

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.

- **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 delivered through EPI programmes.

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 recommends ACTs for the treatment of uncomplicated *P. falciparum* malaria. Artemisinin partial resistance and resistance to some partner drugs do pose a challenge in parts of South-East Asia. However, there are still highly efficacious ACTs available that can cure all strains of malaria.

MPAC conclusions: Available ACTs in Africa remain fully efficacious for the treatment of malaria. Considering the evidence, 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 antimalarial activity or with no or varying amounts of artemisinin.

Recalling the World Health Assembly resolution WHA60.18, which calls for the progressive removal of oral artemisinin-based monotherapies, MPAC recognized the threat of the widespread use of non-pharmaceutical forms of *A. annua* in fuelling the development of artemisinin resistance. MPAC encouraged countries and partners to continue to improve access to quality-assured treatments, including ACTs, in malaria-endemic countries. An essential part of this access is for countries to have a strong regulatory system in place to protect patients from counterfeit and substandard treatments and to ban the promotion of such products for the prevention and treatment of malaria.

MPAC 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 was particularly concerned about the public dissemination of unverified claims that could mislead health authorities and populations at risk for malaria. 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.

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

Background: GMS countries substantially reduced the number of malaria cases from 2012 to 2018. In 2018 and the first half of 2019, several countries made significant progress towards *P. falciparum* elimination, especially Cambodia, Myanmar and Thailand. From January to June 2019, approximately 79% of cases in the GMS were *P. vivax* or combined cases of *P. vivax* and *P. falciparum*. The remaining cases are concentrated in small geographical areas among forest goers, necessitating a focused and tailored strategy for these populations, including prophylaxis. Priorities in the GMS include targeting high-risk populations such as forest goers and mobile/migrant populations; monitoring drug efficacy and implementing effective national treatment guidelines; and strengthening cross-border collaboration through the regional data-sharing platform and partner coordination. WHO continues to support NMCPs to address challenges and priorities through the Mekong Malaria Elimination programme, which supports communication, partner coordination and cross-country activities.

MPAC conclusions: 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; furthermore, *P. vivax* has become the dominant species in most GMS countries. Elimination of drug-resistant *P. falciparum* and the reduction of *P. vivax* cases remain key challenges for malaria elimination in the GMS. MPAC recommended the continued monitoring of drug efficacy and the update/implementation of national treatment guidelines, including replacing ineffective first-line treatments, implementing a single low dose of primaquine for reducing transmission *P. falciparum*, and implementing *P. vivax* radical cure. The Committee supported the implementation of activities targeting high-risk populations, including forest goers in remote areas and mobile/migrant populations, according to local situations and considering structural drivers. MPAC noted that monthly case data sharing and quarterly surveillance data analysis have been established in all GMS countries through the WHO regional data-sharing platform. The Committee recommended the implementation of case-based surveillance, timely feedback surveillance data and foci actions at subnational levels in all GMS countries.

MPAC noted that the anticipated continuing support for malaria elimination in the GMS from the Global Fund grant for the Regional Artemisinin-resistance Initiative presents an important opportunity to achieve impact in the subregion and encouraged GMS countries to make the political commitment necessary to achieve their goals.

Update on the Strategic Advisory Group for malaria elimination (SAGme)

Background: In 2016, at the request of the WHO Director-General, a group of scientists and public health experts from around the world was brought together to advise WHO on future scenarios for malaria, including whether eradication was feasible. The members of the SAGme analyzed trends and reviewed future projections for the factors and determinants underpinning malaria. The analyses reaffirmed that eradication will result in millions of lives saved and a return on investment of billions of dollars. There were no biological or environmental barriers to malaria eradication identified, and models accounting for a variety of global trends in the human and biophysical environment over the next three decades suggest that the future world will have much lower levels of malaria. However, even with the most optimistic scenarios and projections using current tools, there will still be an estimated 11 million cases of malaria in Africa in 2050.

The SAGme felt that while setting a specific date for eradication is not a promise that can be made, there is a clear agenda, beginning with getting back on track to achieve the goals of the GTS. To help countries reduce malaria burden, eliminate malaria from within their borders and then push towards the vision of eradication, the SAGme called for focused efforts in four areas:

1. R&D for new tools: One of the highest priorities is a renewed R&D agenda to improve the knowledge base and products necessary to achieve eradication. As demonstrated in campaigns against polio and smallpox, implementation research is required until the very end of the programme to adapt strategies to suit local conditions and assess new tools.
2. Access to affordable, good quality, people-centered health services: Health system quality is strongly correlated with malaria progress across the spectrum of malaria endemicity. A strong governance framework will be needed to bring together health systems infrastructure, service delivery, civil society and communities.
3. Surveillance and response: A reliable, rapid and accurate surveillance and response system will be fundamental for dealing with the changes in transmission likely to result from global megatrends in urbanization, climate change and population growth.
4. Subnational, national and regional strategies: Strategies are needed to accurately define populations at risk, ensure that populations at risk are covered with effective interventions to prevent infections, and guarantee that all malaria patients get the care they need in a timely and comprehensive fashion.

