Global **Malaria** Programme

WHO Malaria Policy Advisory Committee (MPAC) meeting

OCTOBER 2018

MEETING REPORT

SUMMARY

On 17–19 October 2018, the WHO Malaria Policy Advisory Committee (MPAC) convened to review updates and progress, and provide guidance with respect to specific thematic areas of work carried out by the Global Malaria Programme (GMP).

The meeting included eight sessions focused on 12 topics: (1) a report from the Malaria Elimination Oversight Committee (MEOC) and the E-2020 Global Forum; (2) an update on malaria elimination in the Greater Mekong subregion (GMS); (3) an update on antimalarial drug efficacy and resistance in the GMS; (4) an update on the GMP policy-making and dissemination process review; (5) an update on the RTS,S Malaria Vaccine Implementation Programme (MVIP) and framework for decision-making; (6) an update on the 10+1 approach including the analytical framework; (7) a proposed Evidence Review Group (ERG) on the community effect of insecticide-treated nets (ITNs); (8) an update from the ERG on border malaria; (9) a review of the outcomes from the technical consultation on the research requirements to support policy recommendations on highly sensitive point-of-care diagnostics for P. falciparum malaria; (10) a proposed technical consultation on the role of parasite genetics in malaria surveillance to optimize the response by national programmes; (11) a proposed technical consultation on engaging the private sector in malaria case management in high-burden countries; and (12) a proposed technical consultation on external competence assessment for malaria microscopy.

The key outcomes/recommendations of MPAC to GMP included:

- **MEOC and E-2020:** MPAC noted that the MEOC identified cross-border issues as a major challenge for almost all malaria-eliminating countries and supported the MEOC's proposal to highlight operational research as one of the themes of the subsequent Global Forum. MPAC re-emphasized the importance of malaria-eliminating countries

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convening independent national elimination advisory committees to help drive the elimination agenda.

- **Elimination in the GMS:** MPAC was pleased with the progress being made in reducing morbidity and mortality in the GMS and appreciated the presentation of more granular data from countries. Given that falciparum malaria in the GMS has been reduced to foci, MPAC emphasized the need to improve implementation in the remaining endemic areas, where cases are highly concentrated in at-risk populations. MPAC requested that the WHO Secretariat provide a specific progress report on *P. vivax* elimination with data disaggregated by species at the next MPAC meeting. MPAC previously recommended the establishment of an Independent Oversight Board for malaria elimination in the GMS and urged that this independent board be convened without delay to support countries in identifying and addressing key challenges that remain.

- **Antimalarial drug efficacy:** MPAC noted that drug resistance remains a major problem in the GMS and emphasized the renewed focus on elimination. The presence of both artemisinin and partner drug resistance in other parts of the world, including Papua New Guinea and Guyana, appears to be due to independent emergence and not spread from the GMS. MPAC supported the convening of the proposed ERG to review evidence on the main drivers of and potential strategies to delay the development of drug resistance.

- **GMP policy-making and dissemination:** MPAC endorsed the review of the GMP policy-making and dissemination processes, and proposed improvements to the processes. MPAC highlighted the importance of this work for ensuring that evidence on new tools and strategies is efficiently reviewed and used to inform timely policy recommendations with the primary goal of preventing malaria cases and deaths. MPAC appreciated the efforts to increase the consistency, transparency and efficiency of the policy-making processes and agreed that a formal mechanism should help to prioritize the need for and types of new tools and strategies.

- **RTS,S malaria vaccine implementation:** The report of the Phase III trial's long-term follow-up (Mal076) was well received and the Committee was reassured by the new results indicating the lack of rebound of malaria in the group of children receiving RTS,S. The Committee noted the progress of the MVIP and appreciated the update on the development of the policy decision-making framework.

- **10 + 1 approach:** MPAC endorsed the approach that places special focus on high burden countries; however, the Committee expressed preference for a descriptor such as "maximizing high-impact for high-burden countries", as part of the GTS continuum from control to elimination. MPAC requested that GMP carefully monitor the progress of the approach and report back at subsequent MPAC meetings on overall progress, including details of the analyses in each of the 11 high-burden countries.

