage with the public health system – access can be provided, but individuals should have a sense of responsibility to participate.

The second focus of debate was the impact of climate change and land-use patterns on both mobile populations and vectors. Deforestation has led to huge plantations across GMS, for example, and it is still largely unknown how different species of mosquitoes are affected. There was widespread concern that current surveillance systems need to be strengthened to capture these changes. It was also felt that pro-active control strategies would be best, but for that better information about large-scale development projects (e.g., dams, plantations) is needed *before* they are underway. However, this information is often highly sensitive and unavailable.

Surveillance: Operation Research Needs and Wants by Dr. Steven BJORGE (Scientist, World Health Organization)

Dr. Bjorge highlighted the importance of distinguishing between surveillance (i.e., case investigation and follow-up) and monitoring and evaluation (i.e., indicators to measure inputs, activities, outputs, outcomes, and impacts). While there can be some overlap, it is important to understand the distinction, and to do both well. He highlighted the data, information systems, and analysis needs of each. One point of interest is that decades ago, there were fully-developed and functioning surveillance systems using data collected with paper and pens, and that while modern computers and software are immensely helpful, many field workers in remote locations are unable to accurately use them. He highlighted new innovative, field-friendly approaches such as using mobile phone text messages and coordinating with non-traditional partners. The chief surveillance challenges in GMS today are mobile/migrant populations and surveillance in areas approaching malaria elimination. He also highlighted the most important and sensitive indicators that should be used.

Discussion again focused on mobile/migrant populations, including the difference between them and incorrect assumptions that *all*, rather than only some groups are actually high-risk. One participant pointed out that there is a great deal of data already, but it is under-utilized. There was some agreement that qualitative research is the major gap.

Case Management Research in GMS by Dr. Prudence HAMADE (Senior Technical Officer, Malaria Consortium International)

Dr. Hamade presented on the characteristics of malaria-affected areas of GMS and the critical diagnosis, treatment, and access to care research topics that would improve malaria case management, including management of severe malaria, eliminating the "last man standing," and non-malaria fevers.

Early diagnosis and treatment was a key point of discussion, because it is essential to reducing morbidity and further transmission, but many people do not seek treatment until the disease has advanced. This

is particularly the case for ethnic minorities in border areas, where malaria is concentrated. There was a call to make malaria diagnostic testing within 24 hours of fever onset an indicator for the region. Unfortunately, "even if we provide everything in the village, they still come too late even if it is free and available. [Ethnic minorities] wait until they are really sick." There were calls to make health services more culturally appropriate and sensitive to encourage earlier treatment. Better surveillance is critical, and there was some debate on the efficacy of microscopy in the field. It can be effective when there is good training and field supervision as in Thailand, but the experience in Africa has shown high inaccuracy and so is probably not the best approach for areas that are remote. The comparative success of VHWs in different countries was discussed – they have been sustained and effective in Cambodia, but systems in Vietnam and Lao PDR have collapsed when start-up funding was exhausted.

There is optimism that artemisone may be efficacious in treating malaria strains common in GMS, because it has double-peroxide bonding and so might be less subject to resistance. Clinical trials are underway.

How to Control (and Eliminate) Plasmodium Vivax Malaria? A Challenging Issue by Dr. Didier MENARD (Head of Molecular Epidemiology Unit, Institut Pasteur Cambodge)

Dr. Menard highlighted the biological characteristics of *P. vivax* and their implications for control and elimination, including that a higher proportion of sporozoite-positive mosquitoes bite before bedtimes (thus reducing the efficacy of bednets). There are also particular treatment challenges, including lack of molecular markers for resistance to particular drugs. Primaquine is the only drug currently available to prevent malaria relapse, but persons with G6PD deficiency may rapidly haemolyse when taking this medication. With more than 500 different mutations of G6PD deficiency identified, use of primaquine for radical cure will require very complex research.

Artemisinin Resistance in Cambodia: New Diagnostic Assay and Mechanism by Benoit WITKOWSKI (Post-Doctoral Researcher, Institut Pasteur Cambodge)

Dr. Witkowski described how classical assay approaches to artemisinin drugs might become less effective, because cell cycle arrest (quiescence) represents a new selectable mechanism of resistance that is not captured by traditional screening tests. A hypothesis is that less sensitive ring forms of *Plasmodium falciparum* drive increased PCT (parasite clearance time), and so new in vitro assays are needed that would be able measure the effect of the early ring forms going into a period of hibernation to avoid being killed by the artemisinin.