Eradication must remain the global vision. This can only be achieved through the reduction of the global burden of malaria and progressive elimination of malaria in countries and regions. Even if the ambitious targets of the GTS are achieved, there will still be much more to be done, with an estimated 32 million cases remaining in 55 endemic countries in 2030. The SAGme recommended reinforcing the GTS with a dynamic series of rolling five-year and 10-year plans. These rolling plans would have clear targets and be subject to rigorous review to ensure responsive modifications to the strategy guided by an evolving risk-assessment and decision-making framework for eradication. With such a high-profile renewed and sustained effort, the platform to launch a successful and time-limited eradication effort can be established.

MPAC conclusions: The Committee congratulated the SAGme on its comprehensive efforts and excellent executive summary and looked forward to the compendium to be published later this year. MPAC agreed with the conclusion that malaria

eradication remains the vision and endorsed GMP and WHO efforts to push forward this agenda. MPAC acknowledged and endorsed the call for a renewed and increased R&D effort and suggested that GMP actively engage the malaria community in enhancing the awareness of the need for continued and innovative research, including new knowledge on the biology, new tools and innovations in implementation and operations. The Committee endorsed the SAGme's recommendation to set ambitious rolling five-year and 10-year goals and to critically evaluate progress on a regular basis, making course corrections. MPAC acknowledged the Lancet Commission's report and recognized the strong alignment in terms of the immediate strategy, including the call for additional R&D.

Update on the informal consultation to reconsider the formulation of malaria policy guidance

Background: WHO uses evidence-informed processes to develop guidance to control malaria. The most robust evidence comes from randomized controlled trials (RCTs), although information from a range of study designs may feed into the policy-making process. RCTs generate evidence under tightly controlled conditions, which led to some malaria policies being overly prescriptive, stipulating that interventions should only be deployed in conditions matching those in the RCTs. The net result is that malaria control efforts may be overly constrained by the way that policy guidance is currently formulated.

As malaria control improves, the underlying heterogeneity in malaria risk is revealed. To further improve control and to maximize the impact of the limited resources available, a problem-solving approach is needed. Such an approach involves the deployment of the most appropriate intervention packages for the range of settings within a country, and implies the need for guidance that allows flexibility in the implementation of recommended tools and strategies.

An informal consultation on 17–18 September 2019 explored the advisability of moving from an approach that formulates guidance based on the conditions in which specific studies were conducted to one that draws on the transferability of study findings to inform policy recommendations. The specific objectives were:

1. to explore how policy recommendations emerging from WHO guideline development processes can be reformulated to increase generalizability, where appropriate, and support problem-solving approaches in malaria control;
2. through consideration of specific examples, to explore the need for – and feasibility of – reformulating malaria policy recommendations; and
3. to articulate principles to guide the formulation of malaria guidance.

Key outcomes of the informal consultation included the identification of common themes and recommendations to prioritize for early review; identification of principles to apply when considering the modification or broadening of existing recommendations or the development of new recommendations that extend beyond available evidence; and the development of a consensus statement.

MPAC conclusions: MPAC reviewed and was generally in agreement with the consensus statement emerging from the consultation, with some minor modifications: The past 15 years have seen a substantial decline in malaria cases and deaths, thanks to the scaling up of essential interventions, driven by increased investment and reduced

commodity costs. This decline has resulted in increased heterogeneity in malaria burden, which demands the effective use of limited resources and better targeting of interventions. Countries are working to develop detailed national strategic plans with robust stratification and tailored subnational intervention mixes, adapted to the local context and available resources to achieve national targets.

The goal remains universal coverage¹ with an appropriate mix of interventions for at-risk populations. There is broad recognition that in many cases, the resources available are not sufficient to fund all of the elements of these national strategic plans. In this situation, countries must make difficult choices, trying to make the best use of the limited resources available. The process of stratification and defining appropriate intervention mixes for each stratum requires additional data and therefore increased investments in the collection of routine data and surveillance systems. MPAC agreed with the conclusions from the consultation:

- Intervention prioritization should not be driven solely by sequentially optimizing single interventions for maximal coverage.
- Instead, intervention prioritization should be based on local evidence and aligned to the specific needs of different epidemiological strata/settings, as defined in the country's national strategic plan.

This new data-driven approach moves away from a one-size-fits-all perspective driven by the national strategic plan. It will be critical that countries monitor and document the impact of these stratified approaches through enhanced surveillance, both to learn from the process and to identify and rapidly mitigate potential problems.

