Global **Malaria** Programme

WHO Malaria Policy Advisory Committee (MPAC) meeting

OCTOBER 2019

MEETING REPORT

SUMMARY

On 2–4 October 2019, the World Health Organization (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 14 topics: (1) an update on the "High burden to high impact" approach and the "One WHO Africa malaria programme"; (2) an update on the RTS,S Malaria Vaccine Implementation Programme; (3) an update from the Malaria Vaccine Advisory Committee; (4) the use of non-pharmaceutical forms of *Artemisia*; (5) an update on malaria elimination in the Greater Mekong Subregion; (6) an update on the Strategic Advisory Group on malaria eradication; (7) an update on the informal consultation to reconsider the formulation of malaria policy guidance; (8) a technical consultation to review the role of drugs in malaria prevention for people living in endemic settings; (9) an update on the technical consultation on malaria case management in the private sector in high-burden countries; (10) an update on the technical consultation on institutionalizing integrated community case management; (11) an update on the technical consultation on genomic surveillance; (12) an update on the technical consultation on *Anopheles stephensi*; (13) the revision of the WHO classification of glucose-6-phosphate dehydrogenase variants and the International Classification of Diseases; and (14) an update on Malaria Elimination 2020 and STOP-Malaria.

The key conclusions of MPAC to GMP included:

- **"High burden to high impact" (HBHI) approach:** Reflecting the Director-General's request for MPAC to prioritize advising WHO on how to restore and maintain progress in the 11 HBHI countries, the Committee chair and membership noted the considerable progress that had been made by countries since the last update and congratulated GMP, the regional offices, countries and partners involved.

World Health Organization

- **RTS,S malaria vaccine implementation:** MPAC strongly supports the MVIP and reaffirmed the statement that was approved in August, which will be posted on the GMP website.

- **Malaria Vaccine Advisory Committee (MALVAC):** MPAC expressed strong support for the re-establishment of MALVAC and for strengthening the pipeline of vaccines with a long-term perspective, recognizing vaccines as an additional powerful tool to combat infectious diseases.

- **Use of non-pharmaceutical forms of *Artemisia:*** MPAC agreed with WHO's position against the promotion or use of non-pharmaceutical forms of *Artemisia* for the prevention or treatment of malaria. MPAC members were deeply concerned about the potential life-threatening consequences for malaria patients receiving treatments with suboptimal and/or unknown antimalarial activity or with no or varying amounts of artemisinin and requested that WHO work with the ministries of health and drug regulatory authorities to ensure that safe and effective antimalarial medicines are readily accessible. MPAC recommended that GMP adopt communications strategies that have been used effectively by other WHO programmes to counteract negative campaigns, such as the anti-vaccination campaign.

- **Elimination in the Greater Mekong Subregion (GMS):** MPAC noted that GMS countries significantly reduced the number of malaria cases from 2012 to 2016, but the level of decline did not continue in 2017–2018; the Committee recommended the implementation of case-based surveillance, timely feedback surveillance data and focused actions at subnational levels in all GMS countries.

- **Strategic Advisory Group on malaria eradication (SAGme):** The Committee congratulated the SAGme on its comprehensive efforts and excellent executive summary. The committee further agreed with the conclusion that malaria eradication remains the vision and endorsed GMP and WHO efforts to push forward this agenda.

- **Reconsidering the formulation of malaria policy guidance:** MPAC reviewed and was generally in agreement with the consensus statement emerging from the consultation, with some minor modifications. MPAC requested that the WHO GMP Secretariat support countries in the prioritization exercise and that country programmes and funders embrace the flexibilities and additional data required to optimize the allocation of limited resources for maximum impact.

- **Review of the role of drugs in malaria prevention:** MPAC supported the convening of the technical consultation and suggested that it consider how the goals of malaria prevention could be achieved by using drugs in the context of Universal Health Coverage (UHC).

- **Malaria case management in the private sector in high-burden countries:** MPAC endorsed the recommendations from the technical consultation and supported the calls to identify short-term goals and approaches in addition to long term regulatory changes which might be included in the upcoming Global Fund applications to support interventions.

- **Institutionalizing integrated community case management (iCCM):** MPAC expressed its enthusiastic support for the work to institutionalize and sustain iCCM as a fully integrated delivery strategy within ministries of health and the primary

healthcare strategy. However, MPAC also noted key areas of concern likely to be central to the effectiveness and sustainability of iCCM, including the security of drug supply, particularly for pneumonia and diarrhoea; supportive supervision; and adequate training, including logistics and management issues.

- **Genomic surveillance:** MPAC complimented GMP on the comprehensive and informative technical document and recognized the great potential of genetic surveillance to detect changes in transmission and the emergence and spread of new foci of drug resistance.