Discussion on the presentations of Dr Menard and Dr Witkowski concerned ACT-resistant genetics, and how this research was collaborating with biochemistry studies underway in Myanmar and elsewhere. Dr. Witkowski clarified that his tool is highly experimental and still under design, so it would be premature to test the technique in other areas. A need to more effectively distinguish between repeated dormant cycles and re-infections is critical, and to be able to treat the parasite during its dormant stages.

Mathematical Modeling of Pf Elimination by Dr. Richard MAUDE (Research Physician, Mahidol-Oxford Research Unit)

Dr. Maude presented an introduction to mathematical modeling for malaria elimination, and then led participants through models for Cambodia, particularly those designed to make predictions and explore scenarios for "last man standing" artemisinin resistance, optimizing strategies for Pf elimination, spatial models, and internet models. These models can be used to optimize malaria-control strategies.

In response to questions, Dr. Maude explained how these models are more robust than the ones he had published the previous year. There was great interest in the sensitivity of these models for malaria elimination, and particularly using MDA to purge the "last man standing" and locate areas where malaria is rebounding.

Breakout Groups: Identification and Prioritization of Operational Research Questions

Each group was asked to formulate 5-6 research questions under their assigned topic. Participants were asked to score their research questions according to various criteria, but this proved more useful for building consensus than for ranking per se. All the small groups identified shortcomings in the ranking methodology, typically because the most imperative questions were often the most difficult and/or expensive to assess and thus ended up with a low ranking. It was agreed in the end to report on the questions, but not the points assigned to them.

The agreed and prioritized Regional Operational Research framework is presented in Figure 1.

Plenary Discussion

Participants returned to the topic of early diagnosis and appropriate treatment of malarial and non-malarial fevers, and particularly the issues surrounding drug resistance. There was also the question of appropriate screening and treatment for people with G6PD deficiency. There have been some important clinical trials in China, but published only in Chinese – these findings should be disseminated and similar studies considered in GMS. There was also disagreement about when and whether standby treatments should be available or promoted for forest workers. Vietnam's experience with this approach should be evaluated and disseminated.

Innovative personal protection was agreed to be a critical area – and behavior change needs to go beyond health-seeking behavior and bednets. We need to explore what personal protection measures are both effective and acceptable to various populations, and there was lively debate about the measures that have impact on a population versus individual level.

Many of the most critical social and biomedical research questions are very difficult and/or expensive to investigate, and within a context of limited funding there is a range of opinions on whether to prioritize the most urgent gaps or to improve existing monitoring and surveillance systems. At the same time, non-traditional funding streams may be available for new topics, particularly climate change. Predicting

malaria outbreaks (and therefore, what level of RDT and ACT supplies should be stockpiled) are notoriously difficult to accurately predict, and only likely to become more so as the climate changes. While we recognize that changing land-use patterns are more influential on vectors and migration in the short term, there may be possibilities to tap into funding to explore environmental factors overall. One participant reported that the Global Fund's research funding is under-utilized, and strongly encouraged participants to "think big" when applying for grants. Translating research into practice is another critical issue, and there were calls for integrating not only health information systems, but delivery systems especially at the local level. There were strong calls for regional-level operational research, and submitting joint research funding applications to the Global Fund or other funding agencies. An easily-accessible research database that would include not only findings but downloadable research protocols is seen as invaluable, but previous efforts along these lines have had problems because they were not maintained. There was a discussion regarding testing artemisinin resistance using monotherapies, which was felt to be important but ethically dubious.

Summary, Next Steps, and Closing Remarks

Dr. David SINTASATH from Malaria Consortium summarized the central themes of the conference. Based on the presentations from the countries in the GMS, there is a wide range of OR conducted or being conducted in the region. Participants identified several priority areas, i.e., vector control; diagnosis and treatment; G6PDdeficiency,*Pv*, and PQ use; vulnerable populations; M&E and surveillance (including for elimination and resistance); and health systems (including the private sector). Priority research questions were formulated for each area, although it is important to consider the limitations and interpretations of any exercise to prioritize key topics or questions. Despite these inherent challenges, the groups engaged in constructive discussion and deliberations on key areas and prioritized questions of needed operational research in the region.