MPAC appreciated the concept of “universal coverage”; in striving to save lives, reduce disease and ultimately eradicate malaria. The Committee encouraged work towards universal coverage of the right mix of interventions, recognizing that the coverage of individual interventions will vary by setting. 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.

Technical consultation to review the role of drugs in malaria prevention for people living in endemic settings

Background: A meeting is planned to review the use of medicines for malaria prevention in endemic countries and to identify opportunities to increase their impact.

Three groups of drug-based strategies are currently recommended by WHO for malaria prevention:

1. Chemoprophylaxis, which is the administration of a medicine, at predefined intervals, to prevent either the development of an infection or progression of an infection to manifest disease. This intervention is used in non-immune travellers or specific risk groups;

¹ Universal coverage for malaria vector control is defined as universal access to and use of appropriate interventions by populations at risk of malaria.

2. Mass drug administration (MDA), which is the delivery of malaria treatment to every member of a defined population or geographic area at the same time to:
 - a. mitigate the worst effects of malaria in epidemic situations or exceptional complex emergencies (e.g., civil unrest, Ebola outbreaks), or
 - b. accelerate progress towards the interruption of transmission;
3. Intermittent preventive treatment (IPT), in which a full treatment course of an antimalarial drug is given to a target group (e.g., infants (IPTi), pregnant women (IPTp), or children under 5 living in intensely seasonal transmission settings (SMC)), regardless of whether the recipient is infected with malaria.

In addition, multicentre studies are evaluating the potential of post-discharge malaria chemoprevention to reduce re-admission and death among children discharged from hospital with anaemia. Several studies have evaluated the potential of IPT in school children.

The term chemoprevention is used to reflect the general approach of using malaria drugs to prevent disease. The IPT strategies and associated policy recommendations were developed during the 1990s and 2000s. However, their implementation has been fragmented and, as a group of strategies, their impact has not been maximized. SMC, recommended in 2012, has been rapidly implemented at a large scale, but large coverage gaps exist and questions have surfaced about the potential to expand the SMC approach to other age groups or settings with longer transmission seasons.

Specific objectives for the upcoming meeting are:

1. to define strategies to maximize the impact of malaria medicines on mortality, morbidity and transmission, based on existing policies for malaria chemoprevention and experience with their implementation;
2. to define the evidence gaps and priority research needed to update WHO policies on malaria chemoprevention.

MPAC conclusions: 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 UHC. Other suggestions for topics to be included in the consultation were:

- Consider the potential to enhance impact by considering additional interventions such as azithromycin including for the prevention of malaria in pregnancy.
- Highlight research questions regarding malaria post-discharge, including factors indicating vulnerability such as inequity, physical factors and poverty, among others.
- Review the safety and cost-effectiveness of mefloquine for chemoprophylaxis, e.g., in troops requiring long-term chemoprophylaxis.
- Identify the factors that have impeded the scale-up of IPTi implementation and how to address those barriers in the future.

- Provide clear guidance for drug developers for R&D with respect to high-risk populations, including pregnant women and young children, particularly in terms of safety, dosing adjustments and new formulations.
- Disseminate WHO recommendations on the use of MDA against *P. falciparum* and develop new recommendations on the use of MDA against *P. vivax*, covering settings with different endemicity levels, including eliminating countries.
- Recognize and review strategies to address the low coverage of malaria chemoprevention among specific high-risk groups within vulnerable populations, e.g., the low coverage of IPTp among primigravidae and adolescents.

Update on the technical consultation on malaria case management in the private sector 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 consultation concluded that the private sector plays an important role in delivering malaria care in many high-burden countries, both in urban areas and in remote rural areas underserved by formal health care facilities. A large proportion of patients with fever first seek treatment through private health care providers, especially pharmacies, authorized and informal drug shops, and other medicine sellers. The quality of case management in these facilities varies widely and is often poor, especially in terms of access to quality ACTs and malaria diagnostic testing prior to treatment.

The private sector could be a valuable source of data for national surveillance systems, particularly where they are a common source of care; however, there is very little experience in including these providers in national HMISs. The integration of the private sector into national efforts to reduce malaria was seen to be an important area of intervention, paving the way for the sector's wider involvement in supporting countries to achieve UHC.

Based on the high proportion of patients accessing care for febrile illness in the formal and informal private sectors, participants were asked to identify the main bottlenecks in accessing quality malaria case management in the private sector in their country and to prioritize steps to reduce barriers, promote best practice and increase access. The following common themes were identified:

- **Promotion:** Governments, NMCPs and other key stakeholders need to generate demand among the population for better quality care in the private health sector. Behavior change and communication activities targeting the general public need to continue to promote malaria diagnostic testing and compliance with the results.
- **Quality of care:** The confidence of all stakeholders in the quality of care that can be delivered by the private sector can be enhanced through: 1) accreditation systems for drug shops; 2) training in malarial and non-malarial fever case management and professional development schemes for private health care providers; 3) supervision of private health care providers, ideally by existing government health care workers; and 4) increasing the availability and affordability of quality diagnostics and medicines.