- **ERG on the community effect of ITNs:** MPAC agreed that conducting a comprehensive review of the community effect of ITNs is an important task, but felt that it would be useful to first see the conclusions from the ongoing literature review in order to determine whether there is sufficient new evidence to warrant an ERG meeting.

- **ERG on border malaria:** MPAC agreed with the definitions of border and transnational malaria as presented, and endorsed the conclusions from the ERG

on border malaria including the analytical framework. MPAC noted the issue of border screening and requested WHO to determine whether there is sufficient evidence of impact to make a recommendation.

- **Research requirements to support policy recommendations on highly sensitive point-of-care diagnostics (hsRDTs) for *P. falciparum***: MPAC reaffirmed its previous conclusion that there is insufficient evidence to determine whether detection of low-density infections using hsRDTs would have a significant impact on transmission. MPAC advised that these tools should be further evaluated through research activities and are not recommended for deployment in routine malaria control or elimination programmes until such evidence is generated.

- **Technical consultation on the role of parasite genetics in malaria surveillance:** MPAC welcomed the idea of GMP hosting a technical consultation on parasite and vector genetics to assess its potential relevance to malaria programme work. Members noted that this is a dynamic and rapidly changing area, and there is value in active engagement to keep abreast of developments and to help steer the focus.

- **Technical consultation on engaging the private sector in malaria case management:** MPAC supported the proposed technical consultation on engaging the private sector in malaria case management in high-burden countries.

- **Technical consultation on external competence assessment for malaria microscopy:** MPAC strongly supported the proposed technical consultation on external competence assessment for microscopy.

BACKGROUND

The WHO Global Malaria Programme (GMP) convened the Malaria Policy Advisory Committee (MPAC) for its 14th meeting in Geneva, Switzerland on 17–19 October 2018. MPAC convenes biannually in Geneva to provide independent strategic advice to WHO on policy recommendations for malaria control and elimination. The Committee is supported by standing Technical Expert Groups (TEGs) and ad hoc Evidence Review Groups (ERGs), whose work focuses on thematic areas and specific research questions in order to generate sufficient evidence to provide guidance. Over the course of the two-day meeting's open sessions, 18 MPAC members, seven national malaria control programme (NMCP) managers, the WHO Secretariat and over 30 observers discussed updates and progress in the work areas presented. Recommendations were discussed in the Committee's final closed session on Day 3.

The meeting participants were reminded of the procedures governing WHO's assessment of the MPAC members' declarations of interest. It was noted that the GMP Secretariat had requested and received feedback from all of the experts present at the meeting regarding their declarations of interest. The following members disclosed various interests – Professor Graham Brown, Professor Gabriel Carrasquilla, Professor Maureen Coetzee, Professor Umberto D'Alessandro, Professor Abdoulaye Djimde, Professor Azra Ghani, Professor Brian Greenwood, Professor Caroline Jones, Professor Kevin Marsh, Doctor Neena Valecha, and Professor Dyann Wirth. The GMP Secretariat reviewed the disclosures and determined that there were no conflicts of interest with respect to the topics presented for decision at the meeting and the participating MPAC members.

UPDATES FROM THE GLOBAL MALARIA PROGRAMME

The GMP Director opened the meeting by highlighting the increasing trend towards separation of countries into two distinct groups: high-burden countries and countries close to elimination. Moreover, while the world is likely to meet the 2020 milestones of the Global Technical Strategy (GTS) elimination targets, it is unlikely to meet the morbidity and mortality targets. He called for an urgent and credible response, which is presented in detail in the summary of Session 5. Other updates provided by the Director included data to guide action on the response to the continuing problem of malaria-associated anaemia, which will be included in the World Malaria Report 2018; the Malaria Threats Map; the dramatic drop in cases and deaths in the GMS; the increase in reports of *An. stephensi* in new and potentially troubling geographies that will be discussed by an ERG in early 2019; and key meetings held and documents launched since the last meeting.

