On 10–12 April 2019, the World Health Organization (WHO) Malaria Policy Advisory Committee (MPAC) convened to review updates and progress in malaria control and elimination, and to provide guidance on specific thematic areas of work carried out by the Global Malaria Programme (GMP).

The meeting’s eight sessions focused on 11 topics including: 7 updates for guidance (the “High burden to high impact” approach; malaria elimination in the Greater Mekong Subregion; the Strategic Advisory Group on malaria eradication; the GMP policy-making and dissemination process; the Evidence Review Group on mass drug administration; the Malaria Elimination Oversight Committee and STOP-Malaria; the outcome of the technical consultation on external competence assessment for malaria microscopy); 2 updates for information (drug efficacy and resistance; and the Evidence Review Group on malariogenic potential); one update for approval (the RTS,S Malaria Vaccine Implementation Programme and framework for decision-making); and one new process for approval (prioritization of new topics for policy recommendation development).

The key conclusions of MPAC included:

- **“High burden to high impact” (HBHI) approach**: MPAC commended the work of the national malaria control programmes (Ministries of Health) and WHO and partners in support of countries to implement a coordinated response to accelerate progress against malaria. The discussion highlighted the need to move away from short-term technical assistance towards long-term capacity-building, which needs to be embedded in all elements of the approach.

- **RTS,S malaria vaccine implementation and decision-making framework**: MPAC endorsed the proposed “Framework for Policy Decision on RTS,S/AS01 Malaria Vaccine”, noting that the timing of
the suggested analysis will be based on the accumulation of events, currently expected approximately 24 months after introduction. Following MPAC endorsement, the framework is now fully approved by both advisory bodies.

- **Drug efficacy and resistance:** MPAC appreciated the update and noted that the presence of mutants for resistance to artemisinin identified in countries such as Guyana and Papua New Guinea, among others, did not spread from the Greater Mekong Subregion. MPAC noted with concern the issue of poor quality of dihydroartemisinin-piperaquine (DHA-PIP) being used in Africa, with a particular focus on the stability of the DHA component. MPAC requested that WHO propose a course of action to improve the availability of prequalified DHA-PIP to address this urgent risk of spreading resistance.

- **Elimination in the Greater Mekong Subregion:** MPAC noted the considerable progress in the subregion and commended countries, regional offices, and the Mekong Malaria Elimination Programme. The discussion emphasized the continued importance of cross-border collaboration, including collaboration on the regional data-sharing platform, forest malaria, and mobile and migrant populations. MPAC encouraged continued attention to developing and testing specific interventions for resident and transient forest goers, including chemoprophylaxis.

- **Strategic Advisory Group on malaria eradication (SAGme):** MPAC commended the SAGme on its continued progress towards completing its charge and compiling the work packages, acknowledging the important ways forward that have been identified. There was considerable discussion on the conclusion by the SAGme that megatrends favour eradication and concern that this conclusion may be based on the current relationships between malaria transmission and factors like urbanization and climate change. It was noted that these relationships are likely to change over time as vectors adapt to urbanisation, a trend already observed in Africa, and the invasion of vectors into new geographic areas (including An. stephensi into Africa and Sri Lanka).

- **GMP policy-making and dissemination:** MPAC congratulated GMP on improvements to its policy-making and dissemination processes. MPAC welcomed the improved coordination between the WHO Prequalification Team and GMP to reduce timelines, and suggested that formalized scientific advice should include written documentation on the performance criteria and evidence required. MPAC noted that the pre-read documentation and presentation were oriented around potential new products and that it will be important to ensure that the proposed policy pathway also facilitates the development of policy recommendations for new strategies that are agnostic of product. The Committee highlighted the need for global guidance to be flexible enough to enable countries to target resources where they are most needed, as well as the importance of ensuring country input into the entire policy-making process.

- **Prioritization of new topics for policy recommendation development:** MPAC appreciated GMP’s efforts to be more transparent and inclusive in prioritizing the topics for the development of policy guidance and highlighted the need to ensure that country and regional voices are heard. Furthermore, MPAC recognized the differential prioritization of guidance needs in the different regions and asked GMP to propose a strategy to address this issue. MPAC also suggested that criteria for prioritization would be useful, recognizing that capacity and resources are limited.
• **Evidence Review Group (ERG) on mass drug administration (MDA):** MPAC appreciated the work of the ERG and agreed that in this transition period, the MDA recommendations should follow the process and methodology of the WHO Guidelines Review Committee and new GMP Guideline Development Group (GDG). As a result, recommendations listed in the ERG report are not endorsed by MPAC and will be resubmitted for approval by MPAC after full policy recommendation process has been completed.

• **ERG on malarriogenic potential:** MPAC welcomed the results of the ERG on malarriogenic potential and acknowledged that the work will need to continue as new data become available.

• **Malaria Elimination Oversight Committee (MEOC) and STOP-Malaria:** MPAC appreciated the work of the MEOC and the countries that are on track to meet the 2020 elimination milestone of the Global Technical Strategy for Malaria 2016–2030 (GTS). MPAC called on GMP to convene a technical consultation on zoonotic malaria to examine the biology, transmission, classification and implications for control and elimination. The proposed STOP-Malaria pilot programme was strongly endorsed by MPAC. There was a suggestion to consider expanding the programme to HBHI countries, but it was also acknowledged that the technical expertise and skills required in high malaria transmission settings are quite different from those developed in the successful STOP-Polio model.

• **External competence assessment for malaria microscopy consultation:** MPAC endorsed the external competence assessment of the malaria microscopy programme and suggested that GMP invest in an e-learning platform to support training in addition to competence assessment.

**BACKGROUND**

The WHO Global Malaria Programme (GMP) convened the Malaria Policy Advisory Committee (MPAC) for its 15th meeting in Geneva, Switzerland on 10–12 April 2019. MPAC convenes twice annually in Geneva to provide independent strategic advice to WHO on policy recommendations for malaria control and elimination. Over the course of the two-day meeting’s open sessions, 13 MPAC members, four national malaria control programme managers, the WHO Secretariat and over 40 observers discussed the updates and progress in the work areas presented. Conclusions and recommendations to GMP were discussed in the final closed session of the Committee on day three.

