

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

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-piperazine 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 MVIP team is engaging with funders to secure funding for the second phase of the 6-year programme, from 2021 to completion of the pilots.

MPAC conclusions: The report of the Mal076 results was well received, and the Committee noted that children living in areas with moderate to high perennial malaria transmission who receive three or four doses of RTS,S appear to benefit for at least seven years after vaccination and do not have an excess risk of clinical or severe malaria. This important result provides further reassurance on the absence of a rebound effect on immunized children and reinforces the safety profile of the vaccine. Other approaches to control malaria should accompany use of the vaccine.

The Committee noted the MVIP's progress and appreciated the update on the development of the policy decision-making framework. MPAC requested that the

decision-making framework include acceptability data. It also noted the recommended data sources for the different components of the safety evaluation and the need to secure funding to complete the pilots.

Update on the 10+1 approach including the analytical framework

Background: Progress in reducing the global malaria burden has stalled. The *World malaria report 2017* estimated that there were 216 million cases (95% CI 196–263 million) of malaria in 2016, marking a return to 2012 case levels. The number of deaths estimated in 2016 (445 000; 95%CI 402 284–486 548) is similar to that of the previous year. Globally, we are not on track to meet the mortality and morbidity milestones for 2020 set out in the GTS. The WHO African Region continues to bear more than 90% of the burden of disease, accounting for most of the increases in cases between 2012 and 2016. Around 70% of the globally estimated cases and 71% of the estimated deaths in 2016 occurred in 10 countries in sub-Saharan Africa (in alphabetical order: Burkina Faso, Cameroon, Democratic Republic of the Congo, Ghana, Mali, Mozambique, Niger, Nigeria, Uganda and United Republic of Tanzania) and in India.

The 10+1 approach is characterized by the following four key response elements that work synergistically to improve the current business model:

1. Galvanize national and global political attention to reduce malaria deaths: a successful technical response relies upon a broader societal shift that integrates the powerful role of affected communities, high-level national political leadership and the complementary role of global advocates.
2. Drive impact in country through strategic use of information: NMCPs and technical partners will use a context-specific analytical framework to identify challenges that affect malaria control in areas of high malaria burden and tailor locally appropriate responses.
3. Establish best global guidance, policies and strategies suitable for a broad range of contexts: National and subnational decisions will be guided by global guidance. All available evidence will be analyzed to identify the appropriate mix of technical interventions across a broad range of subnational contexts.
4. Implement a coordinated country response: based on the analysis of each country's unique context, ministries of health will work with in-country technical and implementing partners to refine and align their approach for reducing malaria mortality and morbidity in the high-burden target areas.

The attainment of the GTS targets will be the measure of success. In addition, more efficient and effective use of resources can help to establish long-term national commitments to increase the volume and impact of domestic funding for health, complemented by incremental global finance. Better malaria control in these and other high-burden countries will contribute to potential demographic, social and economic dividends in the coming decades.

MPAC conclusions: 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”, as part of the GTS continuum from control to elimination. MPAC noted that this endorsement does not imply a disregard for countries with smaller populations at similarly high risk for malaria or an intention to reduce global efforts in other places malaria is present. MPAC highlighted the value of strategic use of information to guide decision-making for prioritization and efficient

use of available resources. MPAC further noted the critical leadership role of local stakeholders and NMCPs, the primary health care strategy and multisector approach, and the crucial need for technical support and capacity-building in the number and range of skills at all levels including guidance for tailored approaches.

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. The report should include information on NMCP contributions and leadership, methods for prioritization of resource allocation, responses from partners, capacity-building at all levels, and how progress will be made in the context of existing health delivery systems. MPAC requested early analysis of progress and the effects of the approach, both in areas of highest burden and in other parts of the countries.

MPAC further requested GMP to lead the development of an evidence-based common analytical framework to enable the identification of strata and the monitoring of changes in disease burden when intervention strategies change. MPAC encouraged analysis of some countries in Africa and subnational areas of India where trends of malaria case reductions have continued, so as to understand how these areas differ from the 11 focus countries. Some analyses are underway as part of the Strategic Advisory Group on malaria eradication, however, additional comparative analyses should not be undertaken if they impede analyses that directly inform action in high-burden settings.

