Meeting Report

NINTH MEETING OF THE GREATER MEKONG SUBREGION THERAPEUTIC EFFICACY STUDY NETWORK

15–16 September 2021
Virtual meeting

World Health Organization
Western Pacific Region

WORLD HEALTH ORGANIZATION

REGIONAL OFFICE FOR THE WESTERN PACIFIC

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Convened by:

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NOTE

The views expressed in this report are those of the participants of the Ninth Meeting of the Greater Mekong Subregion Therapeutic Efficacy Study Network and do not necessarily reflect the policies of the conveners.

This report has been prepared by the World Health Organization Regional Office for the Western Pacific for Member States in the Region and for those who participated in the virtual Ninth Meeting of the Greater Mekong Subregion Therapeutic Efficacy Study Network from 15 to 16 September 2021.

CONTENTS

KEYWORDS

Antimalarials – therapeutic use / Drug resistance / Malaria-prevention and control / Mekong valley

ABBREVIATIONS

ACPR	adequate clinical and parasitological response
ACT	artemisinin-based combination therapy
AFRIMS	Armed Forces Research Institute of Medical Sciences
AL	artemether-lumefantrine
AQ	amodiaquine
AS-AQ	artesunate-amodiaquine
AS-MQ	artesunate-mefloquine
AS-PPQ	artesunate-piperaquine
AS-PY	artesunate-pyronaridine
AS+SP	artesunate+sulfadoxine-pyrimethamine
eCDS	electronic Communicable Disease System
CMPE	Center for Malaria, Parasitology, and Entomology (Lao People's Democratic Republic)
CNM	National Center for Parasitology, Entomology and Malaria Control (Cambodia)
COVID-19	coronavirus disease 2019
CQ	chloroquine
DHA-PPQ	dihydroartemisinin-piperaquine
DHIS	District Health Information System
DVBD	Division for Vector Borne Diseases (Thailand)
ECAMM	External Competency Assessment of Malaria Microscopists
EQA	external quality assessment
ERC	Ethics Review Committee
G6PD	*glucose-6-phosphate dehydrogenase*
glurp	*glutamate-rich protein*
GMS	Greater Mekong Subregion
HRP	histidine-rich protein
iDES	integrated drug efficacy surveillance
IMPE	Institute of Malariology Parasitology and Entomology Quy Nhon (Viet Nam)
IPT	intermittent preventive treatment
K13	*Kelch 13*
LLIHN	long-lasting insecticidal hammock net
LLIN	long-lasting insecticidal net
MME	Mekong Malaria Elimination programme
MMS	malaria management system
MORU	Mahidol-Oxford Research Unit
msp	merozoite surface proteins
NIMPE	National Institute of Malariology, Parasitology and Entomology (Viet Nam)
NIPD	National Institute of Parasitic Diseases (China)
NMCP	National Malaria Control Programme (Myanmar)
NMP	national malaria programme
NRA	national regulatory agency
NTG	national treatment guideline
PCR	polymerase chain reaction

pLDH	parasite lactate dehydrogenase
PMI	U.S. President's Malaria Initiative
PPQ	piperaquine
PQ	primaquine
PY	pyronaridine
QA	quality assurance
QC	quality control
RAI	Regional Artemisinin-resistance Initiative
RDT	rapid diagnostic test
RSC	Regional Steering Committee
SOP	standard operating procedure
TDA	targeted drug administration
TES	therapeutic efficacy studies
TQ	tafenoquine
UNOPS	United Nations Office for Project Services
WHO	World Health Organization

SUMMARY

On 15 and 16 September 2021, the World Health Organization (WHO) Mekong Malaria Elimination (MME) programme hosted the virtual Ninth Meeting of the Greater Mekong Subregion Therapeutic Efficacy Studies Network with representatives from national malaria programmes (NMPs), focal points from Greater Mekong Subregion (GMS) countries, as well as technical experts and partners. Representatives from the GMS Member States – Cambodia, China, the Lao People's Democratic Republic, Myanmar, Thailand and Viet Nam – attended the workshop to monitor the results of therapeutic efficacy studies (TES) and integrated drug efficacy surveillance (iDES) from the past year, review the efficacy of antimalarial drugs, identify alternative artemisinin-based combination therapies (ACTs) to revise of national treatment guidelines (NTGs) and prioritize future needs of the countries, as necessary.

The main discussion points included the results of recent TES and iDES, future priorities and activities given the present results, ways to continue monitoring drug efficacy in malaria-free and near elimination settings, the risk of *Plasmodium falciparum* histidine-rich protein 2 (pfHRP2) and pfHRP3 deletions and the effective management and monitoring of *P. vivax* malaria in the GMS.