- ***Anopheles stephensi:*** MPAC had previously agreed on the potential threat posed by *An. stephensi* to malaria control and elimination and appreciated the publication of the Vector Alert. The discussion noted challenges to managing the threat, potential mechanisms for dissemination, the need for more proactive awareness and the dynamic nature of vector populations, which makes it necessary to enhance country vector surveillance capacity to rapidly detect incursions of new vector species and to continuously update distribution maps.

- **Revision of the WHO classification of glucose-6-phosphate dehydrogenase (G6PD) variants and the International Classification of Diseases (ICD)-11:** MPAC endorsed the need to convene the proposed technical consultation and proposed an additional objective: to investigate what assessment of G6PD activity should be required prior to administration of primaquine or tafenoquine, and whether G6PD testing needs to be repeated before administering each course of treatment with those drugs.

- **Malaria Elimination 2020 and STOP-Malaria:** MPAC recognized the continued progress of countries moving towards elimination and appreciated WHO's work to support countries to achieve elimination and certification of malaria-free status.

BACKGROUND

The WHO Global Malaria Programme (GMP) convened the Malaria Policy Advisory Committee (MPAC) for its 16th meeting in Geneva, Switzerland on 2–4 October 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, 14 MPAC members, five national malaria control programme (NMCP) managers, the WHO Secretariat and over 28 observers discussed 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 members present at the meeting regarding their declarations of interest. The following members disclosed various interests: Professor Graham Brown, Professor Thomas Burkot, 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 reflecting on the two World Health Assembly endorsed strategies related to malaria: the *Global Technical Strategy for Malaria 2016–2030* (GTS) and the *Global Vector Control Response 2017–2030*. Although the world is not on track to meet the 2020 milestones for reducing malaria cases and deaths, it is likely that the elimination targets will be met. Two initiatives focus specifically on supporting countries' acceleration towards the global targets: the "High burden to high impact" (HBHI) response and E-2020. GMP hosted the 3rd Global Forum of malaria eliminating countries in China and supported the certification of Algeria and Argentina as malaria-free which was awarded by the WHO Director General at the World Health Assembly in May. A new area of work is the development of the "One WHO Africa malaria programme" in close coordination with the WHO Regional Offices for Africa (AFRO) and the Eastern Mediterranean (EMRO), which aims to ensure WHO's capacity to support countries. Another key area is the evolution of WHO policy guidance on malaria to enable countries to optimize the impact of national programmes based on local contexts. The summary of the Strategic Advisory Group on malaria eradication (SAGme) was launched in September and the compilation of the work packages will be published by the end of the year. The RTS,S Malaria Vaccine Implementation Programme (MVIP) has now been launched in the three selected African countries (Ghana, Malawi and Kenya), and the Rapid Access Expansion Programme of integrated community case management (iCCM) offers an opportunity to increase case management coverage to the most vulnerable populations.

As part of the broader WHO transformation process to optimize support to Member States, GMP has defined its mission – to provide global leadership on malaria and ensure that Member States have the best guidance and strategic support to implement malaria programmes, progressively realize universal health coverage (UHC), and collectively achieve the GTS goals and targets. GMP's four major functions are: 1) to play a leadership role in malaria, effectively supporting Member States and rallying partners to reach UHC and achieve GTS goals and targets; 2) to share the research agenda and promote the generation of evidence to support global guidance on new tools and strategies to achieve impact; 3) to develop ethical and evidence-based global guidance on malaria with effective dissemination to support their adoption and implementation by NMCPs and other relevant stakeholders; and 4) to monitor and respond to global malaria trends and threats.

SUMMARY OF THE MPAC SESSIONS

Update on the "High burden to high impact" (HBHI) approach

Background: The HBHI approach is a targeted malaria response in the 10 highest burden countries in Africa and India that reaffirms commitment and refocuses activities – initially in the highest burden countries – to accelerate progress towards the GTS goals through four response elements: political will to reduce malaria deaths, strategic information to drive down the burden, better guidance for more targeted and efficient use of resources for optimal impact, and coordinated response. These elements build on a foundation of effective health systems and involve a multisectoral response. The three presentations focused on the overall progress in the 11 high-burden countries with respect to the four response elements of the approach, and presented preliminary results from the review of available data for response element two (strategic information), and a related initiative, the "One WHO Africa malaria programme".

Initial country meetings involving all relevant country stakeholders were held in eight of the 11 countries. During the meetings, countries conducted a self-assessment to question their status quo and think critically, and then produced a log frame of objectives to be achieved and activities to be carried out. Partners and stakeholders were very supportive with a high level of engagement during the process, resulting in increased visibility and political attention for malaria in most countries. Countries identified their needs in the strategic use of information and development of better guidance. The national Roll Back Malaria partnerships were reconstituted or set up in countries where they were not present. Strong NMCPs tend to be supported by strong in-country partnerships.