The meeting participants were reminded of the procedures governing WHO’s assessment of MPAC members’ declarations of interest. It was noted that the GMP Secretariat requested and received feedback from all the experts present at the meeting regarding their declarations of interest. The following members disclosed various interests: Professor Graham Brown, Professor Thomas Burket, Professor Gabriel Carrasquilla, Professor Umberto D’Alessandro, Professor Abdoulaye Djimde, Professor Azra Ghani, Dr Caroline Jones, Professor Patrick Kachur, and Dr Dyann Wirth. The GMP Secretariat reviewed the disclosures and determined that there were no conflicts of interest with respect to the topics for decision at this meeting.
UPDATES FROM THE GLOBAL MALARIA PROGRAMME

The GMP Director opened the meeting by reminding participants that the malaria-endemic world is becoming increasingly divided into two distinct groups: high-burden countries and countries close to elimination; and that while the world is likely to meet the 2020 elimination milestones of the GTS, it is unlikely to meet the morbidity and mortality targets. He provided a brief summary of the data from the World Malaria Report 2018 and highlighted the “High burden to high impact” (HBHI) approach, which was launched by WHO and the RBM Partnership to End Malaria at the end of 2018 to support countries with a high malaria burden (HBHI was discussed in detail in Session 2). Other updates provided by the Director included the progress made by malaria eliminating countries supported by the E-2020 initiative, progress in the Greater Mekong Subregion (GMS), updates from the Strategic Advisory Group on malaria eradication (SAGme), highlights of the work on policy-making, the imminent start of the Malaria Vaccine Implementation Programme (MVIP), and key meetings and documents launched since the last meeting.

SUMMARY OF THE MPAC SESSIONS

Update on the “High burden to high impact” approach

Background: The HBHI approach is a targeted malaria response that aims to reaffirm commitment and refocus activities initially in the highest burden countries to accelerate progress towards the GTS goals through four response elements: political will, strategic information, better guidance for more targeted and efficient use of resources for optimal impact and coordinated response. Building on a foundation of effective health systems and a multisectoral response, these four mutually reinforcing response elements will support the implementation of prioritized operational plans derived from evidence-informed national malaria strategic plans. In the 10 highest burden countries of Africa, national governments are convening a broad array of global and national partners to kick-start their country-led approach. The process has already started in Uganda and Nigeria, pioneering the way forward for other countries to learn from their experiences.

Representatives from Nigeria, Uganda and India presented key updates from their national programmes and examples of using the HBHI response elements to help accelerate progress with coordinated support from partners. In Uganda, commitment from all levels of the political system is translating into appropriate actions. The President has called for the establishment of a national malaria fund, and civil society has been mobilized to contribute to the Mass Action Against Malaria initiative. In Nigeria, a high-level National Malaria Dialogue is planned for July 2019 to establish increased political responsibility at national and state levels to allocate appropriate levels of domestic funding. India reported 3 million fewer cases in 2017, achieving a 24% reduction compared to 2016. The presentation demonstrated that India’s programme had identified the ingredients necessary to drive down malaria, including strong national leadership and funding, a coordinated response to malaria, a high level of political commitment and the use of strategic information to stratify districts for adequate response. India’s success will provide an example for other countries to follow.

MPAC discussion: MPAC commended the work of the national malaria control programmes (Ministries of Health) and WHO and partners in supporting countries to implement a coordinated response to accelerate progress against malaria. The Committee recognized the value of meaningfully engaging civil society and
empowering communities, but cautioned that this should be done to increase ownership. MPAC noted the need to actively engage academia to ensure that national technical expertise and locally applicable knowledge are used more effectively. MPAC noted that the HBHI approach provides an opportunity to share best practices and to learn from other country experiences. The India experience demonstrates the value of the four response elements, which, when modified to suit the local context, will be applicable to African countries.

MPAC noted that while countries can achieve greater impact with existing tools and resources, achieving elimination will likely require the introduction of new tools. Such new tools should be evidence-based and available to underserved populations. The discussion highlighted the need to move away from short-term technical assistance towards long-term capacity-building, which will need to be embedded in all elements of the approach. MPAC raised the importance of countries sharing their data and information to facilitate planning and cross-border collaboration. MPAC noted the risk of trying to address too many priorities at once, but recognized that the full value of the HBHI approach will be accrued by taking forward all four interdependent and mutually reinforcing response elements in parallel.

**Update on the RTS,S Malaria Vaccine Implementation Programme (MVIP) and Framework for Policy Decision**

**Background:** The MVIP was developed in response to the 2016 WHO recommendation to pilot implementation of the RTS,S/AS01 malaria vaccine. The MVIP is supporting the introduction of the malaria vaccine in selected areas of Ghana, Kenya and Malawi, as well as the evaluation of the programmatic feasibility of delivering a four-dose schedule, the vaccine’s impact on mortality, and its safety in the context of routine use. The primary aim of the Programme is to address outstanding questions related to the public health use of the RTS,S/AS01 malaria vaccine in order to enable a WHO policy decision on the broader use of the vaccine in sub-Saharan Africa. The Programme is jointly coordinated by GMP, the Immunization, Vaccines & Biologicals (IVB) Department and the WHO Regional Office for Africa, in close collaboration with other WHO departments and country offices, ministries of health in pilot countries, PATH and other partners. Introduction of the malaria vaccine is country-led and was launched in April 2019.

A Working Group was established, including representatives from the WHO advisory bodies involved in the policy review that led to the 2016 WHO malaria vaccine position paper. The Working Group reviewed the data and information that had emerged since the 2016 decision and developed the “Framework for Policy Decision” document to present to WHO’s Strategic Advisory Group of Experts (SAGE) on Immunization and MPAC. The Framework provides recommendations on how the data generated by the MVIP can be used to inform WHO policy decisions as such data become available. The Framework provides an opportunity for discussion and alignment prior to key time points for SAGE’s and MPAC’s recommendations to WHO on the broader use of RTS,S/AS01. The following points represent a summary of the Working Group’s recommendations:

1. The SAGE and MPAC should consider recommending a step-wise approach for reviewing and making policy decisions on the broader use of RTS,S/AS01 based on emerging pilot data.

