Malaria Policy Advisory Group Meeting

4–5 March 2024, Yaoundé, Cameroon
Background document for Session 5

Strategy to respond to antimalarial drug resistance in Africa

Updates and identification of needs

Mutations in *PfKelch13 (K13*) associated with delayed clearance post-treatment with artemisinin-containing regimens are on the rise in the Horn of Africa and Eastern Africa. In the Horn of Africa, the 622I mutation has been identified in multiple countries, including Eritrea, Ethiopia, Sudan and Somalia. Notably, the 622I mutation is present in parasites exhibiting hrp2/3 deletions, making them challenging to detect through conventional hrp2-based Rapid Diagnostic Tests (RDTs). In Uganda, various K13 mutations seem to be proliferating, with certain areas showing a prevalence of validated markers indicating partial resistance to artemisinin in the majority of sampled parasites. Meanwhile, in Rwanda, the 561H K13 mutation is spreading, although the 675V mutation is more prevalent in western Rwanda. The 561H mutation has also been identified in Tanzania, particularly in Kagera, near the Rwandan border. With a prevalence exceeding 5% of a validated marker for artemisinin partial resistance and evidence of delayed clearance, four African countries have now confirmed artemisinin partial resistance: Eritrea, Rwanda, Uganda and the United Republic of Tanzania. In Ethiopia and Sudan, artemisinin partial resistance is suspected as studies have detected >5% patients carrying K13 mutations (622I) validated to be associated with artemisinin partial resistance but delayed clearance has yet to be confirmed.

Since the latest MPAG meeting, several initiatives have been undertaken to advance the implementation of the *Strategy for the response to antimalarial drug resistance in Africa*. In November 2023, two regional meetings for Africa were held in Uganda. The first meeting was a regional stakeholder meeting for countries across Africa aimed at aligning intervention priorities to assist countries in addressing resistance. During this meeting, key drivers of antimalarial drug resistance were discussed along with necessary interventions to respond at the country level. The second meeting focused on surveillance of drug efficacy and resistance for countries in Eastern Africa and the Horn of Africa. The meeting provided technical updates on methods of surveillance of drug resistance and efficacy, and results of country studies on drug efficacy and resistance were shared, including plans for future studies and research. Additional activities conducted include an assessment evaluating the factors that may contribute to resistance in Rwanda and devising a strategy to address these challenges.

A crucial priority is ensuring the accuracy of data generated by therapeutic efficacy studies, which inform drug policy decisions. The *Strategy for the response to antimalarial drug resistance in Africa* highlights different interventions needed to support this. These include strengthening of subregional networks for monitoring efficacy and resistance, and enhancing capacity of national teams to generate better quality and standardized data on antimalarial drug efficacy and parasite resistance. Planned activities to support these objectives encompass updating the document "Methods for Surveillance of Antimalarial Drug Efficacy," serving as a reference for national programs and investigators assessing medicine efficacy. In addition, we plan to establish a roster of consultants trained to support Therapeutic Efficacy Studies (TES) in line with WHO study protocols. Furthermore, we plan to expand the ongoing WHO External Quality Assessment (EQA) scheme for malaria molecular diagnostics, managed by UK-NEQAS, to include molecular K13 markers of artemisinin resistance.