The key conclusions of the meeting included:

- **Overview of GMS malaria elimination:** From January to July 2021, the GMS countries recorded a 26% reduction in malaria cases compared to the same period in 2020. At the same time, *P. falciparum* + mixed cases fell by 55%, and *P. vivax* cases dropped by 19%.

- **Drug efficacy:** In 2021, quality TES and monitoring were completed in four GMS countries: Cambodia, the Lao People's Democratic Republic, Myanmar and Viet Nam. As malaria case numbers continue to drop, iDES continues to be implemented nationwide in Thailand and rolled out in Viet Nam and the Lao People's Democratic Republic. Cambodia started an iDES pilot in three districts in one province. While artesunate-pyronaridine (AS-PY) is registered as an alternative ACT and a second-line drug, its use is limited in Cambodia and the Lao People's Democratic Republic due to supply issues.
    - **Cambodia:** Artesunate-mefloquine (AS-MQ) and AS-PY continue to demonstrate efficacy for *P. falciparum* and *P. vivax* malaria. In 2020, TES indicated that the efficacy of AS-MQ remains high.
    - **Lao People's Democratic Republic:** AS-MQ and AS-PY remain efficacious. Data on artemether-lumefantrine (AL) from 2019-2020 show high efficacy compared to 2018 against *P. falciparum* and *P. vivax* malaria with a larger sample size than was achieved in 2018. Molecular data indicated fewer K13 mutations compared to 2018 except in Champassak province, there is mefloquine sensitivity in all samples assayed, and plasmepsin2 copy number is decreasing, showing a reversal of piperaquine (PPQ) resistance.

      Myanmar: AL, AS-PY and dihydroartemisinin-piperaquine (DHA-PPQ) remain efficacious. Similarly, chloroquine (CQ) for *P. vivax* cases also remains efficacious.
    - **Viet Nam:** AS-PY and AS-MQ are efficacious. In September 2020, treatment failures with DHA-PPQ led to two additional provinces (Phu Yen and Khanh Hoa) switching to AS-PY. Molecular data indicate PPQ resistance along the provinces bordering Cambodia.
    - **Thailand:** DHA-PPQ for *P. falciparum* cases is efficacious where data is available, except in Sisaket province, bordering Cambodia, where AS-PY is the first-line treatment. CQ + primaquine (PQ) for *P. vivax* cases also remain efficacious.

- **Quality control in TES and iDES:** Adherence to WHO's quality assurance (QA) and quality control (QC) protocols are mandatory. Common deviations should be noted to avoid incorrect or missing information. QA and QC were maintained through regular monitoring and communications between WHO country staff, NMP investigators and the WHO regional drug resistance monitor despite pandemic restrictions.
- **Efficacy monitoring in a malaria-free setting:** iDES is feasible as a routine activity in a "prevention of reestablishment" setting. The continuous training of relevant health staff, particularly in microscopy, is essential to ensure the effectiveness of iDES among imported cases.
- **pfHRP2/3 deletions:** Histidine-rich protein 2 (HRP2) is a protein expressed only by *P. falciparum* and is the target for the most used rapid diagnostic tests (RDTs). HRP2 RDTs generally have the highest sensitivity of the RDTs for *P. falciparum* malaria. However, parasite strains in several countries have been identified that have deletions in the genes encoding HRP2 or the similar HRP3 protein. Studies done in the past on the Myanmar-China border detected the presence of parasites with pfHRP2/3 deletions. Surveys and studies are needed to map the prevalence and impact of pfHRP2/3 deletions in the subregion. NMPs should keep note of anecdotal evidence or formal complaints regarding false-negative RDTs as this may indicate the presence of pfHRP2/3 deletions.
- **Effective management and monitoring of *P. vivax* malaria:** The efficacy of drugs for treating *P. vivax* in the GMS ranges from 94.7% to 100%. But there are challenges in the 14-day PQ radical treatment and monitoring for relapse or reinfection beyond day 28/42 in iDES. Routine TES for *P. vivax* infections looks at efficacy and resistance to the treatment of the asexual blood stages parasites.
- **Supervised treatments:** Supervised treatment is required for TES and iDES. In iDES, countries are adapting to local conditions to find ways of assuring that the treatment is taken. The first dose of treatment under iDES is always supervised by health staff; documentation for patients taking subsequent doses is sometimes inadequate. If iDES shows high numbers of treatment failures, confirmatory studies should be done and a change in first-line treatment should be considered.