Preliminary results from the review of available data indicated that most countries did not have a single national malaria data repository linking routine data with non-routine data to trigger actions and support national malaria control activities. There is the need to develop data repositories at national and subnational levels. Progress reviews, including subnational and national impact evaluations, midterm programme reviews and surveillance system assessments, have been initiated in all countries. Stratification and intervention mix analyses are planned for all countries. Key findings from an initial data analysis included the following:

- 43% of the 540 million people in the high-burden countries live in urban areas – a factor that should be considered when planning the intervention mix required.
- There is a high correlation between under-5 all-cause mortality and malaria burden.

The "One WHO Africa malaria programme" aims to provide fit-for-purpose, in-country, international support. This support will include a short-term relocation of the GMP Director to AFRO, placement of one national professional officer (NPO) with relevant skills in each of the 47 endemic countries, consolidation of the resources and capacity of the two WHO regions overseeing African countries, and a deliberate integration of malaria within the health system. It is proposed that the NPOs be deployed to the ministries of health, not to WHO country offices.

MPAC conclusions: Reflecting the Director-General's request to MPAC to prioritize advising WHO on how to restore and maintain progress in the 11 HBHI countries, the Committee chair and membership noted the considerable progress made by countries since the last update and congratulated GMP, the regional offices, countries and partners involved. In addition to this dedicated session, HBHI support and actions were discussed in nearly all subsequent sessions. The Committee noted that this approach should not detract from full implementation of the Global Technical Strategy in all other endemic countries.

It was appreciated that the 11 HBHI countries' reforms and efforts are deliberately intended to provide learnings that can be applied in other settings and that prioritizing the most hard-to-reach and disadvantaged populations is consistent with an approach of progressive universalism. The discussion emphasized the need to support countries to mobilize political will and develop management and an intersectoral approach at national and subnational levels. Members supported the effort to elevate NMCPs and programme managers within the hierarchies of their local ministries.

MPAC was concerned that the health management information systems (HMISs) of most countries do not include data from the private sector and from community health workers (CHWs), even though a significant number of patients are seen by these providers. The Committee felt there is a need to take advantage of digital technologies to improve malaria data collection. MPAC noted with interest the results

of the initial analysis, including the proportion of population residing in urban areas, and emphasized the importance of using data to inform decision-making on the most appropriate intervention mixes for the range of transmission scenarios in countries. The discussion pointed out the need to consider annual population growth in the data analysis. MPAC further noted with concern that even though countries regularly collect data on vectors, they were not using those data for decision-making. MPAC emphasized the urgent need for capacity-building of subnational implementers charged with making decisions on the most appropriate intervention mix in various contexts.

MPAC congratulated GMP for the "One WHO Africa malaria programme", particularly for the proposed short-term relocation of the Director to AFRO to provide direct support to countries. MPAC also endorsed the intention to assign NPOs directly to the ministries of health rather than to WHO country offices.

Update on the RTS,S Malaria Vaccine Implementation Programme (MVIP)

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

WHO welcomed the launch of the world's first malaria vaccine by the Government of Malawi on 23 April 2019, the Government of Ghana on 30 April 2019 and the Government of Kenya on 13 September 2019. Vaccine uptake and coverage are being closely monitored through countries' routine health information systems. The data and feedback received so far suggest good acceptance of the programme by health care workers, caregivers and communities, and generally high demand in areas where communication and sensitization efforts have been strong. Early supervisory visits have identified areas for improvement, and the national immunization programmes (Expanded Programme on Immunization (EPI)) are taking measures to address these issues. There were few reported adverse events following vaccination in Ghana - 40 out of almost 52,000 vaccine doses and more than 28,000 children vaccinated; and 31 in Malawi out of almost 32,000 vaccine doses in more than 18,000 children vaccinated. None of the reported severe adverse events were related to the vaccine. It is anticipated that the first analysis on safety could be done in late 2021, although the timing may change according to the implementation of the program. A recommendation may be issued as early as 2022, and may be able to support maintaining vaccine production.

MPAC conclusions: MPAC strongly supports the MVIP and reaffirmed the statement that was approved in August, which is posted on the GMP website and annexed to this report. During the discussion, it was clarified that RTS,S is cost-effective compared to other malaria control interventions and to other Gavi-supported vaccines, including PCV13, even at higher prices than anticipated. Another point raised was that analyses of Demographic and Health Survey (DHS) data from 27 countries found that 28 million children who did not sleep under a bed net received the DPT vaccine, indicating the potential of the malaria vaccine to reach 60% of the children not covered by other key interventions.

MPAC questioned whether there had been any reaction from anti-vaccination activist groups following the launch of the pilot implementations. There was some social media activity in Ghana claiming that all vaccines are poisonous, but the Ministry of Health responded quickly and strongly, and there have been no further issues.