- **Policy and regulation:** Country policies and regulations should be reviewed and revised to ensure consistency on where mRDTs can be sold and who can perform them, and where antimalarials can be accessed and who can prescribe and/or sell them, taking into account client care-seeking practices and supporting the extension of quality malaria testing to ensure the rational use of malaria medicines. Guidance should be developed and behavior change promoted to ensure that health care providers and patients know what should happen in the event of a negative malaria test result.
- **Market information:** The lack of detailed current information on private sector antimalarial and RDT market dynamics, especially outside the large urban areas, should be addressed and results should be disseminated among all stakeholders. As countries differ, each needs to undertake an in-depth market review, with periodic updates to monitor progress and inform future actions.
- **Surveillance:** Simple systems should be developed to allow the private sector to be fully integrated into national malaria surveillance systems, and providers should be supported to report complete, accurate and timely data through training, supervision and appropriate incentives.
- **Pricing and incentives:** Countries should ensure that quality-assured products crowd out poor-quality and inappropriate products through pricing and other measures that make them preferred by patients and providers. The cost to the caregiver/patient of the testing and treatment package should be affordable and promote appropriate case management, and taxes and tariff systems for finished products should be aligned so that diagnostics are not disadvantaged compared to quality ACTs or other pharmaceutical products.
- **Coordination:** As different stakeholders are not always aligned on how to involve the private sector in delivering quality case management, it is necessary to bring all groups together to work out ways to overcome this constraint, under the stewardship of government.

The consultation concluded that WHO guidance on malaria case management in the private sector should be brought together into a Roadmap (similar to the TB Roadmap) for integrating the private health care sector into national strategies to improve malaria case management. This guidance should provide direction to ministries of health and other national agencies on how best to engage the private sector to deliver quality diagnosis and treatment, and contribute to surveillance and routine reporting of malaria.

MPAC conclusions: MPAC endorsed the recommendations from the technical consultation. Key discussion points included the recognition of the huge diversity in the private sector, acknowledging that these variations are to some extent country-specific. There is a need for each country to have information on malaria case management at multiple levels of its private sector to identify who is doing what and what might be feasible in each context. MPAC supported the WHO-wide approach, in coordination with partners including the Global Fund, USAID and World Bank, to systematically engage the private sector, including the development of survey methods and indicators to collect, map and collate information and promote best practices to improve the quality of care in the private sector across a series of programmes.

MPAC supported the calls to identify short-term goals and approaches in addition to longer term regulatory changes which might be included in the upcoming Global Fund applications to support interventions. MPAC recognized the need to identify the purpose of engaging the private sector and to develop guidelines for improving case management and enhancing reporting to fully map the malaria burden.

Update on the technical consultation on institutionalizing integrated community case management (iCCM)

Background: In 2017, 5.4 million children under the age of 5 died. Nearly half of these deaths occurred in sub-Saharan Africa, where pneumonia, diarrhoea and malaria remain the main causes of death among children aged 1–59 months. Achieving UHC and reaching the child health-related Sustainable Development Goal (SDG) targets will require strong primary health care (PHC) systems and the institutionalization of community health systems. Community Health Workers (CHWs) can effectively deliver a range of preventive, promotive and curative health services, contributing to increased access and reduction in inequities. Since 2012, WHO and UNICEF have recommended iCCM of childhood illness as a community-level component of a comprehensive strategy for Integrated Management of Newborn and Childhood Illness (IMNCI). By targeting hard-to-reach, vulnerable populations and supporting extension of the formal health system to the community level, iCCM increases access to life-saving interventions for malaria, pneumonia and diarrhoea, and promotes rational use of medications, home care, immunization and use of ITNs. To date, over 30 countries have implemented iCCM – mostly at the subnational level – with the support of global development partners, including substantial investments from the Global Fund and the RMNCH Trust Fund through the malaria and Resilient and Sustainable Systems for Health (RSSH) allocations. However, many countries struggle to maintain an acceptable level of quality of care and coverage. Along with proper integration of iCCM in PHC, adequate planning, budgeting and resource mobilization remain a major challenge.