SUMMARY OF THE MPAC SESSIONS

Report from the Malaria Elimination Oversight Committee (MEOC) and the E-2020 Global Forum

Background: An update was provided on the Global Forum held in Costa Rica and progress made by the 21 malaria-eliminating countries that first convened in 2017 to exchange ideas, experiences and lessons learned; report on progress towards elimination; and share updated policy guidance. An analysis of the 17 countries that eliminated malaria between 2000 and 2015 showed that 75% of the countries had reported 100 or fewer cases 3 years before reaching zero. Progress towards elimination was discussed for each of the 21 countries, on the basis of which countries were classified as "on track" to achieve zero cases by 2020 (if they reported fewer than 100 cases in 2017), "somewhat off track" (if they reported between 100 and 1000 cases in 2017), or "off track" (if they reported more than 1000 cases); meanwhile, Paraguay was certified as malaria-free. The next Global Forum is planned for June 2019 in China.

The MEOC was established to provide independent operational and programmatic advice and oversight monitoring of malaria elimination. The MEOC met after the Global Forum. Key conclusions and recommendations from the meeting included significant concern over the increases and stagnation reported in some E-2020 countries in recent years; commitment to following the cross-border issue closely; the recommendation that national programmes should analyse barriers to accessing preventive measures, diagnosis and treatment; and emphasis on the importance of independent national elimination advisory committees. At the next meeting in February 2019, the MEOC will focus on countries with 100 or fewer cases, where extra assistance may be helpful for meeting the 2020 milestone.

MPAC conclusions: MPAC noted that the MEOC identified cross-border issues as a major challenge for almost all malaria-eliminating countries and supported the MEOC's proposal to highlight operational research to address bottlenecks as one of the themes of the subsequent Global Forum. MPAC re-emphasized the importance of malaria-eliminating countries convening independent national elimination advisory committees to help drive the elimination agenda and provide a link to support countries.

MPAC noted that GMP is currently finalizing an analytical framework to help countries identify the best mix of interventions to apply in specific contexts based on malaria epidemiological data and malariogenic potential, and a surveillance assessment tool to assist them in strengthening their surveillance system to ensure the early identification and treatment of all cases in order to prevent onward transmission.

Finally, MPAC noted the issue of *P. knowlesi* (the topic of a previous ERG), which has the potential to confound the picture in countries that have eliminated human malaria but are reporting significant numbers of *P. knowlesi* cases. *P. knowlesi* is not currently considered a human parasite, as there is no evidence of sustained human–mosquito–human transmission. GMP will work with researchers and look at examples of other zoonotic diseases to guide how to move forward with the certification of countries reporting *P. knowlesi* cases.

Update on malaria elimination in the Greater Mekong subregion (GMS)

Background: An update was provided on malaria elimination in the GMS, highlighting the progress, key challenges, activities in 2018 and future priorities. Between 2012 and 2017, GMS countries have significantly reduced the number of malaria cases and deaths. As a result, malaria cases are now concentrated in small geographical areas. In 2018, however, the number of cases in some areas of Cambodia and adjacent countries has increased. Possible reasons for the increase include that the village health worker network is not fully functional in some places, there was a delayed switch from DHA-piperaquine to mefloquine-artesunate, and that there is insufficient coordination between partners and the national programmes. To address the increase in cases, there is a need for stronger focus of programmatic activities and the strengthening of technical and operational support. Major common challenges in the GMS include project implementation among forest-goers in remote areas that are disproportionately affected by malaria; monitoring and addressing multidrug resistance; and improving surveillance. As GMS countries approach elimination, the relative importance of *P. vivax* cases is likely to increase. In 2018, almost 60% of cases were *P. vivax* or combined cases of *P. vivax* and *P. falciparum*.

WHO continues to support NMCPs to address new challenges and priorities. Key areas of support include technical support at subnational levels to improve operations, support to monitor drug efficacy and update treatment guidelines, support for the implementation of the Ministerial Call for Action, and support to assess the implementation of new approaches and tools.

