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Report on the

# Sixth intercountry meeting of national malaria control programme managers from HANMAT and PIAM-Net countries

Cairo, Egypt
13–14 August 2014

World Health Organization
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## 1. INTRODUCTION

The spread of resistance to antimalarial drugs presents a major challenge to health systems. To meet this challenge, there is need for updated quality information on antimalarial drug treatment efficacy for policy-makers. Monitoring the therapeutic efficacy of antimalarial medicines can generate the information needed for evidence-based malaria treatment policies.

The World Health Organization (WHO) has established two subregional networks for countries endemic with *falciparum* malaria: the Horn of Africa Network for Monitoring Antimalarial Treatment (HANMAT) comprising Djibouti, Saudi Arabia, Somalia, Sudan and Yemen from the WHO Eastern Mediterranean Region, along with Eritrea, Ethiopia and South Sudan from the WHO African Region, and the Pakistan–Islamic Republic of Iran–Afghanistan Malaria Network (PIAM-Net). These networks aim to ensure continuous monitoring of the therapeutic efficacy of antimalarial medicines using updated WHO protocols. In most network countries, WHO supports activities and studies on drug efficacy testing at sentinel sites. In 2013, the gene for artemisinin resistance (K13 gene) was discovered and WHO was given the mandate to coordinate the tracking and mapping of the gene.

The sixth intercountry meeting of national malaria programme managers from the countries of HANMAT and PIAM-Net was organized by the WHO Regional Office for the Eastern Mediterranean in Cairo, Egypt, from 13 to 14 August 2014. The meeting aimed to disseminate information and update antimalarial drug monitoring mechanisms and treatment policies in countries. National malaria programme managers and focal points for case management attended from Afghanistan, Djibouti, Eritrea, Ethiopia, Islamic Republic of Iran, Pakistan, Saudi Arabia, Somalia, South Sudan and Sudan, as well as staff from the US Naval Medical Research Unit 3 (NAMRU-3). WHO staff from headquarters, regional and country levels also attended the meeting. The programme and list of participants are included as Annex 1 and 2, respectively.

## 2. UPDATE ON ARTEMISININ RESISTANCE AND MONITORING EFFICACY, AND PLANS FOR ITS CONTAINMENT

*Dr M. Warsame, WHO headquarters*

There are several tools available for monitoring drug efficacy and resistance, including in vivo studies using the WHO protocol (2009), pharmacokinetic studies, in vitro studies and studies of molecular markers. However, in vivo study results are the gold standard used to determine whether a change in treatment policy is required. Treatment failure in an individual patient is not always due to drug resistance, but may be due to other factors, including inadequate dosage, drugs of poor quality, pharmacokinetic factors, and patient immunity and non-compliance. Polymerase chain reaction (PCR) analysis must be conducted on samples from patients with treatment failure to determine whether treatment failure during follow-up was due to true recrudescence or re-infection.

Regular monitoring is needed for early detection of changes in treatment efficacy. Consistent monitoring every two years at the same sentinel sites, according to WHO protocol, allows for analysis of trends over time. The early detection of artemisinin resistance in Cambodia

was achieved when delayed parasite clearance was first observed in Pailin province. Recent studies have determined that artemisinin resistance is likely to be spreading and emerging independently, making "containment" of the problem more complex. Currently, artemisinin resistance is limited to the South-East Asia Region. The risk of further spread and emergence of artemisinin resistance can be reduced by scaling-up diagnostic testing, removing monotherapies and sub-medicines that do not meet quality standards from global markets and following the recommendations outlined in the Global plan for artemisinin resistance containment.

## 3. COUNTRY PRESENTATIONS OF THERAPEUTIC EFFICACY STUDY RESULTS

### 3.1 Afghanistan

The number of confirmed cases for both *Plasmodium falciparum* and *P. vivax* malaria has steadily decreased from 2002 to 2013. Since 2003, therapeutic efficacy studies (TES) have been conducted in three sentinel sites in Faryab, Nangarhar and Takhar provinces. This year, the malaria control programme is monitoring the efficacy of artemether-lumefantrine (AL) for the treatment of uncomplicated *P. falciparum* and *P. vivax* in four health facilities in Nangarhar and Kunar provinces. The study, which targets a sample of 100 patients each with *P. falciparum* and *P. vivax*, will conclude in November 2014.

### 3.2 Djibouti

In 2013, artesunate + sulphadoxine-pyrimethamine (AS+SP) was removed from Djibouti's national treatment policy due to concerns about possible resistance to SP**.** Challenges faced by the Djibouti national malaria control programme include: government procured treatments without proof of quality control; patient preference for treatments despite negative diagnostic results; patient preference for injected medicine over tablets. Djibouti has recently replenished their supply of medicine and rapid diagnostic tests for both species).