   **Step 1:** A WHO policy recommendation on the use of RTS,S/AS01 beyond the pilot countries could be made if and when:

   i. concerns regarding the safety signals observed in the Phase III trial (related to meningitis, cerebral malaria and sex-specific mortality) are
satisfactorily resolved by demonstrating either a lack of a significant risk during RTS,S/AS01 pilot implementation or an assessment of a positive risk–benefit profile despite adverse event(s); and

ii. either severe malaria or mortality data trends are assessed as consistent with a beneficial impact of the vaccine;

Based on current assumptions across the three MVIP countries related to the expected rate of accumulating events and the timing of vaccine introduction, the required data on safety and impact trends could be available approximately 24 months after RTS,S/AS01 vaccine introduction in the Programme. Once there are preliminary data on event rates, updated estimates can be confirmed within a statistical analysis plan.

Step 2: Adjustments or refinements to the policy recommendation for broader use of RTS,S/AS01 can be made based on the final MVIP dataset, with particular focus on the value of the fourth dose. This final dataset is expected to be available approximately 50 months after the start of vaccination in the third MVIP country.

2. There is a need to resolve safety concerns over meningitis, cerebral malaria and sex–specific mortality to establish the risk–benefit profile of the vaccine, as reassuring safety data are required for a policy recommendation.

3. The policy recommendation for broader use could be made in the absence of data showing a vaccine impact on mortality. Impact on severe malaria is an acceptable interim surrogate indicator for impact on mortality to support a policy recommendation if assessed as consistent with a beneficial impact.

4. A policy recommendation for broader use of RTS,S/AS01 need not be predicated on attaining high coverage (including coverage of the fourth dose). For a newly introduced vaccine, high coverage is frequently not attained until several years after the start of implementation.

5. Barring substantial adverse impact on the coverage of other vaccines or malaria control interventions, the impact of RTS,S/AS01 introduction on the coverage of other vaccines or malaria control interventions will not be major factors influencing a vaccine recommendation. Rather, these indicators should inform strategies for implementation, including opportunities for improvement.

6. Cost–effectiveness estimates should be regularly refined as data become available for increasingly precise calculations and presented at appropriate time points.

7. Expansion within MVIP countries should be synchronized with the recommendation for broader use across sub-Saharan Africa.

8. In the context of the step–wise approach to policy recommendations, the pilots should complete the data collection to establish the public health value of the fourth dose and assess the vaccine’s impact on mortality.

9. Conflicting data among the MVIP countries would require careful investigation into the reasons for such differences. The pilots should continue with plans for analysis, even if data are delayed or not available in all countries.

10. Criteria are suggested that could result in WHO not making a recommendation for use of the RTS,S/AS01 vaccine in routine immunization programmes or that may lead to a decision to defer a policy recommendation to a later time point.
The Framework was endorsed by SAGE during its meeting on 3 April 2019 which was attended by the MPAC chair with other MPAC members participating electronically. The chair of SAGE participated in the MPAC session by phone.

MPAC conclusions: MPAC endorsed the proposed “Framework for Policy Decision on RTS,S/AS01 Malaria Vaccine”, noting that the timing of the suggested analysis will be based on the accumulation of events, currently expected approximately 24 months after introduction. MPAC suggested that the framework document be more concise and that background information should be moved to an accompanying annex. MPAC was informed that an analytical plan is being developed to describe how and when the analyses will be conducted during the course of the pilot including data from household surveys, and community and hospital surveillance systems. Household surveys will inform Information, Education and Communication (IEC) and other mechanisms to address any potential reductions in malaria control interventions that might occur as a consequence of the vaccine implementation. MPAC agreed with the importance of addressing this potential risk, but felt that it should not preclude a recommendation to proceed with implementation if the safety and impact data are supportive. MPAC reinforced the importance of collecting incremental cost-effectiveness data to inform decisions about potential further deployment. Following MPAC endorsement, the framework is now fully approved by both advisory bodies.

Update on drug efficacy and resistance

Background: The situation of antimalarial drug efficacy and resistance focused on special cases. The session included updates on definitions, partial artemisinin resistance, case reports, piperaquine resistance in Africa and advice on data sharing, methods to assess the origin of parasites, the quality control of circulating dihydroartemisinin-piperaquine (DHA-PIP) and marketing of artemisinin-piperaquine. Key definitions included:

- **Antimalarial resistance**: the ability of a parasite strain to survive and/or multiply despite the administration and absorption of a drug given in doses equal to or higher than those usually recommended but within tolerance of the subject;

- **Multidrug resistance (MDR)**: resistance to more than two antimalarial compounds of different chemical classes; usually referring to *P. falciparum* resistance to chloroquine, sulfadoxine-pyrimethamine, and a third antimalarial compound; and

- **Artemisinin resistance**: delayed parasite clearance following treatment with an artesunate monotherapy or with an artemisinin-based combination therapy (ACT); partial resistance would be more appropriate wording.

Reports of partial artemisinin resistance in Guyana, Papua New Guinea, India, Equatorial Guinea, Rwanda and the Horn of Africa were discussed. It is important for investigators reporting resistance to use consistent definitions and to share data with WHO for confirmation. Different methodologies are used to assess the origin of parasites; it would be useful to standardize the minimum information needed to confirm the origin of resistant parasites before publishing findings. Where WHO has investigated, results indicate de novo emergence and potential clonal expansion.

Currently, one DHA-PIP product is prequalified (and another is under evaluation). However, this product is difficult to procure, leaving many generic, non-prequalified compounds of varying quality available on the market. DHA is unstable at temperatures above 30°C, in humid conditions and when in contact with partner medicines. This results in treatment that is effectively piperaquine monotherapy, leading to selection
of resistant parasites; infections with increased copy numbers of Pfplasmepsin2–3, a molecular marker of piperaquine resistance, have been detected in some African countries. There is an urgent need to support quality control of the generic DHA-PIP compounds circulating in Africa and discourage the use of non-prequalified products such as artemisinin-piperaquine.