Proposed ERG on the community effect of insecticide-treated nets (ITNs)

Background: ITNs constitute one of the two core interventions recommended by WHO for malaria vector control (the other being indoor residual spraying [IRS]). The current ITN recommendation is based on evidence of public health value that was generated through cluster randomized trials. Most, but not all, of these studies have shown that ITNs provide both personal protection to people sleeping under the net and protection to community members who are not sleeping under a net. The latter type of protection has been termed 'mass effect' or 'community effect'. The evidence on this community effect has never been systematically reviewed in order to estimate how the absolute and relative magnitude of the effect may vary across settings and with coverage and varying levels of insecticide resistance.

In the context where prioritization of one intervention and the level of coverage at which it is deployed will come at the expense of coverage and/or quality of another intervention, further clarity on the community effect of ITNs is becoming fundamental to inform WHO policy recommendations. Of specific interest in this context are the extent to which a community effect of ITNs has been documented, and the relationship between this effect and varying levels of coverage. Another critical question is the relative degree to which insecticide resistance may be reducing (a) personal protection and (b) the community effect. This issue is critical but hard to measure; moreover, it may be different for different resistance mechanisms as well as across varying levels of transmission intensity. The objectives of the proposed ERG are:

1. to conduct a systematic review of the available evidence on the community effect of ITNs, which will include an analysis of the presence/absence/variations of this effect depending on geographical setting, coverage level and the prevalence/intensity of pyrethroid resistance;
2. to review the WHO glossary to verify whether definitions regarding ITNs and their personal and community effect are appropriately captured; and

3. to advise WHO on whether the findings from the review of the evidence base on the community effect of ITNs warrant a revision of current WHO guidance on the deployment of ITNs.

MPAC conclusions: MPAC agreed that conducting a comprehensive review of the community effect of ITNs is an important task, but felt that it would be important to see the conclusions from the ongoing literature review in order to determine whether there is sufficient new evidence to warrant an ERG meeting. It was highlighted that there is at least one ongoing study that could contribute additional data in this area once it is completed next year. MPAC emphasized that this evidence might be especially crucial to discussions about prioritizing or targeting interventions such as for the 'high burden to high impact' approach. It was also highlighted that any WHO communication on the deployment of ITNs should not undermine the current recommendation of achieving high-level coverage of vector control interventions.

Evidence Review Group on border malaria

Background: Border malaria is defined as malaria transmission or potential for transmission that takes place across or along borders between countries sharing a land border. Border malaria can extend through the adjacent administrative areas along the international border or up to a specified distance from an international border. Countries nearing elimination often find their last few cases occurring along international borders with countries that have not achieved substantial reductions in malaria transmission. An ERG on border malaria was convened to review evidence on characteristics of malaria transmission in border areas, factors that contribute to transmission, and current interventions to reduce border malaria. Experiences and lessons from other communicable diseases with a risk of cross-border transmission were reviewed.

Summarized conclusions and recommendations from the ERG are:

1. Many countries nearing elimination refer to cross-border malaria as a significant challenge. Two related but distinct issues are associated with cross-border malaria: movement of people infected with malaria parasites across international borders, and malaria transmission that crosses or occurs along international land boundaries.
2. "Border malaria" is defined as malaria transmission or potential for transmission that takes place across or along borders between countries sharing a land border. Border malaria can extend up through the adjacent administrative areas along the international border or up to a specified distance from an international border. "Transnational malaria" is defined as the importation of malaria parasites across international borders, which may include airports and sea ports.
3. Border malaria can occur whether or not there is a differential in transmission between countries. Countries nearing elimination often find their last few cases occurring along international borders with countries that have not achieved elimination and malaria transmission persists because control and prevention activities are not equal or optimized throughout the shared focus.
4. There is not a one-size-fits-all approach for addressing border malaria. Multiple factors, including political unrest, differences in social and economic development, weak surveillance and response systems, insufficient access to health services, and differences in national malaria policies, treatment-seeking

behaviours and other factors can contribute to malaria transmission in border areas.

