
**Delaying Artemisinin Resistance in India, Asia, and Africa Consultation (March,2014) under the auspices of the National Institute of Malaria Research and the Public Health Foundation of India to take stock of the regional artemisinin resistance situation and to help shape the on-going global response. This was supported by the DFID under the Knowledge Partnership Programme. This communication brief has been developed based on the deliberations from the workshop.**

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# Health and Disease Control

## ARRESTING ARTEMISININ RESISTANCE: KEY TO SUSTAIN GAINS IN REDUCING MALARIA DEATHS

## Introduction

Malaria is one of the oldest parasites ever known to mankind.

After thousands of years, it remains the world's most pervasive infection, affecting at least 91 different countries.

The disease causes fever, shivering, joint pain, headache, and vomiting. In severe cases, patients can have jaundice, kidney failure, anemia, and can lapse into a coma and even death.

## Malarial Disease Burden

* Malaria is caused by Plasmodium parasites which spread to people through infected female Anopheles mosquitoes which bite mainly between dawn and dusk. There are four parasite species that cause malaria in humans: Plasmodium falciparum, Plasmodium vivax, Plasmodium malariae and Plasmodium ovale.

* According to the latest WHO estimates (December 2014), there were about 198 million cases of malaria in 2013. The total burden of disease from malaria was estimated by WHO to be 46,486,000 Disability Adjusted Life Years (DALYs) lost which the combined toll of death, illness, and disability from the disease.

* Malaria mortality rates have fallen by 47% globally since 2000 and by 54% in the WHO African Region.

* India estimated 128 million suspected malaria cases of which only around 7 percent confirmed cases were recorded (WHO, 2014).

* Marked increase in use of **Arteminsin Combination Therapies** (ACTs) along with rapid diagnostics and Insecticide treated bed nets substantially reduced incidence and number of deaths due to Malaria.

## What is Artemisinin Resistance?

Malarial parasite developed resistance to chloroquine, widely used anti-malarial prior to Artemisinin based therapies. Artemisinin is an extract of a traditional Chinese herbal medicine and its effectiveness as an antimalarial was confirmed in 1971. Since the mid-1990s, Thailand and Cambodia, and eventually almost all countries where malaria is endemic, have taken advantage of this drug by adapting national drug regimens to recommend artemisinin combination therapy (ACT), as first-line treatment for uncomplicated malaria. The intent is for Artemisinin to quickly clear most parasites from the bloodstream, leaving the partner drug (like sulphadoxine, pyrimethamine, lumefantrine) to kill those that remain.

Artemisinin resistance is a consequence of continued use of irrational treatment protocols, inadequate compliance by patients, substandard/spurious drugs and availability of oral monotherapy products (Arteminisn only). The emergence of resistance to antimalarial medicines is initiated by rare spontaneous mutations that give survival advantages to the parasite when exposed to a specific antimalarial compound. The WHO recommends phasing out of oral artemisinin-based monotherapy.

Similar to the spread of resistance to chloroquine and other antimalarial medicines in the past, there is a possibility that artemisinin resistance will spread or develop independently around the world.

## Current Geographic Spread and Epidemiological Demarcation

**Artemisinin-resistant malaria has been documented in five countries in the Greater Mekong Subregion: Cambodia, Thailand, Vietnam, Myanmar and Laos. It appears to be replay of the chloroquine resistance story—spread from the epicenter in Cambodia. Containment plans have been developed but challenges persist as evident by analysis of molecular markers in the region. Mapping of resistance in a geographical region would allow one to craft a credible response-**

**•Tier I areas are those for which there is credible evidence of artemisinin resistance**

**•Tier II areas have significant inflows of mobile and migrant populations from tier I areas or shared borders with tier I areas.**

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**•Tier III areas are defined as P. falciparum endemic areas which have no evidence of artemisinin resistance and limited contact with tier I areas.**

## Consequences of Artemisinin resistance

In the Greater Mekong sub-region, patients with resistant parasites still recover after treatment, provided that they are treated with an ACT containing an effective partner drug and ensuring compliance.

However, there is a real risk of parasites developing resistance to all available medicines.

Concerns for the near future include the potential for artemisinin resistance, either from cross border spread, particularly from nearby Thai-Myanmar and Thai-Cambodia borders; or from de novo (independent emergence) resistance in India, possibly because of failure of combination drugs placing additional pressure on artemisinins.

Widespread emergence of resistance to first line drugs would cause a serious setback to the goal of reducing deaths due to Malaria.

## The Response

*Global Plan for Artemisinin Resistance Containment (GPARC) is intended to mobilise global and local stakeholders for the containment and ultimate elimination of artemisinin resistance where it has emerged and for the prevention of its emergence in or spread to new locations.

**i. Stop the spread of resistant parasites:** In areas for which there is evidence of artemisinin resistance, an immediate, comprehensive response with a combination of malaria control and elimination measures is needed to stop the survival and spread of resistant parasites.

**ii. Increase monitoring and surveillance to evaluate the artemisinin resistance threat:** Regular geographic monitoring and surveillance are critical to identify new foci

rapidly and to provide information for containment and prevention activities.

**iii. Improve access to diagnostics and rational treatment with ACTs:** Increasing access to affordable, quality point of care diagnostics and treatment with ACTs improves clinical outcomes and limits opportunities for resistance to both arteminsin and partner drugs.

**iv. Invest in artemisinin resistance-related research:** Research is important to improve understanding of resistance and the ability to manage it. At the same time programmes need to invest in researching of new therapy options.

**v. Motivate action and mobilize resources:** Successful implementation of the GPARC will depend on motivating many stakeholders at global, regional and national levels to support or conduct the recommended activities.

## The Way Forward

• Increasing access to rapid diagnostic testing and quality treatment remains essential for moving toward elimination.

• Complete ban on manufacture, sale of oral artemisinin mono-therapies, and promotion of evidence based rationale therapeutics, strengthening drug regulatory systems so as to weed out substandard and spurious antimalarial medicines in the region.

• Capacity building of wide range of malaria treatment providers in public, private or community for adherence to ACT protocols and patient education especially compliance.

• Collaborate with research networks to understand nature of parasitic mutations and track movement of mutant genes.

• Create a surveillance system to quickly identify new areas of resistance emergence as a second line of defence.

DFID is supporting a number of programmes to contain spread of AR such as through GFATM's Regional Artemisinin Initiative (RAI); tracking resistance to artemisinin collaboration, TRAC research project which supports Mahidol Oxford Research Unit (MORU); co-financing the Regional Malaria Trust Fund through the ADB; supporting the WHO Global Malaria Programme (GMP) and the WorldWide Antimalarial Resistance Network (WWARN).

*KPP is a South-South cooperation programme promoting knowledge sharing in the areas of Food Security, Resource Scarcity and Climate Change; Health and Disease Control; Trade and Investment; and Women and Girls. KPP is funded by the Government of UK's Department for International Development (DFID) and managed by a consortium led by IPE Global Private Limited under its Knowledge Initiative. The main objective of KPP is 'Gathering and uptake of evidence on issues central to India's national development that have potential for replication in LICs and impact on global poverty'.*
*For more on Artemisinin Resistance, visit http://ipekpp.com/kp/hndc/AR%20final%20KP.pdf*

Contact: Dr Dinesh Agarwal, M.D.
Policy Lead – (Health and Disease Control)
IPE Global House, B – 84, Defence Colony, 110 024, New Delhi, India, Phone: 0091 11 4075 5974; Direct: 0091 11 4075 5933 E-mail: dagarwal@ipeglobal.com; kpp@ipeglobal.com Website: www.ipekpp.com

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