**MPAC conclusions:** MPAC appreciated the update and noted that the presence of mutants for resistance to artemisinin identified in countries such as Guyana and Papua New Guinea, among others, was not the result of spread from the GMS but arose independently. Key questions raised during the session were on the need for investigators and countries to share information with WHO on a potential public health concern; the need for methodologies to identify the origin of resistant parasites; the need to identify if other potential mechanisms in addition to Pfkelch13 are involved in artemisinin resistance; and the need to consider the half-life of a drug when evaluating the drug efficacy of an ACT.

MPAC noted with concern the issue on the quality of DHA-PIP used in Africa, with a particular focus on the stability of the DHA component. It was noted that there is a lack of availability of WHO prequalified product and that many countries are procuring non-prequalified products. MPAC requested that WHO propose a course of action to improve the availability of prequalified DHA-PIP to address this urgent risk of spreading resistance.

**Update on malaria elimination in the Greater Mekong Subregion (GMS)**

**Background:** Countries of the GMS are accelerating towards their shared goal of malaria elimination by 2030. The six countries – Cambodia, China (specifically Yunnan Province), the Lao People’s Democratic Republic (PDR), Myanmar, Thailand and Vietnam – have achieved remarkable progress. Between 2012 and 2017, the reported number of malaria cases fell by 75% and malaria deaths by 93%. In 2018, the total estimated cases in the GMS remained the same (1% decline) compared to the previous year. Cases are mostly concentrated in a few provinces of Cambodia, Lao PDR and Vietnam. The number of P. vivax cases increased by 32% compared to 2017, while countries made significant progress towards P. falciparum elimination, particularly Cambodia (26% decline), Myanmar (34% decline) and Thailand (39% decline), and China reached zero locally transmitted malaria cases in 2017. The remaining challenges include inadequate case management among high-risk populations (e.g., forest goers in remote areas), delays in rolling out radical treatment for P. vivax malaria, low utilization of insecticide-treated nets (ITNs), and increased population movement into areas of active transmission.

During the 71st World Health Assembly in May 2018, the GMS Ministers of Health signed the Ministerial Call for Action to Eliminate Malaria in the GMS before 2030, renewing their commitment to hastening elimination. The Call for Action urges rapid implementation of the WHO Strategy for malaria elimination in the GMS (2015–2030). This subregional strategy, adopted by GMS Ministers of Health in 2015, aims to eliminate P. falciparum malaria by 2025 and all species of human malaria by 2030.

**MPAC conclusions:** MPAC noted the considerable progress in the Subregion and commended countries, regional offices, and the Mekong Malaria Elimination Programme. There has been significant progress towards P. falciparum elimination, which GMS countries aim to achieve by 2025. The discussion emphasized the continued importance of cross-border collaboration, including collaboration on the regional data-sharing platform, forest malaria and mobile and migrant populations. MPAC
noted that progress in reducing *P. falciparum* cases has been faster than against *P. vivax* (as anticipated), and where increases have occurred, they appear to be *P. vivax*. The use of single-dose tafenoquine might ultimately prove valuable in the radical cure of vivax malaria, but will require a quantitative G6PD testing format before it can be recommended and widely deployed. The continued predominance of falciparum malaria relative to vivax malaria in Viet Nam was noted. This discrepancy may be related to two policies: 1) widespread deployment of 14 days of primaquine for radical cure without G6PD testing which reduces vivax and 2) reliance on DHA-PIP (which appears to be compromised) for falciparum malaria. MPAC encouraged continued attention on developing specific interventions for forest goers, including chemoprophylaxis.

**Update on the Strategic Advisory Group on malaria eradication (SAGme)**

**Background:** The SAGme convened for its fourth meeting to present the preliminary findings and conclusions of six work packages and initial development of overarching conclusions. Members of each work package group met during the first day of the meeting to receive feedback, guidance and course corrections from the Advisory Group to determine the next steps, and presentations to the plenary were completed on the second day. Preliminary conclusions were discussed and will contribute to a final document to be submitted to the WHO Director-General. The SAGme determined that one additional meeting would be required in 2019 to allow sufficient time to digest the findings and foster thoughtful reflection on the final conclusions and recommendations of the SAGme.

The SAGme’s preliminary conclusions were:

1. Global megatrends are likely to contribute to reductions in malaria, but they will not be sufficient to eradicate malaria by 2050, even with a full scale-up of current effective interventions.

2. More can be done with current tools, but new tools are needed to achieve eradication.

3. Good, people-centred health systems will be fundamental to achieving eradication.

4. The willingness of Member States to embark on eradication is likely to be affected by the consequences of and reflections on the polio transition.

5. It will not be possible to estimate costs until the strategy is clearer.

6. Targets for the GTS are achievable, and if achieved will contribute significantly to eradication, but achieving GTS targets alone will not get the world to eradication.

7. In sum, in preparation for the launch of a successful malaria eradication campaign, the GTS 2030 targets must be met along with several key conditions.

It was agreed that the most effective way to capture the contributions of all work packages would be through a final report coordinated by the GMP Secretariat. An interim outline and draft executive summary will be presented at the next meeting.
**MPAC conclusions:** MPAC commended the SAGme on continuing its progress towards completing its charge and compiling the work packages, acknowledging the important ways forward identified. The Secretariat confirmed that malaria eradication remains the ultimate goal and that the 1955 resolution is reinforced by the GTS vision of a world free of malaria. There was considerable discussion on the SAGme’s preliminary conclusion that megatrends favour eradication as the relationships between the transmission system and factors like urbanization and climate change are likely to change over time. Key examples are the adaptation of *Anopheles gambiae* to less pristine urban and peri-urban breeding sites and the expansion of *An. stephensi* to the Horn of Africa. There was a suggestion to consider how to capture the global political and cultural dimensions that influence effective progress or reversals, but it was acknowledged that such an analysis would not be straightforward.