5. Eliminating countries should consider the problem of malaria along international borders early in order to shorten the long tail of elimination. More resources should be directed to border areas to ensure that prevention, diagnosis, treatment, surveillance and response are of high quality.
6. Bordering countries should conduct joint mapping of health services and risk assessments to inform responses best-suited to the situation and optimize activities.
7. Informal data-sharing and coordination at the border district level can be efficient and effective. WHO should explore new modalities for scaling up cross-border coordination and collaboration with neighbouring countries. The concept of “Special Intervention Zone” developed for onchocerciasis elimination should be considered.

MPAC conclusions: 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 also agreed that the concept of the “Special Intervention Zone” or a “Buffer Zone” could be useful in promoting collaboration between countries to achieve elimination. MPAC noted the issue of border screening and requested that WHO determine whether there is sufficient evidence of impact to make a recommendation.

Outcomes from the technical consultation on the research requirements to support policy recommendations on highly sensitive point-of-care diagnostics for *P. falciparum*

Background: Recently, next-generation, highly sensitive rapid diagnostic tests (hsRDTs) for *P. falciparum* have become commercially available. These tests claim a limit of detection that is 10-fold more sensitive than that of conventional rapid diagnostic tests (RDTs). In May 2017, WHO convened an ERG on low-density malaria infections that highlighted the scarcity of data on the relative contributions of low-density *P. falciparum* and *P. vivax* infections to onward transmission in human populations. It was concluded that it would be difficult to determine the impact of identifying and treating these infections through active test-and-treat based interventions in a number of endemic settings. Subsequently, MPAC recommended that hsRDTs only be used for research purposes until there is evidence that the detection of low-density infections using these tools will have a significant impact on clinical outcomes, public health or transmission. GMP convened a technical consultation in June 2018 to identify the evidence required to develop recommendations on the use of highly sensitive point-of-care tests (HSPOCTs).

The following conclusions and draft recommendations were presented to MPAC for consideration (please see the ERG report for full draft recommendations):

1. Determining the role of HSPOCTs in surveillance and elimination strategies, and in the prevention or treatment of malaria in pregnancy (MiP) will require impact studies assessing the public health and clinical benefit, including evaluation of the effects on patient and/or community outcomes, diagnosis and treatment, as well as cost-effectiveness.
2. Any new malaria diagnostic tests, including both HSPOCTs and RDTs, should ideally meet the ASSURED (Affordable, Sensitive, Specific, User-friendly, Rapid

and Robust, Equipment-free, Delivered) criteria. Impact studies should follow independent HSPOCT performance assessments through i) laboratory studies using well-characterized reference samples, and ii) a systematic review of field-based accuracy studies across a range of transmission settings.

3. The following studies were identified as priorities in determining the clinical accuracy of HSPOCTs and the impact of their use in surveillance and elimination strategies and in the prevention and treatment of MiP:
 - a. to define the sensitivity and specificity of the assay for the detection of malaria in different settings and use case scenarios, studies comparing HSPOCTs to RDTs using quality-assured methods as reference standards were proposed;
 - b. to assess the potential applications of HSPOCTs in accelerating elimination, cluster randomized trials were proposed comparing HSPOCTs to conventional RDTs when used in mass test-and-treat strategies;
 - c. to assess the potential role in surveillance for elimination, studies were proposed evaluating the effectiveness of HSPOCTs vs. conventional RDTs in identifying additional foci of transmission through reactive case detection or proactive case detection; and
 - d. to provide preliminary evidence on the impact of first-trimester low-density malaria infections detectable with HSPOCTs on pregnancy outcomes, a retrospective study of samples from a cohort of women, followed from pre-conception through to delivery, is ongoing. High-quality evidence on the potential role of HSPOCTs in testing for MiP will require individually randomized controlled trials.
4. In areas of low transmission, there are limited data on the natural history of infection and longitudinal infection dynamics. Studies are currently being implemented and planned in African settings to understand the epidemiology of low-density infections in relation to clinical illness, detectability throughout the course of infection, acquisition of protective immunity, and duration of infectiousness.
5. Several other applications for HSPOCTs were considered but determined to be of lower priority. These include the use of HSPOCTs in border screening to prevent importation of malaria parasites, in clinical case management, and in intermittent test-and-treat strategies for MiP.

MPAC conclusions: MPAC reaffirmed its previous conclusion that there was insufficient evidence to determine whether detection of low-density infections using hsRDTs would have a significant impact on clinical outcomes, public health or 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.