With the aim of promoting the institutionalization of iCCM within PHC systems and comprehensive child health programming, WHO and UNICEF co-organized the technical consultation on institutionalizing iCCM to end preventable child deaths from 22 to 26 July 2019 in Addis Ababa, Ethiopia. The meeting consisted of two connected parts: 1) institutionalizing iCCM to end preventable child deaths and 2) implementing malaria HBHI approaches and iCCM to accelerate reduction of child mortality. The main conclusions and recommendations were as follows:

- iCCM is an effective strategy for reducing morbidity and mortality of common childhood diseases by improving equity in access to and coverage of PHC. Countries with a high burden of under-5 mortality should integrate iCCM into national health policies, strategies and national health sector development plans.
- A national community health policy/strategy should be in place, containing clear, official guidelines for recruiting and motivating CHWs, along with a job description, as well as clear criteria for implementing iCCM with a focus on the hardest to reach populations.
- Domestic and external funding should be targeted at systems strengthening, with an inclusive focus on malaria, pneumonia and diarrhoea, as well as community- and facility-based provision of care.
- iCCM should be included in the national costing exercise and the annual health sector budgeting processes, with specific budget lines.
- To promote institutionalization and sustainability, funding agencies should coordinate iCCM funding with ministries of health and support the ministry of health's iCCM implementation plan, instead of funding isolated projects in different parts of the country.
- iCCM is a key component of a functional PHC system, ensuring a continuum of care from community to health facilities and referral facilities, and delivery of quality care at all levels, including at referral facilities to manage severely ill children referred from the community.

- Attaining the highest level of quality of care at the community level is dependent on competent CHWs empowered through training and mentoring, consistent supply of tools, diagnostics and medicines, and motivation and supervision support as part of the PHC system.
- The supply chain for iCCM should be fully integrated into the existing national supply management system, and iCCM medicines and diagnostics should be part of health facility and district-level quantification, procurement and distribution.
- Supportive supervision of CHWs from the nearest health facilities is core to quality iCCM and needs to be budgeted for and included in district implementation plans. District management teams should promote integrated supervision.
- Government-led, harmonized, streamlined monitoring and evaluation systems need to include quality information and data from community activities to guide action at the local level and ensure accountability and sustained improvement of iCCM programming.
- Community engagement is key to the institutionalization of iCCM. Local communities are central to the planning, implementation and uptake of quality iCCM services

The second part of the consultation focused on the implementation of the HBHI approach and iCCM to accelerate the reduction of child mortality in Africa. The discussion and deliberations were framed according to the four HBHI response elements: 1) political will to reduce malaria mortality; 2) strategic use of information; 3) better guidance, strategies and policies; and 4) coordinated action at country level. The participants raised strong concerns over the limited financial support for the procurement of non-malaria iCCM commodities, namely amoxicillin and ORS+zinc, which could compromise the effectiveness of iCCM programmes in reducing child mortality. The immediate next steps following the technical consultation are:

- to finalize the recommendations for institutionalizing and scaling up iCCM as part of the HBHI approach;
- to update the 2012 UNICEF iCCM joint statement, ensuring wide dissemination, policy adoption and implementation;
- to develop an iCCM district operational manual based on best practices and lessons learned.

MPAC conclusions: MPAC expressed its enthusiastic support for the work to institutionalize and sustain iCCM as a fully integrated delivery strategy within ministries of health. MPAC recognized that CHWs need to be effectively integrated into a functional health system; if the PHC and secondary facilities are dysfunctional, then communities will quickly lose faith in the CHWs. MPAC 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.

It will be important to identify who has ownership of the iCCM strategy within WHO and at country level, as countries will need to develop context-specific algorithms to guide diagnosis and treatment within the iCCM framework. MPAC also noted the need to ensure that CHW records and reporting are integrated into the wider HMIS.

Update on the technical consultation on genomic surveillance

Background: Emerging evidence indicates that genetic epidemiology can create new opportunities for malaria surveillance, prevention and control. In June 2019, GMP convened a technical consultation to review the evidence from research studies on the use of genetics in epidemiology to determine their potential role in the development of future policies and for use by NMCPs to improve programmes. The technical consultation also aimed at establishing a list of global research priorities for the future strategic use of genetic epidemiology.

Strategic next steps

1. The table of research priority areas (Table A1 in the consultation report – MPAC pre-reads) identified during this meeting should be made available online and updated on an annual basis by WHO with help from research networks and individuals.
2. A database of researchers and institutions involved in policy-relevant malaria genetic epidemiology studies should be developed by WHO and updated annually.
3. The use of genetics in epidemiological surveillance shares several overlapping themes across the spectrum of transmission in terms of understanding gene flow in insecticide and drug resistance. Studies should maximize these linkages so that common data generation platforms and samples can be used, wherever possible.
4. In addition to research studies, there are opportunities to explore drug and insecticide resistance monitoring sites: collecting genetic samples during case detection and investigations in elimination settings, and in burden reduction settings, passive case detection systems and household surveys could become the mainstay for genomic surveillance. A structured approach that will not add unnecessary burden to health systems is needed.
5. Stakeholders should work with researchers to ensure that study protocols are designed to generate evidence in formats relevant to policy and programmes. For example, studies exploring the relevance of genomic surveillance metrics must include a comparison to metrics currently recommended by WHO and used by countries in terms of their relevance, reliability, accuracy, precision, cost and sustainability. WHO should work with networks of researchers during the study design stage.
6. Established global databases should be harnessed to develop information products relevant for policy and country operations. WHO should work with groups such as the Wellcome Sanger Institute and BROAD on appropriate information products once policy relevance has been established.
7. Investment in regional and national capacities for genetic epidemiology should be sought. WHO should work with researchers and funders such as the Bill & Melinda Gates Foundation, the United States President's Malaria Initiative, the Global Fund and others on pathways to increase national capacity.