MPAC conclusions: MPAC was pleased with the progress being made in reducing morbidity and mortality in the GMS and appreciated the presentation of more granular data from countries, as previously requested. Given that falciparum malaria in the GMS has been reduced to foci, MPAC emphasized the need to ensure strong implementation in the remaining endemic areas, where cases are highly concentrated in at-risk populations such as forest-goers, migratory workers, military, and other mobile populations. MPAC noted that new strategies to deal with forest malaria such as pre-treatment are being used to enhance the impact of existing control strategies. MPAC supported innovation in the strategies being deployed to tackle forest malaria, but stressed that these innovative strategies need to be carefully monitored and their impact assessed in order to provide the evidence needed for future policy recommendations.

Since the primary goal of malaria elimination in the GMS is to address *P. falciparum* multidrug resistance, MPAC urged that a strong focus on the elimination of falciparum malaria be maintained in order to ensure the achievement of elimination by 2020 in areas with multidrug resistance. MPAC requested that the WHO Secretariat provide a specific progress report on *P. vivax* elimination with data disaggregated by species at the next MPAC meeting.

MPAC previously recommended the establishment of an Independent Oversight Board for malaria elimination in the GMS and urged that this independent board be convened without delay to support countries in identifying and addressing key challenges that remain.

Update on antimalarial drug efficacy and resistance in the GMS

Background: Despite the delayed response to artemisinin in some areas of the GMS and reports of "partial" resistance to artemisinin, artemisinin-based combination therapies (ACTs) remain the most effective treatment for uncomplicated falciparum malaria. Routine monitoring must continue in order to ensure that the recommended ACTs remain effective, that timely changes to national treatment policies are implemented, and that artemisinin resistance is detected early. Assessment of K13 propeller region mutants will greatly facilitate the tracking of artemisinin partial resistance as it emerges. In the context of multidrug resistance in the GMS, including artemisinin partial resistance and partner drug resistance, elimination of falciparum malaria has become a high priority. The role played by artemisinin resistance in the development or selection of partner drug resistance needs to be further evaluated.

Key updates presented included an update on artemisinin partial resistance markers; the relationship between partial artemisinin resistance and partner drug failure; the spread of DHA-piperaquine resistance; and the efficacy of other ACTs. Conclusions from the presentation were that:

- the intensive regional malaria elimination campaign in the GMS is critical;
- surveillance for artemisinin and partner drug resistance in the GMS should be strengthened;
- there is a critical need for surveillance outside the GMS to detect de novo resistance or the introduction of resistant parasites; and
- where surveillance signals a potential threat to leading ACTs, effective alternative ACTs should be identified and implemented before resistance reaches a critical level.

An ERG was proposed to look at the evidence on the main drivers of drug resistance development and to identify proactive strategies to delay the development of drug resistance.

MPAC conclusions: MPAC noted that drug resistance remains a major problem in the GMS and that the situation has not changed markedly in the past six months; MPAC emphasized the renewed focus on elimination as well as the importance of continued close monitoring. The presence of both artemisinin and partner drug resistance in other parts of the world, including Papua New Guinea and Guyana, appears to be due to independent emergence and not spread from the GMS. MPAC supported the convening of the proposed ERG on drug efficacy and response.

The discussion highlighted two key points:

- The issues of DHA-piperaquine ineffectiveness and its potential to drive artemisinin and piperaquine resistance should be addressed as a priority. MPAC requested WHO to work with GMS countries to review and update national guidelines, especially in areas where therapeutic efficacy studies (TESs) show high treatment failure rates.

- There is an urgent need to implement the WHO policy recommendation to use single low dose primaquine as a gametocytocide in *P. falciparum* malaria in Cambodia. MPAC noted the lack of prequalified primaquine in the required dosage and requested WHO to work closely with GMS countries to address the logistical and regulatory challenges related to the use of single-dose primaquine. MPAC further encouraged documentation of the community effect of single-dose primaquine treatment for *P. falciparum* in reducing malaria transmission.

