Global **Malaria** Programme

WHO Malaria Policy Advisory Committee (MPAC) meeting

APRIL 2018

MEETING REPORT

SUMMARY

On 11–13 April 2018, the WHO Malaria Policy Advisory Committee (MPAC) convened to review updates and progress, and provide guidance with respect to specific thematic areas of work carried out by the Global Malaria Programme (GMP).

The meeting included eight sessions focused on 15 topics: (1) an update on the guidelines for malaria prevention through vector control; (2) an update on the Mekong malaria elimination programme; (3) an update on the Malaria Elimination Certification Panel and Oversight Committee; (4) a proposed Evidence Review Group on determining non-inferiority of insecticide-treated net and indoor residual spraying products within an established class; (5) an update on key developments associated with the evaluation process for vector control tools; (6) a proposed Technical Consultation on research requirements to support WHO policy on highly sensitive malaria diagnostic tests; (7) a proposed Evidence Review Group on malaria control in humanitarian emergencies; (8) a proposed Evidence Review Group on assessment of malariogenic potential to inform elimination strategies and prevent re-establishment of transmission; (9) an update on the Evidence Review Group on malaria mortality estimates; (10) a proposed Evidence Review Group on mass drug administration in areas of moderate transmission and complex emergencies; (11) an update on the malaria capacity building initiative; (12) an update on the RTS,S malaria vaccine implementation programme and framework for decision-making; (13) an update on the Strategic Advisory Group on malaria eradication; (14) an update on a Technical Consultation on universal access to core malaria interventions in high-burden countries; and (15) a discussion on the "10 + 1" initiative among high-burden countries.

At the closing session, the key outcomes/recommendations of MPAC to GMP included:

- **Vector control guidelines:** MPAC appreciated the work of the team in consolidating the first edition of the guidelines for malaria prevention

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through vector control, which draw on systematic reviews and grading of available evidence. MPAC provided significant feedback on the draft, commenting on some basic structural elements and offering suggestions for revision. The document will be submitted to the WHO Guidelines Review Committee in May 2018, with a view to publication in late 2018.

- **Elimination in the Greater Mekong Subregion:** MPAC appreciated the update on malaria elimination in the GMS, noting the granularity of the data presented. The overall progress in decreasing the number of cases and deaths in the subregion was noted, but MPAC expressed concern about the increase of cases in Cambodia.

- **Malaria Elimination Certification Panel and Oversight Committee:** MPAC was supportive of the newly established Committees: one to certify malaria elimination and the other to support elimination activities. MPAC approved the approach of an abbreviated process to certify countries that have reported zero cases for 15 or more years and agreed that it was important to continue monitoring the status of certified countries through the current practice of routine data reports.

- **ERG to develop methods to assess the non-inferiority of insecticide-treated net and indoor residual spraying products within an established class:** MPAC supported the proposed ERG and members of the Committee appreciated that this approach to enhancing programmatic guidance on new vector control products faces a number of challenges. MPAC raised a number of questions, including outcome indicators, for the ERG to consider.

- **Developments associated with the evaluation process for vector control tools:** MPAC appreciated the work that has been undertaken to simplify and bring clarity to the pathway for assessing the public health value of new vector control tools, as well as the clear explanation of the prequalification process and initiatives taken by WHO to enhance the functioning of the Vector Control Advisory Group.

- **Research requirements for policy on highly sensitive malaria diagnostic tests:** MPAC endorsed the proposed Technical Consultation with some suggestions for consideration.

- **Malaria control in humanitarian emergencies:** MPAC endorsed the proposed ERG pointing out the need to ensure consistent definitions of humanitarian emergencies and complex emergencies, and the need to ensure complementarity with the ERG for mass drug administration in areas of moderate transmission and complex emergencies and with previous WHO recommendations on MDA.

- **Malariogenic potential to inform elimination strategies:** MPAC endorsed the convening of the ERG. MPAC felt that it was important to maintain the focus of the ERG on those countries nearing elimination and moving to prevent re-establishment of transmission at either the subnational or national level.

- **Malaria mortality estimates:** MPAC appreciated the work of the ERG and the progress made to improve the methodology for estimating malaria mortality. MPAC also highlighted the importance of a communication strategy that can ensure transparency on the uncertainties and complexities of estimates, effectively convey changes in estimates due to changing data and/or methods, and foster the involvement of country programmes.