MPAC was asked to provide guidance on key research areas/questions and the strategic next steps.

MPAC conclusions: MPAC complimented GMP on the comprehensive and informative technical document and strongly suggested publishing a version of the document in a widely read journal in addition to dissemination via the normal WHO channels. MPAC noted that there have been significant advances in this field and that applications for the use of *pfhrp2/3* deletion surveillance are ready for implementation at the NMCP level and

have immediate policy application. MPAC encouraged GMP to facilitate this process. Longitudinal surveillance of *pfhrp2/3* deletions will enable NMCPs to anticipate the need to change RDTs. Genetic surveillance for parasite drug resistance markers is already in use in many NMCPs, and MPAC encouraged GMP to establish standard operating procedures that include the correlation of genetic markers with phenotypic data to enable standardized reporting and eventual recommendations for changes in drug regimens. MPAC further noted that the use of parasite genetic surveillance in national and subnational elimination settings has great potential to add evidence to distinguish imported from indigenous cases and encouraged GMP to facilitate access to this technology.

MPAC noted the great advances made in genetic analysis of anopheline mosquitoes, particularly the detection of insecticide resistance markers and the role of gene flow in understanding the spread of insecticide resistance. MPAC saw great potential in the future use of genetic markers to detect insecticide resistance in operational settings; however, it recognized the need for additional research to understand the relationship between phenotype and genotype. MPAC also stressed the importance of accurate morphological identification of mosquito species prior to genetic confirmation of species identities.

MPAC recognized the great potential of genetic surveillance to detect changes in transmission and the emergence and spread of new foci of drug or insecticide resistance. MPAC acknowledged the need for additional research to establish the relationship between specific genetic markers and standard epidemiological indicators. MPAC strongly encouraged GMP to work with partners to establish a standard set of markers and operating procedures so that data can be shared across programmes and knowledge generated in one country can inform other countries as they address similar issues. It was noted that NMCPs should be encouraged to collect dried blood spots and mosquito samples – whenever possible leveraging other ongoing activities – for use in genetic surveillance, as longitudinal samples provide an exceptionally useful form of data. In addition, for countries approaching elimination, genetic data on extant parasites will better enable the distinction between imported and indigenous cases. MPAC also noted that genetic surveillance might be particularly useful in situations of fragile or rapidly changing transmission settings and suggested that future technical consultations include such situations.

Update on the technical consultation on *Anopheles stephensi*

Background: In recent years, *Anopheles stephensi*, an efficient urban malaria vector for both *P. falciparum* and *P. vivax*, has been reported in four countries outside of the previously known geographical range, which was considered to be confined to certain countries in South-East Asia and large parts of the Arabian Peninsula. The first detection outside the traditional geographical range was reported in Djibouti in 2012, in an area between Djibouti City and the Somali border, and confirmed in a follow-up study from 2013 to 2017. In addition, in 2016, the vector was detected for the first time in Mannar Island in Sri Lanka, five years after the country achieved zero malaria transmission. Subsequently, *An. stephensi* was reported in Ethiopia's Somali Regional State and, most recently, in the Red Sea and Gedaref states in East Sudan.

Anopheles stephensi can be a highly efficient malaria vector in its traditional geographical range, particularly in urban environments. The detection of *An. stephensi* in countries outside its established range poses a potential threat to malaria control and elimination. Given the rapid growth of cities in Africa, the potential establishment of this vector in urban environments could put at risk the reductions in malaria burden achieved since 2000. WHO plays a key role in monitoring threats to malaria control, elimination and prevention of re-establishment, and in providing guidance to Member States on how to manage these threats. Recognizing the emergence and spread of *An. stephensi* as a potential threat, WHO convened a technical consultation to assess the current evidence and to define a response strategy.

The technical consultation recommended that WHO develop a Vector Alert document and post it online to urge WHO Member States and their implementing partners in and around the Horn of Africa, Sudan and the surrounding geographical areas, and Sri Lanka to take immediate action. It was recommended that the Vector Alert summarize the current evidence base on the invasion of *An. stephensi*, and to provide detailed recommendations. Subsequently, in August 2019, WHO released the Vector Alert: *Anopheles stephensi* invasion and spread. As recommended in the technical consultation, the Alert covered the following areas: 1) what should African countries, especially those in and around the Horn of Africa, do now?; 2) what should countries do in areas where the vector has been detected?; and 3) how should interventions be monitored and evaluated?