MPAC agreed that the proposed research agenda was reasonable, and considered ongoing and planned studies to be useful for providing evidence on diagnostic performance in the populations of intended use, cost-effectiveness and impact for specific use. MPAC did caution that for comparative studies to detect transmission impact, research groups may want to consider standard of care as a comparator, rather than mass drug administration or mass test-and-treat interventions with conventional RDTs, as there are limitations to using both of these comparators. MPAC also requested GMP to revisit the relationship between parasite density and clinical signs and symptoms and the desired thresholds for diagnosis of clinical malaria.

Proposed technical consultation on the role of parasite genetics in malaria surveillance to optimize the response by national programmes

Background: An important role of GMP is the identification of priority policy-relevant research questions and the development of normative guidance in the areas of epidemiological, entomological, insecticide and drug-resistance surveillance. Increasingly, molecular epidemiology has become an important source of information on drug and insecticide resistance. With advances in parasite and mosquito genotyping methods, research into the use of parasite and mosquito genetics in understanding malaria transmission has also increased.

GMP proposes to convene a technical consultation on the role of genetic epidemiology in the understanding of drug resistance gene flow, malaria transmission intensity and elimination surveillance. The focus of this consultation will be on parasite genetics given the potential complexity of convening a single consultation that would be effective in discussing the priority research areas and policy and operational implications of both mosquito and parasite genetic epidemiology and surveillance. The objectives of this technical consultation will be:

1. to review the evidence on the role of parasite genetic epidemiology in the understanding of drug resistance gene flow, malaria transmission intensity and elimination surveillance;
2. to identify key research questions relevant to policy and operational national programme activities;
3. to discuss standards for study designs and data access.

MPAC conclusions: MPAC welcomed the idea of GMP hosting a technical consultation on parasite and vector genetics to assess the 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. Since the proposed scope of the consultation was quite broad, MPAC suggested it would benefit from further focus and refinement in order to prioritize areas that might be more pressing for malaria programmes. NMCPs should be engaged to help prioritize the agenda, potentially by contributing input on key transmission or elimination questions to be answered, or by sharing their perceptions on how the technology could help support programmes.

Examples of relevant use cases might include using parasite genetics for transmission measurement, for case classification in the context of border malaria, or in settings of elimination or prevention of reintroduction activities. Another relevant use for vector genetics could be to assess whether imported parasites from distant geographies are compatible with and can infect local malaria vectors. Additionally, the consultation could provide an overview of genotyping methodologies used and opportunities for standardization. In the longer term, compiling a database of parasite genotypes may be valuable for tracking parasite movement and assessing importation in the context of elimination.

MPAC also noted the importance of training needs to support implementation of relevant technology at national or regional levels, and that this may merit discussion with the Special Programme for Research and Training in Tropical Diseases.

Proposed technical consultation on engaging the private sector for malaria case management in high-burden countries

Background: In February 2018, WHO convened a technical consultation on universal access to core malaria interventions in high-burden countries. The aim was to review the current situation and make recommendations on steps to improve access for those at the highest risk of malaria mortality. In relation to access to malaria diagnosis and treatment, the consultation reviewed the services delivered through different platforms, including public sector, private sector and community-based programmes in high-burden malaria countries. In most of these countries, private sector providers play an important role in malaria case management and are often the first place that patients seek treatment.

WHO plans to convene a technical consultation to distil best practices based on research and programmatic experiences, and to map the key steps towards a coordinated public health engagement of the private sector in improving access to malaria diagnosis and treatment. The private health care system in malaria-endemic countries is highly heterogeneous. The private drug retail sector consists of pharmacies, authorized and informal drug shops, and medicine sellers, which handle a large share of malaria treatment-seeking. The focus of the consultation will be on private health care providers in high-burden malaria countries of Africa, and the objectives will be:

1. to review the data supporting the rationale for an international effort to engage the private sector in malaria case management, reporting of cases, and the evidence base showing that this can be done safely and effectively;
2. to review the laws, regulations and policies influencing the use of medicines and point-of-care diagnostic tests in malaria case management;
3. to identify the main bottlenecks and outline steps, including research priorities, to reduce barriers, thereby enabling improved quality of care for malaria across the entire health sector;
4. to draw upon documented lessons learned from major global, regional and country initiatives to improve malaria case management in the private sector;
5. to review results of recent private sector outlet surveys, and the main determinants of supply and distribution mechanisms for malaria medicines and diagnostics in the private sector; and
6. to identify key lessons learned and best practices from other public health programmes – including family planning, tuberculosis and HIV – with a long history of private sector stakeholder engagement.