- **Mass drug administration in areas of moderate transmission and complex emergencies:** MPAC endorsed the proposed ERG with several suggestions for areas to consider in the evidence review.

- **Malaria capacity building initiative:** MPAC strongly endorsed the development of the capacity building initiative and suggested that dedicated resources be identified to ensure that the work moves forward as a priority.

- **RTS,S malaria vaccine implementation programme:** MPAC was encouraged by the progress in the MVIP preparations, which are on track for launching vaccinations by the end of 2018, and in the development of the framework for policy decisions.

- **Strategic Advisory Group on malaria eradication (SAGme):** MPAC noted the substantial progress achieved by the SAGme. MPAC also noted that a Lancet Commission on malaria eradication was recently announced. MPAC expressed concern for the potential overlap of subjects and the declared goal of developing a roadmap for eradication.

- **Universal access to core malaria interventions in high-burden countries:** MPAC appreciated the report from the Technical Consultation and agreed with the conclusions. The discussion covered a range of issues including access to integrated community case management and seasonal malaria chemoprevention at the community level.

- **10 + 1 initiative:** MPAC endorsed the initiative to renew focus on support for high-burden countries and support's WHO's role as a catalyst for countries to renew their commitment and strengthen their programmes in response to recent data indicating that progress has slowed. MPAC emphasized the need to engage countries and key stakeholders to ensure that harmonized and complementary support is provided.

BACKGROUND

The WHO Global Malaria Programme (GMP) convened the Malaria Policy Advisory Committee (MPAC) for its 13th meeting in Geneva, Switzerland on 11–13 April 2018. MPAC convenes twice annually in Geneva to provide independent strategic advice to WHO on policy recommendations for malaria control and elimination. The Committee is supported by standing Technical Expert Groups (TEGs) and ad hoc Evidence Review Groups (ERGs), whose work focuses on thematic areas and specific research questions in order to generate sufficient evidence to provide guidance. Over the course of the two-day meeting's open sessions, 20 MPAC members, seven national malaria control programme managers, the WHO Secretariat and over 50 observers discussed the updates and progress in the work areas presented. Recommendations were discussed in the final closed session of the Committee on day three. After the introductions, the meeting participants were reminded of the procedures governing WHO's assessment of MPAC members' declarations of interest. It was noted that the GMP Secretariat requested and received feedback from all the experts present at the meeting regarding their declarations of interest. The following members disclosed various interests – Dr Thomas Burkot, Professor Gabriel Carrasquilla, Dr Maureen Coetzee, Professor Umberto D'Alessandro, Professor Azra Ghani, Professor Brian Greenwood, Dr Caroline Jones, Professor Kevin Marsh, Dr Neena Valecha, and Dr Dyann Wirth. The GMP Secretariat reviewed the disclosures and determined that there were no conflicts of interest with respect to this meeting and the participating MPAC members.

UPDATES FROM THE GLOBAL MALARIA PROGRAMME

The GMP Director opened the meeting by providing a concise general update on the work of the WHO-GMP units organized according to five key roles: 1) to address key malaria control and elimination strategic questions; 2) to set, communicate and disseminate evidence-based normative guidance, policy advice and implementation guidance to support country action; 3) to coordinate WHO capacity building and technical support to Member States, jointly with regions and countries; 4) to help countries develop and implement robust surveillance systems to generate quality data and use those data to achieve greater impact; 5) to keep an independent score of global progress in malaria control and elimination, including drug and insecticide resistance.

The Director summarized key data from the World Malaria Report 2017, which indicates that, after a decade of significant progress, the fight against malaria has stalled and is at a crossroads. He highlighted the unfinished agenda of intervention coverage gaps and the challenges of insecticide and drug resistance, concluding that: 1) we are not on track to meet the 2020 morbidity and mortality targets set in the Global Technical Strategy for malaria, and 2) there are new challenges and opportunities in estimating the burden of disease. In order to get back on track to meet the 2020 and 2025 targets, there is a need to focus on the 11 countries that contribute ≈ 70% of the global malaria morbidity and mortality, as well as the 21 countries with the potential to eliminate malaria. Key activities under each of the five roles were highlighted, including progress towards elimination in the Greater Mekong Subregion; improvements to the normative guidance pathway for vector control and other guidance launched since the last meeting; the malaria response in complex situations, including Nigeria and South Sudan; the launch of the Malaria Surveillance, Monitoring & Evaluation reference manual; and the work of the Strategic Advisory Group on malaria eradication (SAGme) and the Malaria Vaccine Implementation Programme (MVIP). The GMP update closed with a moment of recognition for Dr Ruth Nussenzweig's recent passing. Dr Nussenzweig provided the first evidence that protection against malaria pre-erythrocytic stages existed and could be effective in protecting against infection, a precursor to the research leading to the RTS,S vaccine. She published more than 200 scientific papers in her lifetime.