MPAC conclusions: 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 continuously update distribution maps. Key challenges noted included insufficient surveillance capacity, which failed to detect the incursion of *An. stephensi* until it was widely disseminated, and the need for guidance on containment and elimination.

MPAC noted that the potential mechanisms for dissemination included both transport with people and long-distance mosquito migration, and highlighted the need for more acute awareness in terms of both the identification of the vector and guidance on its control. It is critical that researchers holding data related to the reporting of public health threats understand their responsibility to ensure that data are acted upon while waiting for formal publication. Several expansions of malaria vectors in endemic areas were noted in the report and during the discussion, emphasizing the need to strengthen surveillance at points of entry.

Revision of the WHO classification of glucose-6-phosphate dehydrogenase (G6PD) variants and the International Classification of Diseases (ICD)-11

Background: Drugs of the 8-aminoquinoline class, e.g., primaquine and tafenoquine, have important roles to play as the only available agents that are effective against liver stages of *P. vivax* malaria; however, their use is limited because of potentially serious side effects in individuals who are deficient in the enzyme glucose-6-phosphate dehydrogenase (G6PD). Administration of drugs to these individuals can cause acute haemolysis leading to severe anaemia.

G6PD deficiency, an X-linked recessive disorder, is more common in malaria-endemic countries. The gene encoding G6PD is highly polymorphic with over 300 variants. Genotyping alone does not assist in diagnosis because there is variable phenotypic expression in heterozygous females depending on X-inactivation patterns, and variable haemolytic risk following exposure to infections, fava beans or certain medicines.

WHO recommends that G6PD status be known for safe use of primaquine as anti-relapse therapy. This will also apply to tafenoquine, once it is recommended for widespread use. Scale-up of safe and effective radical cure for *P. vivax* is dependent upon the corresponding availability of reliable, quality-assured point-of-care G6PD testing and expansion of our knowledge on the haemolytic risk of various G6PD variants.

A G6PD classification scheme was originally proposed in 1971 by Yoshida et al. This became known as the WHO classification scheme, although the authors never claimed any mandate from WHO. It was slightly revised in 1985 by a WHO Working Group and published, as below, in 1989.

- Class I – associated with chronic non-spherocytic haemolytic anaemia (CNSHA)
- Class II – severely deficient: less than 10% residual activity
- Class III – moderately deficient: 10–60% residual activity
- Class IV – normal activity: 60–150%
- Class V – increased activity

These classifications are somewhat arbitrary and do not account for recent advances in knowledge or the availability of new G6PD point-of-care diagnostic tests at various stages of development. For example, the threshold of 10% activity that separates class II from class III may need revision, as a large number of G6PD variants currently classified as class II and class III have the same clinical manifestations. Furthermore, the definition of “normal” G6PD activity, which was originally set at >60%, has subsequently been set at >70% (for clinical trials with tafenoquine) and >80% of normal (in a WHO consultation on point-of-care G6PD tests in 2015). This definition therefore needs to be reviewed based on the current knowledge of variants and haemolytic risk. The revision of the G6PD classification scheme will be coupled with the revision of the ICD-11, which defines G6PD very narrowly, as only a specific form of acute haemolytic anaemia and not as a genetic metabolic disorder.

The WHO Genomics Initiative, hosted by the WHO Department of Service Delivery and Safety, identified the revision of the WHO G6PD classification scheme as a priority and proposed that GMP convene a technical consultation to revise the classification. The proposed objectives of the consultation are to: 1) revise the most widely used classification of G6PD variants; 2) discuss requirements for defining new variants; and 3) propose a new categorization of G6PD for ICD-11, including classification of G6PD variants and clinical manifestations. The results will immediately impact work on establishing policy and product specifications for point-of-care G6PD tests to guide the use of 8-aminoquinolines for radical cure of *P. vivax*.

MPAC conclusions: 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.

Other key points noted during the discussion included that national programme managers are primarily interested in having a test that gives a yes/no answer as to whether an 8-aminoquinoline drug can be used for treatment. The Committee also noted that it is likely that manufacturers of G6PD tests and 8-aminoquinoline drugs will ask WHO for advice on the cut-off level of G6PD activity required prior to the use of either primaquine or tafenoquine for the treatment and/or prevention of malaria. Therefore, the consultation should investigate appropriate safety cut-off levels for the use of these drugs in different situations. It was also noted that G6PD deficiency is of relevance beyond being a contraindication to 8 aminoquinoline drug administration, for example, in neonatal screening in relation to kernicterus in the newborn, for which MPAC recommended consultation with the WHO Department of Maternal Neonatal and Child Health.