MPAC noted that the current global situation is consistent with observations at the end of the 20th century eradication effort, in that the most concerning settings remain rural tropical Africa and forests in Southeast Asia and South America. The Committee recommended that the presentation of economic benefits should be communicated in terms of absolute numbers rather than relative growth in global gross domestic product. MPAC observed that elimination country by country is the current paradigm, but that subnational elimination should also be promoted. The importance of continuing research and development until malaria is eradicated is captured in the conclusions of the SAGme, but the need for continued basic research must also be clearly articulated. MPAC noted that setting an unrealistic date for eradication has the risk of reducing credibility with both Member States and potential funders.

**Update on the GMP policy-making and dissemination process**

**Background:** In May 2018, GMP launched a deep review of its malaria policy-making and dissemination processes with the aim of ensuring the timely delivery of high-quality and evidence-based guidance to Member States. This initiative gathered input from a broad range of stakeholders, seeking to better understand the needs and perceived bottlenecks, and highlighted areas requiring improvement such as a perceived lack of transparency, inconsistencies in review standards, and lengthy timelines. At the beginning of 2019, GMP launched internal workstreams to lead the implementation of the recommendations in three main areas of work: better anticipation, policy development and optimizing uptake.

A key part of the process will be a consensus-building effort to identify the unmet and partially met public health needs related to malaria to frame the prioritization of WHO’s work. A horizon-scanning process that identifies new evidence to support the development of new or updated policy recommendations will be formalized. Part of this process will be to engage with product development partnerships and tool developers on their target product profiles, jointly with the WHO Prequalification (PQ) Team, to provide formalized scientific advice on the performance criteria and evidence needed to support a policy recommendation and a PQ assessment. Where priority gaps exist, WHO may lead a process to develop preferred product characteristics to stimulate innovation. To streamline the process, GMP is exploring whether sufficient data for products other than vector control are available at the time of submission for registration to a stringent regulatory authority to trigger the policy recommendation development. For vector control products not covered by WHO policy recommendations, generation of data on epidemiological impact is required before WHO can consider issuing a new policy recommendation. Guidance on study designs and assessment of trial data is supported by the Vector Control Advisory Committee. The modification of PQ eligibility criteria is another opportunity to streamline so that the prequalification and MPAC recommendation processes can operate in parallel. The vision is to have a simultaneous launch of the policy recommendation and PQ listing to facilitate the procurement and introduction of new effective, safe and quality tools for impact at country level.
As part of the work to clarify the policy-making process, GMP has clarified the work of its advisory bodies. MPAC remains GMP’s highest level advisory body. For the development of policy recommendations, GMP will convene a single Guideline Development Group (GDG) to ensure consistency and coherence across the department. The GDG will also rely on Evidence Review Groups (ERGs) to support their work. Finally, other advisory bodies will continue to advise GMP on specific areas of technical work, including the Malaria Elimination Oversight Committee (MEOC), the Malaria Elimination Certification Panel (MECP), the Vector Control Advisory Group (VCAG), the SAGme and ad hoc technical consultations.

GMP has also looked carefully at how to optimize the dissemination of new guidance and uptake at country level. Following advice from the field, the document taxonomy and structure will be simplified and harmonized across the department. A compendium of existing guidance was suggested and has been developed as a quick win to put into context all existing guidance on malaria prevention, diagnosis, treatment, surveillance and elimination. The policy guidance pages on the website are being redesigned to facilitate access at the country level, and a mobile application with malaria guidance is in development as a companion to the World Malaria Report app. GMP will also better engage its own country and regional staff, as well as partner networks, to ensure that new recommendations are reaching countries for consideration of adoption. Implementation will be monitored and feedback loops from end-users developed to increase usability.

As a first step, GMP will increase the level of transparency around its policy-making process with the launch of a new dedicated section on its website. The malaria community will be able to track the development of new and updated policy recommendations after prioritization at MPAC meetings. In addition, open portals for nominations of unmet public health needs and development of new and updated policy recommendations will be piloted. GMP has aligned itself with the broader transformation agenda on norms and standards across the Organization and is viewed by many as a pathfinder for other departments. Staff from the Norms and Standards Division, the PQ Team and the Department for the Control of Neglected Tropical Diseases participated in the session.

**MPAC conclusions:** MPAC congratulated GMP on the work done to improve its policy-making and dissemination processes. The discussion and feedback were grouped into three major areas related to the process, horizon-scanning and country-level needs. MPAC noted that the pre-read documentation and presentation were oriented around potential new products and that it will be important to ensure that the proposed policy pathway also facilitates the development of policy recommendations for new strategies that are agnostic of product. Moreover, the dialogue with regulatory authorities, particularly with respect to European Medicines Agency Article 58, will be important. MPAC welcomed the improved coordination between the WHO PQ Team and GMP to reduce timelines, and suggested that formalized scientific advice should include written documentation on the performance criteria and evidence required. MPAC highlighted that it will be important to further articulate the steps at each stage of the pathway and commended the intention to better link policy recommendations to the corresponding prequalified products.

Related to the horizon-scanning process, MPAC noted the importance of involving research investigators and industry at an early stage and thinking about future and current needs. Developing consensus around priority unmet public health needs related to malaria is a good first step in stimulating innovators to think about the problems and could provide links to a grand challenge type approach. The importance of addressing implementation gaps and using existing tools in a more efficient manner was also raised.
MPAC acknowledged the challenge of developing global-level policy that must be interpreted in local contexts, and raised the importance of addressing capacity gaps in WHO regional and country offices so as to support countries to optimize uptake. The Committee highlighted the need for global guidance to be flexible enough to enable countries to target resources where they are most needed, and the importance of ensuring country input into the entire policy-making process. If countries decide to implement strategies that go beyond current recommendations, they should be guided on data collection to inform future recommendations.