In order to support these OR priorities, the need for human resource capacity building, improved coordination and information sharing, and increased research funding are critical gaps. New tools and strategies have been or are being piloted, including research into issues surrounding migrant/mobile populations, innovative personal protection, and surveillance. BCC and integration with the private sector are cross-cutting needs, as is better operational research with vulnerable and minority populations. In terms of approaches to operational research, more qualitative, mixed-methods, and interdisciplinary research should be conducted to address the complex issues at hand.

Key recommendations are **to improve linkages with and capacity of universities**; encourage **annual research workshops** in every GMS country; ensure that findings are **translated into practice**; and update and share existing databases and information clearinghouses. Symposium participants also emphasized the importance of **attractive career paths for young researchers**, strengthening GMS **ethical review committees**, and **increased funding** for operational research. There was considerable discussion about funding issues, including that research budgets are so often reduced, how to fund trans-national studies,

and the fact that donor research priorities are not consistent with those of NMCPs. Great enthusiasm was expressed for more collaboration on OR for the GMS region.

Appendix 1: Symposium Agenda

Greater Mekong Sub-region (GMS) Malaria Operational Research Symposium
Apsara Angkor Hotel, Siem Reap, Cambodia
4 – 6 October 2010
FINAL AGENDA

Objectives of the meeting

• To share/exchange information about malaria operational research activities recently conducted or planned by national programs;

• To identify country priorities, needs, and gaps in conducting operational research towards strengthening malaria control and elimination;

• To formulate a malaria operational research agenda for the Greater Mekong Sub-region (GMS) with inputs from national programs, partners, research institutions, and other key stakeholders

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Day 1

0830 – 08:45	Welcome address and opening	H.E. Dr Duong Socheat, Director, CNM
0845 – 0900	Introductions and overview of objectives of the meeting	Dr David Sintasath, MC

0900 – 1015 Situation analysis of country's operational research (OR) activities and plans

Each country will briefly present their malaria strategic goals and objectives, current and recently implemented OR, and current knowledge gaps needed to be filled to achieve strategic goals.

Chairperson: Dr Chea Nguon, CNM

- Cambodia
- China
- Lao PDR

1015 – 1045 Tea/coffee break

Chairperson: Dr Wichai Satimai, BVBD

1045 – 1200 Country presentations (con't)

Myanmar
Thailand
Vietnam

1200 – 1300 Group photo and Lunch break

Chairperson: Dr Chansuda Wongsrichanalai, USAID

1300 – 1320	Draft Regional Research Plan of Action in Infectious Diseases of Poverty (2011-15)	Dr Jun Nakagawa, WPRO/TDR
1320 – 1340	Presentation of OR Questionnaire and Results	Ms Diana Picon, MC
1340 – 1530	Group work: Identifying priority areas for operational research	
1530 – 1600	Tea/coffee break	

Chairperson: Dr Manh Hung Nguyen, NIMPE

1600 – 1730	Presentation of Priority Research Areas	Group Rapporteurs
1830 – 2000	Welcome dinner	

Day 2

Chairperson: Dr Jimee Hwang, CDC-Atlanta

0830 – 1230 Current OR advances in a changing malaria epidemiology and resistance containment

Vector control	Dr Marc Coosemans, ITM Antwerp
Migrants and mobile populations	Dr Sylvia Meek, MC
Surveillance	Dr Steve Bjorge, WHO
Case management	Dr Prudence Hamade, MC
Plasmodium vivax/G6PD	Dr Didier Menard, IPC
Plasmodium falciparum elimination	Dr Richard Maude, MORU

1230 – 1330	Lunch break	
1330 – 1345	Summary of Day 1 group work	
1345 – 1730	Group Work: Prioritizing key operational research questions and identifying country needs (including internal and external technical support, HR, financial, IT gaps)	

Day 3

Chairperson: Dr Aye Yu Soe, 3D Fund

0830 – 1000	Group presentations and feedback	Group Rapporteurs
1000 – 1030	Tea/coffee break	
1030 – 1100	Plenary discussion	
1100 – 1200	Summary, next steps, and action points to move agenda forward	D Sintasath, MC

Appendix 2: List of Participants

List of participants
Greater Mekong Sub-region Malaria Operational Research Symposium
4 – 6 October 2010, Apsara Angkor Hotel, Siem Reap, Cambodia

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Appendix 3: Strategies and OR Situation Analysis