Update from the Malaria Vaccine Advisory Committee (MALVAC)

Background: MALVAC was re-established during the ongoing pilot implementation of RTS,S/AS01 so that experts can help WHO rearticulate its vision, product preferences and recommendations on malaria vaccine research and development (R&D) priorities. The goal is to accelerate progress towards next-generation malaria vaccines to provide higher protection and reduce transmission. The MALVAC meeting was convened on 17 July 2019, organized after a two-day consultation on the status of malaria vaccine R&D to which a variety of stakeholders were invited to present their activities and perspectives.

During the MALVAC consultation, priority work packages were discussed. Participants agreed that use case scenarios for next-generation malaria vaccines, for example in different epidemiological settings, and the preferences for associated product profiles should be defined. The role of highly effective short-acting products, such as monoclonal antibodies and seasonal vaccination strategies, was discussed. Guidance on product development pathways, trial design and endpoints should be updated to reflect new knowledge and agreed goals. Intermediate thresholds and consensus stage gates could assist in rational resource allocation and disinvestments from failed projects. The best approach to product combination for the development of highly effective multi-stage, multi-component vaccines should be considered. Drawing from available evidence and understanding, the consequences of delayed acquisition of immunity derived from vaccine-induced reduction in natural exposure should inform the development of strategies to manage the potential associated risks. Both *Plasmodium falciparum* and *P. vivax* will be within the scope of MALVAC discussions. The public availability of malaria vaccine clinical activity landscaping should be further supported. Guidance on R&D will support the production of data packages to enable robust policy decisions and subsequent action.

Following the meeting, MALVAC developed a position statement aimed at highlighting its commitment to supporting R&D efforts towards the availability and use of high-impact malaria vaccines. A vaccine is considered an important tool for further reducing disease burden and sustaining momentum towards malaria elimination. Two complementary approaches are recommended: 1) promotion of the short- to medium-term deployment of first-generation vaccine candidates, and 2) support for innovation and discovery to identify and develop highly effective, long-lasting and affordable next-generation malaria vaccines. For this to succeed, the key will be to identify efficient and cost-effective clinical development, financing and regulatory pathways.

MPAC conclusions: MPAC expressed strong support for the re-establishment of MALVAC and for strengthening the pipeline of vaccines with a long-term perspective, recognizing vaccines an additional powerful tool to combat infectious diseases. MPAC noted that the current malaria vaccine pipeline lacks innovation and expressed support for the development of novel and multiple vaccine constructs. MPAC also noted the opportunities offered by ongoing monoclonal antibody research both in terms of fostering a better understanding of how to design innovative vaccine constructs and in terms of developing potential future interventions. It was recognized that the production, distribution and availability of vaccines lead to improved equity and access to health care.

The use of non-pharmaceutical forms of *Artemisia*

Background: Artemisinin-based combination therapies (ACTs), the most widely used antimalarial treatments, are produced using the pure artemisinin compound extracted from the plant *Artemisia annua*. Currently available ACTs can treat all malaria strains globally, despite partial artemisinin resistance in South-East Asia and resistance to some of the partner drugs used in ACTs. However, for those in need in malaria-endemic countries, ACTs are not always available, are only available at high prices, or are of substandard quality. These difficulties form part of the argument being made to promote *Artemisia* plant materials as affordable and self-reliant medicines against malaria.

Traditional herbal remedies have several limitations, especially for treating potentially fatal diseases such as malaria. The main limitations are related to standardization of plant cultivation and preparation of formulations, dosages, quality assurance, and evidence of clinical safety and efficacy. WHO does not support the promotion or use of *Artemisia* plant material in any form for the prevention or treatment of malaria. WHO's position is based on the following considerations:

- The content of *Artemisia* herbal remedies is often insufficient to kill all the parasites and prevent recrudescence.
- The content of artemisinin in *Artemisia* herbal remedies given for malaria treatment and prevention varies substantially and is affected by variations in the content of the plant material and the preparation method.
- To date, *A. afra* has not been found to contain any artemisinin.
- The few clinical studies carried out to determine the safety and efficacy of these products seem methodologically flawed and consequently their results are not reliable.
- Widespread use of *A. annua* herbal remedies could hasten the development and spread of artemisinin resistance. Resistance is more likely to develop and spread when a parasite population is exposed to sub-therapeutic levels of an antimalarial drug. The low and varying artemisinin content of *A. annua* herbal remedies means that widespread use of these remedies could lead to many people having sub-therapeutic artemisinin levels in their blood.
- Artemisinin has a short elimination half-life, meaning that it only remains in the blood at therapeutic levels for a short time. Therefore, artemisinin is not promoted for malaria chemoprophylaxis or prevention in any form.
- Affordable and efficacious treatments for malaria are available. WHO

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