Update on the GMP policy-making and dissemination process review

Background: Continued progress in reducing malaria morbidity and mortality and ultimately achieving elimination will require the introduction of new tools as well as novel use of existing tools. Timely, evidence-based policies are critical for delivering impact, and GMP is the normative body with the mandate to provide malaria policy guidance on both new tools and strategies to Member States. GMP launched a transformative initiative to review and improve its policy-making and dissemination processes. The objectives of the initiative were to lay out a clear diagnosis of the strengths and challenges of the policy-making and dissemination processes, to develop and assess options for transformation, and finally to develop a customized implementation plan.

Over 80 interviews were conducted with a broad array of stakeholders. The general consensus from the numerous interviews was that GMP has achieved much progress since the introduction of MPAC in 2011, particularly in three areas: organization, evidence, and dissemination. Stakeholders felt that GMP's advisory bodies include high-calibre experts, and the roles and responsibilities of those bodies have become clearer. GMP has moved towards robust evidence-based recommendations, particularly where aligned with the Guidelines Review Committee process. The introduction of newsletters and improvements to the website have facilitated the dissemination of GMP policies.

There is, nevertheless, still room for improvement in three major areas: process length, recommendation consistency, and the use of GMP outputs at local level. The detailed review identified opportunities for improvements mapped along the continuum from research and development to use of policy products at country level, lack of harmonized policy pathways, inconsistent requirements on the strength of evidence, heterogeneous composition of GMP advisory bodies, inconsistent naming and structuring of policy documents, non-optimal dissemination mechanisms and networks to support implementation, lack of guidance on the prioritization of interventions, and lack of guidance to support operational execution.

GMP developed options for addressing these issues and conducted a country survey to test options to improve dissemination. Key actions proposed included formalizing the policy pathways to increase transparency; streamlining and aligning the policy recommendation process for products with the prequalification process;

and standardizing key internal processes with regard to evidence evaluation, safety assessment and quality assurance. In addition, GMP proposed to develop and publish Preferred Product Characteristics, including the associated evidence requirements, in order to improve the transparency surrounding the priority tools and strategies needed to reduce malaria morbidity and mortality, and ultimately achieve elimination.

MPAC conclusions: MPAC endorsed the review of the GMP policy-making and dissemination processes for malaria guidance, and proposed improvements to the processes. MPAC highlighted the importance of this work for ensuring that evidence on new tools and strategies is efficiently reviewed and used to inform timely policy recommendations with the primary goal of preventing malaria cases and deaths. MPAC appreciated the efforts to increase the consistency, transparency and efficiency of the policy-making processes and agreed that a formal mechanism should help to prioritize the need for and types of new tools and strategies.

Update on the RTS,S Malaria Vaccine Implementation Programme and framework for decision-making

Background: The presentation included a brief review of the Phase III trial results and components of the Malaria Vaccine Implementation Programme (MVIP) followed by a presentation of the findings from the long-term follow-up study (Mal076). This open label seven-year follow-up of subjects in the 5- to 17-month-old cohort in three sites demonstrated continued clinical efficacy and protection from severe malaria. There was no evidence of an excess of severe malaria and no evidence of increased meningitis.

Updates on the progress of the pilot implementation included the report that the national regulatory authorities in all three MVIP countries have granted special authorization for the use of the RTS,S malaria vaccine in the pilot areas. The timelines for evaluation activities have led the Expanded Programme on Immunization (EPI) in each country to revise the vaccine introduction dates, shifting from Q3/Q4 2018 to Q1/Q2 2019, and possibly Q3 2019 in the third country. The MVIP Advisory Group and the Data Safety and Monitoring Board have met quarterly and provided guidance to the programme. A comprehensive update on the MVIP was provided to SAGE in April 2018. As suggested by MPAC and SAGE, a Joint Working Group (including members from MPAC, SAGE, the Programme's Advisory Group and modellers) has been constituted and will meet in December to consider a framework for policy decision-making.

Key priorities in the coming months include supporting the EPI to launch the RTS,S vaccination programmes in Q1/Q2 2019 and supporting the evaluation partners to finalize country-specific protocols, conduct the baseline household surveys and ensure that the hospital- and community-based surveillance systems are fit for purpose. The