Cambodia	Goal / General Objectives • Move towards pre-elimination of malaria across Cambodia with special efforts to contain artemisinin-resistant *P. falciparum* malaria (Pf) • Move towards phased elimination of malaria in Cambodia with an initial focus on *Plasmodium falciparum* malaria Specific Objectives / Strategies • Improve access to early diagnosis and treatment (EDAT) with emphasis on detection of all malaria cases • Decrease drug pressure for selection of artemesinin- resistant malaria parasites by improving access to appropriate treatment and preventing use of monotherapies and substandard drugs in both public and private sectors • Improve access to preventive measures and specifically prevent transmission of artemisinin-resistant malaria parasites among target populations • Increase community awareness and behavior change among the population at risk and support the containment of artemisinin-resistant parasites through comprehensive behavior change communication (BCC), community mobilization, and advocacy • Provide effective management and coordination to enable rapid and high-quality implementation of the strategy Recent OR Studies • *In vivo* monitoring of anti-malarials in Cambodia • Field trials to evaluate the performance of a point of care diagnostic for screening G6PD deficiency • In vitro monitoring of drug susceptibility of Pf isolates collected from artemisinin-combined therapies (ACT) efficacy study in Cambodia • Multidisciplinary study of severe malaria and drug resistance in Cambodia • Study of *Pv* and *Pf* malaria in Cambodia • Clinical and laboratory study of artemisinin resistance characterization • Mapping of artemisinin-resistant parasites • Retrospective study of severe and hospitalized malaria cases in Battambang Referral Hospital • Survey for *in vitro* and molecular markers of anti-malarial drug resistance in Cambodia • Mathematical modeling of artemisinin resistance and containment • Uncomplicated malaria and anti-malaria drug resistance in Eastern Cambodia, screening for *Plasmodium falciparum* multi-drug resistance gene (PfMDR1) amplification • Identification of Anopheline vectors in relation to malaria transmission and disease risk in endemic malaria regions of Pursat Province • Large scale field trial (Phase III) to study the efficacy, longevity and fabric integrity and community acceptance of Long-Lasting Insecticidal Net (LLIN) Netprotect ® • Evaluation of field deployable arbovirus mosquito vector assays • Monitoring insecticide resistance in Cambodia

	• Monitoring residual effect of Insecticide-Treated Nets (ITNs) • Entomological survey and evaluation of the different methods of Anopheles collection • A cost-effectiveness and feasibility study of VMWs' (village malaria workers) expanded role in containment • Identify and test innovative solutions to increase access to effective malaria treatment • Focused screening and treatment • A cross-sectional, prospective study to define in outpatients causes of acute fever which are not malaria • Routine screening for malaria in pregnancy • Mobile and migrant situational analysis • Good use of ACTs and rapid diagnostic tests (RDTs) in drug outlets • Positive deviance as a method to improve response to BCC on mobile and migrant workers • Impact of the use of storage cooler boxes in the field to improve storage conditions of RDTs • Anthropological approaches to improve control strategies <u>Current and Planned OR</u> • Anti-malarial efficacy studies • Vector control studies <u>Knowledge Gaps and OR needs</u> • Capacity building of young scientists, is necessary, while strengthening CNM's research center (all results and protocols should be archived), and publish results • How to improve referral systems • Controlling malaria among migrant/mobile populations • Effective and sustainable incentives for health workers and volunteers • Impact of land use and climate change on vector bionomics and vector ecology • Integrated vector management for malaria and dengue fever • Appropriate dosages / treatment regimes for *P. falciparum* and *P. Vivax* • Drug efficacy studies • Mapping of G6PD deficiency in order to safely and effectively prescribe primaquine • Training / outreach strategies for private sector health workers, including pharmacies • How to effectively control counterfeit drugs and enforce the ban on monotherapies
China	<u>Goal / General Objectives</u> • To achieve no indigenous infection of *plasmodium* cases nationwide except some border areas in Yunnan by the end of 2015 • To achieve no local cases in the country by the end of 2020 <u>Specific Objectives / Strategies</u> • Ensure access to early, accurate diagnosis, and prompt, effective, safe treatment through public and private sectors • Ensure full coverage of the population at risk with appropriate vector control measures