Update on the E-2020 and STOP-Malaria

Background: WHO convened representatives of 21 countries with the potential to eliminate malaria by 2020, known as the E-2020, at the third Global Forum of Malaria-eliminating Countries in Wuxi, China on 18–20 June 2019. Countries described their progress towards elimination and the challenges in achieving this goal. Several countries reported significant progress towards elimination: for the first time, Cabo Verde, the Islamic Republic of Iran, Malaysia and Timor-Leste reported zero indigenous cases since the beginning of 2018, while China and El Salvador maintained their malaria-free status, and the certification of Algeria and Argentina as malaria-free was celebrated. The Malaria Elimination Oversight Committee met in the during the Global Forum and made several key recommendations: 1) There is a need for greater emphasis on identifying and characterizing “key populations” for malaria; 2) diagnosis and treatment of malaria must be assured free of charge and without barriers to undocumented and uninsured people; 3) CHWs must be able to diagnose and treat malaria; and 4) WHO should develop an elimination dashboard to include key national programmatic indicators.

In an analysis of the median number of indigenous malaria cases in the years before attaining zero indigenous cases for the 14 countries that eliminated malaria between 2000 and 2015, 75% of countries reported 51 or fewer cases two years before reaching zero. Countries eliminating more recently have had similar rates of decline, but several started from a higher number of cases. The criteria for the selection of countries to join the elimination initiative for 2025 were discussed at a recent meeting of WHO elimination focal points. Key considerations will be an epidemiological threshold, national elimination goals, and potential political commitment and health system indicators. Greater emphasis will be placed on country ownership, and all countries from the E-2020 initiative that have not yet eliminated will be included.

WHO is preparing an operational manual for the certification of malaria elimination to support NMCPs and certification committees; an accompanying standard operating procedure for WHO pre/certification and certification missions is also in development. There are potentially three countries eligible for certification in 2020 (China, El Salvador and Azerbaijan) and seven countries in 2021 (Cabo Verde, Timor-Leste, Malaysia, Tajikistan, Oman, Egypt, and the Islamic Republic of Iran).

WHO launched the STOP-Malaria programme in Botswana in August 2019, modelled on the STOP-Polio programme to support the last mile of polio elimination managed by WHO and the U.S. Centers for Disease Control and Prevention. The programme recruits experienced public health professionals, provides rigorous training in malaria elimination strategies and deploys three STOPpers for one year at the focus/district level. The current deployments are to Cabo Verde, Namibia and Botswana and include a baseline situation analysis using the malaria elimination audit tool and weekly monitoring. The next cohort is expected to be 6–7 professionals, planned to start in May 2020.

MPAC conclusions: 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. MPAC raised the potential to extend the STOP-Malaria programme to HBHI countries based on the lessons learned from the current pilot programme. It was noted that the model is based on subnational surveillance towards polio elimination and that new terms of reference and training would need to be considered to extend the programme’s utility to high-burden settings.

ANNEX 1

Statement by MPAC on the RTS,S/AS01 malaria vaccine

4 October 2019

Globally, 219 million cases of malaria were reported in 2018, and an estimated 435 000 people, including 260 000 African children, died from malaria in 2017. Scale up of WHO-recommended preventive measures resulted in a substantial decline in malaria morbidity and mortality between 2000 and 2015. However, in 2015 and 2016, progress with malaria control stalled and started to reverse, with an upswing in malaria cases, particularly in sub-Saharan Africa. A malaria vaccine such as RTS,S has the potential to help get malaria control back on track, and may prove to be an important addition to current control tools. The RTS,S vaccine, with its reported level of efficacy, has been shown to provide substantial and significant added protection on top of that provided by optimal case management and high coverage of insecticide-treated mosquito nets (ITNs), reducing clinical malaria by 55% during the 12 months following primary vaccination, and by 39% over 4 years. Recent data from long term follow-up are reassuring regarding its long term efficacy and safety. The well-established Expanded Programme on Immunization can reach even the poorest children, who are generally at highest risk of malaria, and suffer the highest mortality rates.

The opportunity to evaluate the feasibility of delivery, safety and effectiveness of the RTS,S vaccine, through pilot implementation in three countries, comes at a critical time in malaria control: no other malaria vaccine has entered phase 3 clinical trials. Additional preventive tools are in the development pipeline, and MPAC looks forward to reviewing their potential to reduce the malaria burden. However the development, evaluation and deployment of these new tools is expected to take several years. Moreover, it is likely that they will also offer only partial protection.

At a time when the downward trend in malaria cases and deaths has stalled, when our current control efforts are threatened by resistance, and when no new intervention approaching the efficacy of RTS,S is available, MPAC looks forward to reviewing the results of the pilot implementations, in accordance with the Framework for Policy Decision on RTS,S/AS01 approved at the April 2019 MPAC and SAGE meetings. If these results are promising, the RTS,S vaccine, in combination with ITNs and other control measures, is likely to be an important additional tool to change the course of malaria incidence and reduce malaria deaths in African children.

All documentation related to this meeting can be found at:
<https://www.who.int/malaria/mpac/oct2019/en/>

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

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