



AMAZON MALARIA INITIATIVE

Malaria in Low-Incidence Settings

MONITORING THE EFFICACY OF AND RESISTANCE TO ANTIMALARIAL MEDICINES

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The emergence of antimalarial resistance is a concern in the Americas. In South America, *Plasmodium falciparum* parasites are resistant to chloroquine, therefore the WHO is concerned that parasites may develop resistance to the antimalarial medicine artemisinin as well as partner medicines in artemisinin-based combination therapies.

According to WHO, there are a variety of methods for evaluating the efficacy of and resistance to antimalarial drugs in low-incidence settings, including *in vivo* studies, *in vitro* tests, and molecular analysis. Data collected through these methods should guide the development of policy on the use of antimalarial drugs in endemic areas.

- *In vivo* therapeutic efficacy studies (TES) of antimalarial medicines continue to be essential to orient changes in malaria treatment policies since they correlate best with patients' clinical response to the drugs. Though *in vivo* studies do not require sophisticated technology, they are not simple to conduct. Moreover, a lower incidence setting poses challenges to their feasibility; for example, it hinders the enrollment and follow-up of patients and/or increases the cost and duration of studies, making it more difficult to ensure the quality of studies. Nevertheless, it is recommended that a TES be conducted at least every three years. Alternatively, a multi-center study may be implemented (involving various locations within the country or in a number of neighboring countries that have similar epidemiological characteristics).
- Other elements of the early warning systems like *in vitro* studies that measure the susceptibility of malaria parasites to antimalarial medicines, as well as testing for molecular markers resistance to antimalarials (for chloroquine, mefloquine, sulfadoxine-pyrimethamine, and artemisinin), may help to track the emergence of resistance and complement the information provided by TES. However, reliable markers are not available for all parasite species.



Photo: John Marmion



Photo: CDC

In vivo, *in vitro* and molecular analysis must follow standard protocols and stringent quality control and quality assurance procedures, as data from these studies helps to evaluate the efficacy or inefficacy of antimalarial drugs. Well trained clinical and laboratory personnel who strictly follow the protocol are essential. Likewise, a laboratory that is capable of conducting molecular biology tests, ascertaining the presence of the drug and its metabolites in serum, and/or doing *in vitro* tests where indicated is key to monitoring efficacy and resistance to antimalarials.

Due to the low rate of transmission of malaria, it is often difficult to obtain enough *P. falciparum* malaria patients for the necessary sample size. In dispersed and mobile populations, the relevance and strategy of studies should be analyzed to ensure the feasibility of ongoing monitoring and to limit drop out as much as possible. Overall, more research and innovation is needed, but is rarely supported in low-incidence settings.

The Amazon Malaria Initiative has published a [Strategic Orientation Document on Monitoring the Efficacy of and Resistance to Antimalarials in the Current Epidemiological Context](#) as a reference for countries in Latin America and the Caribbean on how to best combine available tools for monitoring efficacy and resistance to antimalarials.



Photo: PAHO/WHO

Table 1: How to use the available tool in different epidemiological scenarios

Surveillance with:	High or Moderate transmission	Low or No transmission (pre-elimination or elimination)
<i>In-vivo</i>	<ul style="list-style-type: none"> • Up to 8 sentinel sites • Every 3 years • One arm 	<ul style="list-style-type: none"> • One site at least every 3 years • Multi-center studies • One arm
Molecular markers	Concomitant with <i>in vivo</i> studies	Collect samples every 18 months
<i>In-vitro</i> (ELISA)	Concomitant with <i>in vivo</i> studies	Collect samples every 18 months