	• Strengthen malaria health education, promotion, and community mobilization efforts and change behavior to maximize utilization of malaria control and elimination services • Ensure comprehensive coverage of vulnerable, poor, and marginalized populations at high risk of malaria with appropriate interventions • Strengthen the malaria surveillance system by improving case reporting, massive and active case detection, entomological and anti-malarials resistance monitoring, and ensuring adequate outbreak response capability • Provide effective program management, based on firm leadership commitment, to enable high quality implementation of strategies from malaria control to elimination <u>Recent OR Studies</u> • Study on control strategies for malaria outbreak in Yellow River and Huaihe River areas • Study on epidemic characteristics and control strategies of malaria in Tibet • Surveillance on drug resistance and malaria control in the border areas of Yunnan Province <u>Current and Planned OR</u> • Radical treatment for *Plasmodium vivax (Pv)* • Develop new-style, effective tools for rapid diagnosis of malaria cases • Molecular markers for artemisinin resistance • Techniques in malaria elimination for glucose-6-phosphate dehydrogenase (G6PD) deficiency detection, types, distribution <u>Knowledge Gaps</u> • Improved molecular-based tests for rapid diagnosis in order to find cases with low density of parasites • Molecular study to better understand the epidemiology of *Pv* relapses versus re-infections • Vector control: transmission dynamics, surveillance including resistance to insecticide • Forecasting and early warning system: multi-factor mathematical model • Comparing the efficacy of primaquine (PQ) for vivax malaria treatment, 8-day vs 14-day regimens • Evaluation of methods to improve adherence by patients to full treatment regimens • Health economic evaluation of control strategies • Evaluation of the projects for malaria elimination, how to select indices or indicators <u>OR Needs</u> • Gaps in OR financing (≈ 10 million) • Gaps in human resource and capacity; technical assistance is required to implement OR • Techniques for *in vitro* culture of *Pv* • New techniques for vector control • Tools for surveillance

Lao PDR	Goal / General Objectives • Intensify malaria control efforts, targeting remaining endemic communities and key risk groups, and progressively roll out malaria elimination in selected provinces Specific Objectives / Strategies • Strengthen program management • Maximize access to effective vector control and personal protection measures • Improve access to early, effective diagnosis for malaria • Support routine malaria case management • Strengthen routine Malaria Information System • Maintain malaria epidemic preparedness and response capabilities • Progressively roll out malaria elimination in selected provinces • Maximize utilization of malaria services through BCC and strengthening community mobilization efforts Recent OR Studies • Passive case detection (PCD) survey • Malaria prevalence survey • Bednet survey • Ethnic minority group (EMG) survey • Monitoring anti-malarial drug treatment, policy, and activity in sentinel sites • Malaria indicator survey (MIS) • IEC tools evaluation • LLIN acceptance and bioassay • Evaluation of village health volunteer (VHV) performance with RDT/ACTs Knowledge Gaps • Maintaining village based diagnosis and treatment in high risk areas with Combo RDT for diagnosis and radical treatment with Primaquine for *Pv*infections • Integration of surveillance and response activities within national surveillance systems • Expanding and integration of VHV scope of work (ie, including other diseases – acute respiratory infections, diarrheal disease etc) and harmonizing incentive mechanisms among various stakeholders • Strengthening capacity of central, provincial and district staff in early detection and prompt response of outbreaks • Adopting effective pro-active strategies for addressing external risk factors like deforestation, plantation, mining and hydro dam and road development projects • Health systems strengthening – human resource development, incentives, capacity building at provincial/district levels, integration of service delivery and surveillance & response • Operational research and piloting/integration of recommended results. • Strategies for elimination/pre-elimination • Better supply chain management – SMS pilot • Impact of rapid development on malaria : Plantations, hydro dams, road construction, mining

	OR Needs • Epidemiology of malaria among mobile workers in development projects (mining, rubber plantation, dam construction, etc.) • An investigation of continuing malaria transmission in villages with high ITN coverage and access to EDAT • Mapping of G6PD deficiency in Lao PDR, field-based testing and clinical trials for safe dosage of Primaquine • Entomological mapping, study of vector behavior, insecticide resistance monitoring • An assessment of incentive schemes for improving the performance of VHVs participating in malaria, TB and HIV/AIDS programs • Strengthen supply management at all levels monitoring stocks, including through SMS text messaging • Feasibility studies for suitable malaria prevention methods for forest goers
Myanmar	Goal / General Objectives • Reduction of malaria morbidity and mortality by 50% of the level in 2000 by 2010 • Achieve Millennium Development Goal 6 (MDG6) by 2015 Specific Objectives / Strategies • Information, Education, Communication (IEC) at the grassroots level • Prevention through personal protection and environmental measures • Prevention, early detection, and control of epidemics • Early diagnosis and appropriate treatment • Intersectoral collaboration • Community involvement • Capability strengthening of health staff • Operational research Recent OR Studies • Monitoring efficacy and quality of drugs ◦ 6 sentinel sites established for monitoring efficacy of drugs and monitoring of drug resistant malaria ◦ Treatment efficacy of Coartem ◦ Treatment efficacy of Artesunate – Mefloquine ◦ Treatment efficacy of Artesunate- Amodiaquine • Quality assurance (QA) of RDT & malaria microscopy • Stability of combination tests and the effectiveness of coolboxes in different geographical areas Current and Planned OR • Stability of CareStart combo test and other RDTs • Therapeutic efficacy of ACTs • Level of G6PD deficiency in the community • Potency of anti-malarial drugs on the market • Efficacy of LLINs over time