MPAC conclusions: MPAC supported the proposed technical consultation on engaging the private sector in malaria case management in high-burden countries. Committee members noted that nearly a decade ago this was an area of substantial work and initiatives supported by many partners. While a revitalization of activity in this area is welcome, it will be critical to build on what has already been done. There is increased interest and momentum across the health sector to address this issue in the context of universal health coverage; malaria programmes should seize the opportunity to strengthen coordination and delivery of health services more broadly.

MPAC recognized that the private sector consists of a complex array of entities, such as formal, informal, and accredited drug dispensing outlets, and that this mix and the

relationship with the public sector vary across countries. One potential area for possible rapid expansion of access to quality case management is to engage pharmacy schools and pharmacist organizations in malaria testing and treatment delivery. Given this complexity and variation, strategies for engagement of the private sector must be tailored to individual country contexts and consider at least two key segments that may be amenable to intervention: 1) accredited pharmacies and 2) private sector for-profit clinics and clinicians. It will be important to explore ways to incentivize participation of the private sector in diagnosis, treatment and reporting, and to work with the relevant regulatory authorities in country to develop effective approaches. The private sector should be included as part of the strategic areas of work in the formulation of national strategic plans for malaria.

Proposed technical consultation on external competence assessment for malaria microscopy

Background: The external competence assessment for malaria microscopy (ECAMM) was started by the WHO Regional Offices for South-East Asia and the Western Pacific and has expanded to the WHO Regional Offices for Africa and the Eastern Mediterranean. In these four regions, a total of 182 ECAMM workshops have been completed, each evaluating 12 participants corresponding to almost 2000 microscopists. Based on the experience acquired over a full decade, WHO plans to review the results of the assessment of microscopists and update the current methodology of ECAMM, including the training approaches, standard operating procedures (SOPs) and e-learning teaching support tools. WHO has compiled the results from ECAMM workshops conducted since 2009 to identify predictors of competence and to evaluate the need to refine the current criteria for the certification of competence in relation to detection, species determination and parasite density estimation.

The proposed technical consultation will have the following four objectives:

1. to review the results of ECAMM workshops conducted since 2009 and to evaluate the need for updating the current WHO criteria for certification of competence in relation to detection, species determination and parasite density calculation;
2. to review experiences of combining ECAMM workshops with different forms of microscopy refresher training, and provide guidance on the ideal mix of training plus assessment, as well as recommendations on revised curricula;
3. to review the variants of malaria microscopy SOPs for slide examination in relation to detection, species determination and parasite density calculation to foster harmonization and common SOPs; and
4. to review the e-learning platforms recently developed for malaria microscopy and their potential application for refresher training and self-assessment.

MPAC conclusions: MPAC strongly supported the proposed technical consultation on external competence assessment for microscopy. Although use of malaria rapid diagnostic tests has increased in recent years, globally there are still over 200 million malaria microscopy slides examined each year.

MPAC members expressed their strong appreciation for WHO's work in this area over the years and noted that it was an excellent example of increasing capacity and

quality performance. Members noted the critical importance of quality microscopy in the elimination and prevention of reintroduction phases, as demonstration of quality diagnosis is a criterion for elimination certification. It was suggested that performance assessment of malaria microscopy should be considered along with assessment of microscopy performance for other diseases and include other health workers involved in laboratory diagnosis of malaria, although it was acknowledged that this would be operationally challenging. MPAC also suggested that it would be useful to explore options to assess competence and extend training to the private sector possibly through cascaded training programmes conducted within countries.

All documentation related to this meeting can be found at: <http://www.who.int/malaria/mpac/oct2018/en/>

All previous MPAC meeting reports can be found here: http://www.who.int/malaria/mpac/meeting_reports/en/

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