### 3.3 Eritrea

TES on artemisinin-based combination therapies (ACTs) have demonstrated high cure rates (> 90%) in Eritrea since 2006. Data from the most recent studies (2012/2013) conducted on artesunate + amodiaquine (AS+AQ) are available from four sentinel sites in the Gash Barka region. PCR-corrected treatment efficacy was found to be above 90% in all sites (range: 92.9–100%). The Eritrea national malaria control programme plans to conduct studies in more sites and is planning to conduct studies on *P. vivax*. However, the declining incidence of malaria is making it difficult to achieve the required sample sizes.

### 3.4 Ethiopia

TES results were presented from 2003 onwards. Between 2010 and 2012, studies were conducted on AL in seven sentinel sites. The average adequate clinical and parasitological response (ACPR) for this combination was 99% (range: 96.7–100%). In 2013, the PCR-corrected cure rates of treatment with AL remained high, at 99% and 100%. The national

malaria control programme was advised to test the efficacy of medicines needed to treat *P. vivax*, in particular AL.

### 3.5 Islamic Republic of Iran

The Islamic Republic of Iran is currently implementing a national malaria elimination plan, with the goal of elimination by 2025. There has been a marked reduction in malaria incidence, for both *P. falciparum* and *P. vivax,* over recent years. The most recent TES (2013) of AS+SP had an ACPR of 100%. It was recognized that the caseload in the country is heavily influenced by the neighbouring countries of Afghanistan and Pakistan. Challenges for the national malaria control programme include population movements and security at eastern border areas and the detection and follow-up of imported cases. Currently, all detected cases are reported and tracked through the public health system.

### 3.6 Pakistan

Pakistan has an annual caseload of 300 000 confirmed cases and an estimated 4.5 million cases of clinical (unconfirmed) malaria, most of which are from Punjab province, and many of which are not likely to be malaria. Currently there are four sentinel sites in place for TES. There are several challenges, including an unregulated private sector, inappropriate malaria treatment, with misuse of injection for uncomplicated malaria in the private sector, and control of malaria in border districts, with mass population movement from endemic to non-endemic areas. Selected achievements include increased coverage of diagnosis, provision of treatment to all confirmed cases, activities to increase public awareness on diagnosis and treatment, and partnership building with academia.

### 3.7 Saudi Arabia

Saudi Arabia is currently engaging in a national malaria elimination programme, which has lead to a significant drop in malaria incidence. Challenges faced by the national malaria control programme include follow-up for patients who are not residents (undocumented migrants) and the conduct of research by some academic institutions without coordination with the national programme.

### 3.8 Somalia

Currently there are three sentinel sites in Somalia (in Jamame, Janale and Jowhar), with a fourth planned for 2014 (in Bosasso). In 2011, the PCR-corrected ACPRs in the three sites monitoring AS+SP were 77.8% in Jamame, 99% in Jowhar and 95.6% in Janale. Quadruple and quintuple molecular markers conferring resistance to SP were found in Jamame (60% of samples) and Jowhar (40% of samples). In 2013, TES of AL conducted in Janale and Jowhar found close to 100% ACPR in both sites. Somalia is the first country in the Eastern Mediterranean Region to demonstrate resistance to SP. The national programme has been encouraged to take further steps to update the treatment policy with an effective medicine and to examine the value of using SP for intermittent preventive therapy. It is important that the

malaria indicator survey should be used as the key source of data for making estimates about malaria prevalence.

### 3.9 South Sudan

From August to December 2013, South Sudan conducted TES on AS+AQ and AL (28 days) at three health care centres (in Rejaf, Rubkona and Mapel). Among the 93 cases recruited at one site, 58 patients completed the study. The study is currently on hold and the data has not yet been analysed. Currently, no efficacy data is available on AL, the second-line treatment. The 2013 studies were the first TES to be conducted since 2004, when studies of AS+SP and AS+AQ determined a treatment efficacy of 91.2% and 92.7%, respectively. Many challenges for conducting TES in South Sudan exist, including lack of technical capacity within the country, insecurity leading to patient loss to follow-up, and slow and inadequate recruitment that prolongs study length and cost.

### 3.10 Sudan

In Sudan, sentinel sites have been established at five health centres. Studies were conducted on AS+SP and AL, according to the standard WHO protocol. Most studies conducted on AS+SP (2011–2012) showed a PCR-corrected ACPR above 95%. Studies of AL conducted in two sites in 2010 and 2012 also found a PCR-corrected ACPR above 95%. Data from studies conducted in 2013 have not yet been PCR-corrected; however, ACPR before PCR-correction is above 90%. Molecular analysis of dihydrofolate reductase *(dhfr)* and dihydropteroate synthase *(dhps)* gene mutations in the four sites found that few of the 356 patients had *dhfr* wild type (4%), while 84% had double *dhfr* and triple *dhfr* (11.5%). Triple mutations in the *dhps* gene were observed in all four sites, in particular Kassala (48%). One patient from Kassala was found to have a quadruple *dhps* mutation. When *dhfr/dhps* were analysed together, 23% of patients were found to have quintuple mutants and eight patients among the 352 had more than six mutations.

## 4. ISSUES RELATED TO UNIVERSAL COVERAGE OF DIAGNOSIS AND TREATMENT POLICY

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