	Knowledge Gaps • Stability of RDT (combo tests) • Efficacy of ITN &LLIN over time • Therapeutic efficacy of ACT (continuous monitoring) and comparison among various ACTs • Stability of ACTs (Coartem) • Mapping of artemisinin resistance and primaquine/G6PD deficiency. • Effectiveness and rationale of gametocytocidal drugs like primaquine • Compliance of patients to ACT • Side effects of ACTs, especially Coartem • Level of adherence to national drug policy by health care providers (HCPs) • Effectiveness of BCC activities- video, posters, pamphlets, health education sessions, vendor education, etc. • Level of counterfeit drugs • Human resources and capacity building, especially the how to promote the sustainability of community health volunteers OR Needs • Funding gaps [potential sources: Three Diseases Fund (3DF), Global Fund for AIDS, Tuberculosis, and Malaria (GFATM), others] • Human resources, capacity building, especially community health volunteers • Technical assistance
Thailand	Goal / General Objectives • 80% of the country free of malaria transmission by 2020 Specific Objectives / Strategies • Minimize active malaria transmission areas and limit transmission only to restricted areas • Ensure that malaria patients have access to diagnosis and treatment according to national standard • Reduce multi-drug resistant malaria and prevent its transmission • Ensure that high-risk populations including border areas receive appropriate healthcare • Support research and development for malaria control Recent OR Studies • Developing Quality Assurance / Quality Control (QA/QC) for rapid tests developed for diagnosing malaria • Susceptibility of *An.maculatus* and *An. minimus* to synthetic pyrethroids by WHO using biochemical assay techniques • Cost of QA of malaria microscopy • Effectiveness of social marketing of personal protection products to prevent malaria among agriculturists • Knowledge, attitude and practice (KAP) on malaria management and nursing care in Thai hospitals • Synergism between pyronaridine and retinol in *Pfin vitro*

	• Synergism between quinine and retinol in fresh isolates of *Pf* • A comparative study on residual effects of Cyfluthrin 5 % EW and Permethrin 10 % EC on impregnated bednets against *An. minimus* • Field efficacy and persistence of LLINs in comparison with conventional ITNs • Outcome assessment of training course on microscopy in malaria clinics • Validation of microscopes equipped with a versatile illuminator (the earl-light) in detecting malaria parasites • Characteristics and malaria prevalence among migrant populations in malaria-endemic areas along the Thai-Cambodian border • Low efficacy of 3-day schedules of artesunate-mefloquine combination along the Thai-Cambodian border • Determining new anti-malaria substance for mefloquine resistant *Plasmodium falciparum* malaria by detecting the inhibitors to compete with the cofactor of *Pf* Glyceraldehyde-3-phosphate dehydrogenase (pGAPDH) enzyme activity <u>Knowledge Gaps</u> • Health systems ◦ Early detection for severe malaria at malaria clinics and health centers ◦ How to improve the referral system ◦ Assessment of at-risk people in malaria regional zones ◦ Geographic Information System (GIS) tool for predicting malaria epidemics • Preventive and control measures ◦ Impact of land use and climate changes on vector bionomics and vector ecology by using GIS ◦ Sentinel insecticide monitoring by using WHO standard kit /bottle assay ◦ Resistance mechanism of malaria and dengue vectors and the effect of synergy to enhance susceptibility • Case Management (diagnostics and treatment) including *P. vivax* ◦ Drug efficacy: *in vivo, in vitro* and pharmacokinetic studies ◦ Compliance: social behaviors, side effects /adverse events (pharmacovigilance) ◦ How to improve malaria diagnosis ◦ How to improve QC of malaria diagnosis ◦ New drug development ◦ Gene bank ◦ Monitor anti-malarial drug resistance ◦ How to improve patient compliance to drug regimes ◦ Factors affecting the variability of malaria mortality • BCC (providers and consumers) ◦ Study communication for behavior impact (COMBI) system approaches to prevention • Surveillance (prevalence of malaria, pharmacovigilance, and drug efficacy) ◦ Malaria disease surveillance in hard-core area without using regular insecticide residual spraying (IRS) and evaluation of its impact on malaria morbidity ◦ Evaluate the effectiveness of ITN program ◦ Evaluate the efficacy of LLINs at community level ◦ Investigate the efficacy of IRS to control mosquitoes and sand flies in mixed foci of malaria and leishmaniasis