**Prioritization of new topics for policy recommendation development**

**Background:** As part of the new policy-making process, GMP proposed to present potential topics for developing new or updated policy recommendations over the coming six to twelve months, for discussion and prioritization at MPAC meetings. This initial list was informed by the likely feasibility of conducting the required work in the short to medium term, and did not represent a comprehensive list of all topics requiring the development of new or amended policy recommendations. The four new topics proposed for policy recommendation development were: reactive strategies, housing modifications for vector control, vector control in emergency settings and single-dose tafenoquine for radical cure of *P. vivax* malaria (to be recommended with a point-of-care quantitative G6PD test). Existing recommendations suggested for potential update based on a review of available evidence were divided into recommendations for prevention and recommendations for case management, as follows:

Current recommendations for prevention (malaria vector control and chemoprevention):

- potential revision of the indoor residual spraying (IRS) tables based on an expanded systematic review of the literature;
- formulation of a policy recommendation on the impact of pyrethroid resistance on ITN effectiveness;
- expansion of reviews to include explicit mention of the resources required to implement certain interventions;
- evidence review on pyrethroid-PBO nets, based on the recently published Cochrane review;
- chemoprevention for special risk groups – review of new evidence on intermittent preventive treatment in pregnancy (IPTp) and in infants (IPTi) and seasonal malaria chemoprevention (SMC); and
- chemoprevention in travellers (with International Travel and Health Group).

Current recommendations for case management of malaria:

- treating uncomplicated *P. falciparum* malaria – potential addition of ACT, review of dose recommendation;
- treating uncomplicated *P. falciparum* malaria in special risk groups – complete review of ACTs in the first trimester of pregnancy, in patients <5 kg, in HIV patients and in travellers;
• preventing relapse in *P. vivax* or *P. ovale* malaria – review of recommendation on treatment for people with G6PD deficiency (dosing); and

• update on mass drug administration (MDA) policy recommendations.

Two emerging topics were proposed:

• *An. stephensi* invasion into new geographical areas; and

• testing and treatment at ports of entry.

**MPAC conclusions:** MPAC appreciated GMP’s efforts to be more transparent and inclusive in prioritizing topics for the development of policy guidance and highlighted the need to ensure that country and regional voices are included in the process. Furthermore, MPAC recognized the differential prioritization for guidance needs in the different regions and asked GMP to propose a strategy to address this issue. It was suggested that criteria for prioritization would be useful, recognizing that capacity and resources are limited. The Committee highlighted the need for guidance on monitoring the quality of intervention implementation.

MPAC endorsed the four proposals for development of new policy recommendations, with some suggestions for each:

• Reactive strategies: The Committee agreed that this was an important topic, but that clear definitions of terms need to be provided to clarify the strategies to be reviewed. It was noted that reactive approaches to index cases in elimination settings are highly heterogeneous, requiring different methods in different epidemiologic settings. Moreover, conducting randomized clinical trials to collect evidence may not be possible. Given the large amount of resources being spent in this area, MPAC agreed that it would be useful for the Secretariat to collate and synthesize available evidence to inform policy development. It would also be useful to provide guidance to countries implementing such strategies on the data collection needed to improve guidance in the future.

• Housing modifications for vector control: MPAC agreed that housing modifications have historically and will likely continue to play an important role in malaria transmission but that housing modification is a broad term and that it will be useful to conduct a review of the evidence on which components of housing modifications have an effect in different contexts. A number of questions were raised as to use cases and how to make potential house modification recommendations affordable and implementable.

• Vector control in emergency settings: The evidence review was endorsed, and it was clarified that this generally does not include epidemics or outbreak settings, but applies to natural disasters and man-made disasters that lead to population displacements, food scarcity, and health systems disruption, causing excess mortality and morbidity in affected populations. Vector control in these settings should, ideally, be deployed before an epidemic/outbreak occurs in consultation and partnership with local leaders.

• Tafenoquine: MPAC noted that tafenoquine has been approved by the United States Federal Drug Administration and that it could be an important tool for eliminating *P. vivax* in some areas. It was also noted that while the evidence reviews can be launched, a recommendation will be dependent on the availability of a quantitative G6PD deficiency point-of-care test.
During the session, several other suggestions were made on important topics for new and updated policy recommendations. It was recognized that capacity is finite, so GMP will need to prioritize based on evidence available, potential impact and urgency. Other suggestions included:

- mass screening and treatment in pregnancy compared to IPTp, and at what transmission level IPTp should stop;
- expansion of the proposed scoping on An. stephensi to take a broader look at urban malaria transmission to include the adaptation of the An. gambiae complex to urban polluted breeding sites;
- chemoprevention in special groups, which has particular implications in terms of safety assessment and may include uses outside of current WHO recommendations;
- specification of the duration for which mefloquine prophylaxis can be given safely; and
- strategies to prevent P. vivax relapse, which are a high priority for the Americas.

MPAC strongly endorsed the value of piloting an online policy nomination portal to seek input from countries and partners on other priority topics for policy making.

**Update on the Evidence review group on mass drug administration**

**Background:** In 2015, WHO recommended that the use of time-limited MDA in combination with other malaria control measures could be considered in the following scenarios: in areas approaching interruption of P. falciparum transmission; in the GMS as a component of accelerated malaria elimination efforts; and in epidemics and complex emergencies to reduce morbidity and mortality. Since WHO’s recommendation, new studies were conducted in areas of low to moderate transmission in Africa and in the GMS, generating additional data on the role of MDA in rapidly reducing transmission. WHO convened an ERG to revise and refine the current recommendations on MDA to accelerate malaria elimination, focusing on the evidence emerging from several studies in African countries and the GMS.

The ERG proposed that the existing recommendations on MDA be updated and replaced by the following draft recommendations, which were submitted for consideration to MPAC.

1. Use of MDA to accelerate progress towards elimination of P. falciparum malaria can be considered in areas of very low to low transmission (parasite prevalence <10%) where there is good access to effective treatment and effective implementation of vector control and surveillance, and limited risk of re-introduction of infection. MDA can be considered in small islands (<500 000 population) with moderate transmission (parasite prevalence 10–15%) where there is limited risk of re-introduction of parasites, effective treatment, and effective implementation of vector control and surveillance.

