**Term of Reference**

LABORATORY REAGENT SUPPORT FOR THERAPEUTIC EFFICACY STUDY (TES) FOR FIRST LINE OF ANTI-MALARIA DRUG (DIHYDROARTEMISININ PIPERAQUINE/DHP) IN INDONESIA

**Introduction**

Malaria has historically been one of the main public health problems in Indonesia, but efforts by the Ministry of Health (MoH) within the last few decades has successfully brought down the Annual Parasite Incidence (API) from 4.68 cases per 1,000 inhabitants in 1990 to 1.38 cases per 1,000 inhabitants in 2013. Indonesia is aiming to eliminate malaria by 2030. Nevertheless, malaria still poses a major public health problem in some provinces, especially the eastern part of Indonesia.

Four species of the human malaria parasite are prevalent; the predominant species are *Plasmodium falciparum* and *P. vivax*. To avoid unnecessary antimalarial drug deployment, the MoH has set a treatment guideline in which antimalarial drugs will only be given to cases that are laboratory-confirmed, either by microscopy or rapid diagnostic test (RDT). In Indonesia, follow up of malaria treatment is not common and, therefore, supervisory treatment has been recommended to ensure treatment compliance.

Since the first report of artemisinin treatment failure in Thai-Cambodian border in 2009, the artemisinin resistance cases have spread rapidly across the mainland of Southeast Asia. The artemisinin resistance has manifested as the delay of the parasite clearance. Prolonged courses of artemisinin-based combination therapy (ACT) were reported to be efficacious in areas where standard 3-day treatment are failing. Although there have been reports of delay in parasite

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clearance\(^4\), this has not been linked to artemisinin resistance but may instead be related to the higher parasite load as the parasite is eventually eliminated by day seven. Routine monitoring of the therapeutic efficacy of ACTs is essential for treatment policy and to detect early changes in parasite susceptibility to antimalarial drugs.

PCR adjustment of cure rates initially based on blood-slide microscopy and clinical assessment is necessary as super-infection with additional parasites can occur during the long duration of follow-up treatment, particularly in areas of high malaria transmission. Towards the end of the treatment period, antimalarial drug levels can fall below curative levels, allowing new infections emerging from the liver to establish themselves. Therefore, PCR for the surveillance study is needed to distinguish between treatment failure and new infection. PCR-corrected cure rates have become accepted as the end-points in regulatory clinical trials and for monitoring antimalarial drugs.

The proposed supplies are part of the malaria therapeutic efficacy surveillance (TES) activity in 2018-2019 that was funded and conducted by the national government. There is no funding available through the national malaria programme, National Institutes of Health Research and Development (NIHRD) or Eijkman Institute to procure the laboratory consumables, as their allocated budget has been re-programmed for the COVID-19 response. This study’s output will be reported to WHO and will contribute to local and global knowledge of potential malaria treatment failure and drug resistance.

**Objective**

The aim of this activity is to provide logistic support and delivery of reagent and other laboratory consumables for PCR confirmation of samples enrolled in TES 2018-2019 as part of strengthening malaria drug efficacy surveillance.

**Location and Time**

This activity will be held in collaboration with Eijkman Institute for Molecular Biology, Jalan Diponegoro 69, Jakarta 10430, Indonesia.

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Budget

All expenditures for purchasing reagent and other consumables is expected be covered by WHO.