	◦ Vector surveillance in non-malarial areas by setting up sentinel sites. ◦ Evaluate integrated vector management (IVM) to control vector-borne diseases (VBDs) ◦ Cost effectiveness of integrated vector management to control vector-borne diseases • Private sector ◦ KAP of health officers caring for malaria patients in public and private hospitals <u>OR Needs</u> ◦ Gaps in OR financing: Total = US$900,000, including human resources (PhD, MSc and short-term training, as well as research proposal development.
Vietnam	<u>Goal / General Objectives</u> • Continue to roll back malaria in the high endemic areas and the high risk groups, and develop and strengthen sustainable factors for malaria control <u>Specific Objectives / Strategies</u> • Reduce morbidity < 1.5/1,000 pop. • Reduce mortality < .03/100,000 pop. • No major malaria outbreaks <u>Recent OR Studies</u> • Malaria epidemiological research ◦ Malaria epidemiological stratification for operational intervention across the whole country ◦ Research on appropriate control measures for forest, border malaria and with migrant people such as effectiveness of LLIN face nets for rubber workers, long-lasting insecticide-treated hammocks (LLIHs) for people involved in swidden agriculture and forest-based activities • Research on diagnosis and treatment of malaria ◦ Efficacy of malaria treatment regimens: Artekin and CV artecan (Dihydro artemisinine-Piperaquine) as first line treatment of *Pf*. ◦ Drug-resistant malaria and its resistance mechanism: *Pv* resistance to chloroquine in many places, detection of artemisinin resistance in Binh Phuoc province ◦ G6PD deficiency among ethnic groups of Vietnam • Research on vector control measures ◦ Evaluation trial on the insecticidal and residual effects of insecticides for vector control: to select insecticide for every 5 year planning period: Alphacypermethrine, Lambdacyhalothrine ◦ Evaluation study on the insecticide resistance of the main vectors toAlphacypermethrine, Lambdacyhalothrine • Research on appropriate IEC measures for each ethnic group: selection of suitable IEC materials, languages and channels <u>Current and Planned OR</u> • Malaria control measures for border crossers and seasonal movement people

	• Study on the malaria treatment efficacy of Artequick (artemisinin 80mg – piperaquine 400mg-primaquine 4mg) • Study on the drug resistance of *P.vivax* and *P.falciparum* and identification of drug resistant malaria by polymerase chain reaction (PCR) technique • Study on the epidemiology of*P.vivax,* treatment effectiveness of primaquine 14 days and identification of malaria recrudescence and relapse by PCR technique • Research on G6PD deficiency in some ethnic groups • Study on the mechanism of insecticide resistance of the *Anopheles* by biochemical and PCR techniques • Study on measures to control the *A.epiroticus* resistance to insecticide • Study on the remaining quantity of insecticide relating to the resistance of the vector • Study on the influence of natural and artifical environments (hydro-electric damp, re-forestation, etc.) to the malaria vector <u>Knowledge Gaps</u> • Study on monitoring and case management measures in the artemisinin containment area • Study on monitoring and management of malaria imported cases in the malaria elimination areas • Study on the elimination measures of *P. vivax* in malaria persistent foci in malaria elimination areas • Study on the influence of environment change to the malaria vector • Mapping of G6PD deficiency in the whole country in order to use primaquine safely and effectively • Study of the IEC strategies for malaria control for border crossers and seasonal migrants <u>OR Needs</u> • Training young staff on operational research: research design, research methodology, standard research proposal and paper for international publication • Support budget for operational research; the budget from the government is very limited • International cooperation for research with research institutions and international organizations • Combine research with training of researchers, especially young staff • Training and transfer of advanced techniques applied in the laboratory and monitoring