2. In settings with moderate to high transmission, MDA may produce a short-term reduction in malaria burden, but so far there is no evidence that MDA, with or without additional interventions, will accelerate progress towards elimination. More evidence should be gathered to determine whether repeated rounds of
MDA over multiple years in conjunction with other interventions in these settings could sustain reduced transmission.

3. Mass primaquine prophylactic treatment, requiring pre-seasonal MDA with daily administration of primaquine for two weeks, can be considered as a component of *P. vivax* elimination strategies in temperate regions, taking into consideration G6PD deficiency.

4. Given the threat of *P. falciparum* multidrug resistance and the WHO call for malaria elimination in the GMS, MDA should be considered as a component of accelerated malaria elimination efforts in the GMS where there is good access to effective treatment and effective implementation of vector control and surveillance, and limited risk of re-introduction of infection. Because of the prevalence of multidrug resistance in the region, the options for effective antimalarials that can be used in MDA are limited.

5. Use of time-limited MDA to rapidly reduce malaria morbidity and mortality may be considered for epidemic control as part of the initial response, along with the urgent introduction of other interventions.

6. Use of time-limited MDA to reduce malaria morbidity and mortality may be considered in complex emergencies, during exceptional circumstances when the health system is overwhelmed and unable to serve the affected communities.

7. Medicines used for MDA must be of proven efficacy in the implementation area and preferably have a long half-life. WHO recommends that a medicine different from that used for first-line treatment be used for MDA to reduce the risk of development of resistance. Programmes should include drug safety monitoring during MDA campaigns. Drug efficacy should be monitored after the campaign to identify potential emergence of resistance to the antimalarial medicines deployed for MDA.

8. WHO supports the need for more research on the optimum methods for implementing MDA programmes, promoting community engagement and compliance with treatment, and evaluating the effectiveness of MDA programmes. Modelling can help guide the optimum method for administering MDA in different epidemiological circumstances and help predict its likely impact.

**MPAC conclusions:** MPAC appreciated the work of the ERG and agreed that in this transition period, the MDA recommendations should follow the process and methodology of the WHO Guidelines Review Committee and new GMP Guideline Development Group (GDG). As a result, recommendations listed in the ERG report are not endorsed by MPAC and will be resubmitted for approval by MPAC after the full policy recommendation process has been completed.

MPAC had several comments regarding the ERG recommendations:

- MPAC expressed some concern with the proposed wording of recommendations two, three and four, as they seemed to contradict recommendation one and may be difficult to interpret at country level. MPAC emphasized that current evidence indicates that MDA must be thought of as part of a package together with other interventions, including surveillance and vector control, and that its goal should be to reduce transmission to the point that intensive, case- and focus-based activities can be initiated. The Committee suggested that the proposed recommendations should more clearly articulate what "limited risk of re-introduction" means.
• MPAC also called out areas where more evidence is needed to provide better guidance on MDA to countries, including:

• guidance from GMP on study designs and new approaches to measure the impact of MDA in very low transmission settings, as traditional community-randomized controlled approaches are not always feasible and so implementation can be used to generate evidence through ‘learning by doing’;

• guidance on MDA for *P. vivax* in tropical areas with seasonal transmission;

• specification of the level of intervention coverage needed, frequency, number of rounds and duration; and

• determination of the influence of serial non-compliers on the impact of MDA (experience from Neglected Tropical Disease programmes could be useful).

### Update on the Evidence review group on malariogenic potential

**Background:** Malariogenic potential is the risk of transmission in a given area; it arises from a combination of receptivity (inherent potential of the vector–human ecosystem to transmit malaria), vulnerability (traditionally used within malaria to refer to the risk of importation of parasites) and infectivity (vector–parasite compatibility). Malariogenic potential is a critical factor in determining strategies to achieve elimination and prevent re-establishment of transmission. WHO recommends that countries approaching elimination or working to prevent re-establishment of malaria stratify their geographical units by malariogenic potential to help target appropriate interventions. WHO also recommends that this assessment determine whether vector control can be withdrawn after transmission is interrupted in an area. There is a lack of guidance on methods to measure the components of malariogenic potential and on thresholds relevant for programmatic decisions. WHO convened an ERG to review methods reported in the literature to measure receptivity and vulnerability, and to review evidence on incompatibility between vectors and parasite strains from other regions.

The ERG proposed the following conclusions for consideration by MPAC:


2. Update the WHO *Malaria surveillance, monitoring & evaluation: a reference manual* to:
   a. clearly articulate the importance for entomological surveillance to identify principal versus secondary vectors, given ongoing and likely temporal and spatial changes in vector distribution and abundance; and
   b. provide more detailed guidance on site selection and on the frequency and timing of entomological surveillance in order to inform the assessment of receptivity.

3. Revise other current WHO guidance documents in line with points (1) and (2) in order to ensure consistency.

4. Give priority to further development of methods for assessing malariogenic potential (receptivity, importation risk and infectivity) to ensure that these are applicable and informative for programmatic use.
5. Identify relevant and feasible methods for measurement of the components of malarialogenic potential, interpret these measurements, and develop thresholds to guide programmatic decision-making with regard to maintenance of vector control and intensified surveillance.

6. Further evaluate the issue of infectivity with respect to the mosquito and parasite factors that may reduce vector competence for different strains of *Plasmodium* to determine whether there are programmatic implications for these findings. This may require additional review of evidence in the future.

**MPAC conclusions:** MPAC welcomed the results of the ERG on malarialogenic potential and acknowledged that the work will need to continue as new data become available. There was some debate over both the definitions of the terms and how to measure the components of malarialogenic potential. Because many readers are confused by different meanings of the words vulnerability, infectivity and vectorial capacity, it MPAC suggested that definitions should be restated whenever these terms are used. The proposed modifications will be submitted to the panel that advises on WHO malaria terminology. Key questions for continued work included:

- How should vulnerability, infectivity and vectorial capacity be measured?
- What components does it make most sense to measure?
- Do national programmes need to redefine the terms each time they are used?

MPAC suggested that new serological methods could be useful additions to the parameters, and expressed concerns over not just metrics and measurement but how the data can be used to support country programmes. It was noted that defining vectorial capacity by classic entomological parameters is beyond the capacity of almost all country programmes.

**Update on the Malaria Elimination Oversight Committee (MEOC) and STOP-Malaria**

**Background:** The third meeting of the MEOC was held in February 2019; seven countries (Belize, Bhutan, Cabo Verde, Costa Rica, Malaysia, Suriname and Timor-Leste) considered on track for elimination by 2020 were invited for focused review sessions to examine their programme’s performance and achievements and to identify additional issues that could be addressed to improve effectiveness. Each eliminating country presented on their progress towards elimination and their programme’s activities, successes and challenges. All countries except for Costa Rica reported a reduction in case numbers in 2018 compared with 2017, and two countries (Malaysia and Timor-Leste) reported zero indigenous malaria cases in 2018. The MEOC developed individual country recommendations in collaboration with the national programme managers, WHO and Global Fund staff, as well as overarching recommendations to WHO and partners.

The overarching recommendations from the MEOC meeting included:

1. The MEOC recognized the critical importance of Global Fund resources in helping many countries to achieve elimination, and made the following observations:
   
a. It is vitally important to continue to support surveillance and response plans in countries on the verge of elimination, until certification (and beyond) while countries remain receptive and at risk of malaria importation.
b. Funds could be earmarked to higher burden countries that border eliminating countries in order to reduce transmission in cross-border foci. Alternatively, these areas might be considered and funded as ‘special intervention zones’.

c. It would be helpful to encourage country coordinating mechanisms (CCMs) with shared borders to enter into a formal dialogue.

d. Creating opportunities for WHO to brief members of the Global Fund Technical Review Panel, Technical Evaluation Reference Group and portfolio managers on elimination strategies and challenges that could be better addressed in Global Fund grants would be helpful.

e. Encouraging catalytic and contingency fund mechanisms available on an emergency basis to address outbreaks could support countries close to elimination and prone to outbreaks.

2. WHO should advise countries when they are implementing strategies that are not recommended by WHO (e.g., using long-lasting insecticidal nets [LLINs] and IRS concurrently to target the same vector).

3. The MEOC should study regional initiatives such as the Regional Malaria Elimination Initiative in Mesoamerica to understand how they support elimination.

4. WHO should develop a structured approach to programme auditing.

5. WHO should develop clear and rational criteria for the classification of malaria cases (indigenous, imported, introduced, etc.).

**STOP-Malaria**

At present, many countries with elimination goals lack the skilled human resources and experience with surveillance and response to achieve their objective. Updated national elimination guidelines, tools for case-based surveillance, guidance for focus investigations, reliable supervision and monitoring systems, entomological expertise to inform surveillance and response activities, appropriate data management and analysis capacity, and the communications strategies to engage health providers and communities may all be inadequate to attain elimination and approach certification.

To address the shortage of skilled staff and build such capacity in these countries, GMP, through the WHO regional and country offices, is looking to replicate the successful model of the 20-year-old Stop Transmission of Polio (STOP-Polio) programme, which is part of the Global Polio Eradication Initiative.

The objectives of STOP-Malaria are to strengthen the subnational technical and operational capacity of malaria-eliminating countries to eliminate the last foci of transmission in the country. The initiative will provide an ongoing source of well-qualified, field-oriented technical staff, trained and monitored jointly by the three levels of WHO and the United States Centers for Disease Control and Prevention (CDC). The initiative will also provide additional training to in-country staff to improve their capacity to eliminate malaria transmission. GMP is launching a pilot STOP-Malaria programme to rapidly roll out subnational assistance to five eliminating countries, while testing the basic approach and administrative requirements and preparing a larger proposal to funders that will be needed for a sustained programme. The first STOP-Malaria fellows will participate in training and begin their assignments by October 2019.
MPAC conclusions: MPAC appreciated the work of the MEOC and the countries that are on track to meet the 2020 elimination milestone of the GTS. MPAC noted the challenge of classifying malaria cases as indigenous, imported or introduced, the difficulties in addressing malaria at borders with countries with high endemicity, and the dependence on external funding in some countries. The MEOC brought to MPAC’s attention the issue of zoonotic malaria cases and the potential risk it poses to achieving elimination in Malaysia. The Malaria Elimination Certification Panel (MECP) will consider the implications for Malaysia in the context that, to date, there has been no evidence of human–vector–human infection. MPAC called on GMP to convene a technical consultation on zoonotic malaria to examine the biology, transmission, classification and implications for control and elimination.

The proposed STOP-Malaria pilot programme was strongly endorsed by MPAC. MPAC members appreciated the fact that many potential STOP-Malaria participants might be in a position to apply their experience in elimination settings to high burden malaria settings in their home nations. There was a suggestion to consider expanding the programme to HBHI countries, but it was also acknowledged that the technical expertise and skills required in high malaria transmission settings are quite different from those developed in the successful STOP-Polio model.

Outcome of the technical consultation on external competence assessment of malaria microscopy

Background: The detection of malaria parasites by light microscopy remains one of the main reference methods for diagnosis of malaria worldwide. There are multiple reports of poor microscopy results in malaria-endemic countries as well as in high-income countries where malaria is not present. The diagnostic performance of light microscopy is influenced by multiple factors, including the competence of the microscopist in examining blood films for malaria, the supply of reliable equipment and quality reagents, supportive supervision and cross-checking, the workload of the microscopist and the workplace environment. A model for competence assessment of malaria microscopists was initiated by the WHO Regional Office for the Western Pacific (WPRO) in 2006, and was further refined in 2008 to become the WHO external competence assessment of malaria microscopists (ECAMM). The scheme has been successfully implemented in many countries across four WHO regions with over a decade of activities involving participants from 63 malaria-endemic countries. GMP convened a technical consultation to review progress and provide guidance for the future of ECAMM.

MPAC conclusions: MPAC endorsed the ECAMM programme and suggested that GMP invest in an e-learning platform to support additional training in malaria microscopy in addition to the continued investments in external competence assessment.