SUMMARY OF THE MPAC SESSIONS

Guidelines for malaria prevention through vector control

Background: The guidelines were developed to provide evidence-based recommendations for the effective implementation of each of the vector control options currently available; to inform and guide technical decisions on the appropriate choices of vector control options; and to support the development of evidence-based national malaria vector control policies and strategies. The guidelines will facilitate the use of WHO guidance by bringing together in one document a large number of existing guidance documents on vector control and will inform a research agenda to identify evidence gaps in support of the development of the second edition. The scope of the guidelines includes the core interventions of indoor residual spraying and insecticide-treated nets, supplementary interventions, and the settings and programmatic factors affecting the selection and deployment of vector control interventions.

MPAC conclusions: MPAC appreciated the work of the team in consolidating the first edition of the guidelines for malaria prevention through vector control, which draws on systematic reviews and grading of available evidence. Detailed thematic feedback was provided on the scope of the document, the evolution of updates to the guidelines, concurrent interventions, insecticide resistance management, the evidence base for recommendations, housing, ecotypes and vector control, consistency in messaging, terms, and the anticipated timeline for completion. It was clarified that many of the comments received will be addressed in the revision of the draft document prior to its publication as a first edition. Several major issues that require generation of additional evidence will be included in subsequent editions of the guidelines.

Key issues that were discussed include:

- A request for clarity on the evidence for interventions designed to work at population level compared to those that provide protection at a personal level where evidence of impact at population level is lacking;

- A request to provide detailed deployment scenarios, such as for vector control in humanitarian emergencies or in the prevention of reintroduction phase once malaria has been eliminated;

- The need for cost-effectiveness guidance that considers not just the interventions' impact on cases, but their influence on other factors including insecticide resistance. Currently proposed strategies, such as rotation and sequential use of insecticides, have evidence from agriculture rather than from vector control; more data from vector control will be needed to provide evidence-based guidance for programmes;

- A proposed restructuring for recommendations to be based on vector behaviours rather than ecotypes. This will place the focus on the relationship between vector behaviours and intervention efficacy, recognizing that dominant vectors with very different behaviours co-exist in each ecotype. As vector behaviours are dynamic and change in response to effective interventions, such an approach is complex and will require updating;

- The need to more clearly state that there is currently no evidence on the efficacy of space spraying for malaria control, as some countries continue to implement this approach;

- A request to include a recommendation on factors to consider in the prioritization of implementation of IRS, LLINs or both (e.g. resource implications and cost-effectiveness).

The guidelines incorporating MPAC's input will be submitted to the Guidelines Review Committee in May 2018, with view to publication of the first edition in late 2018. GMP is not planning to send the revised document back to MPAC before it is published. Updates to the online version of the guidelines will be conducted as new data become available. As mentioned in the Director's update, there is a process underway within GMP, and across WHO more generally, to review and standardize the policy making process, including the development of guidelines.

Update on the Mekong Malaria Elimination Programme

Background: An update was provided on the progress towards malaria elimination in the Greater Mekong Subregion (GMS). Although the total number of cases in GMS declined in 2017, cases increased in Cambodia and Viet Nam compared to 2016. The

Mekong Malaria Elimination (MME) Programme has been established to help the six countries of the GMS – Cambodia, China (specifically Yunnan Province), the Lao People's Democratic Republic, Myanmar, Thailand and Viet Nam – accelerate towards their goal of malaria elimination by 2030 at the latest. There are four major issues facing the MME Programme: ensuring sustainable funding, project implementation, monitoring and addressing multidrug resistance, and improving surveillance. Although significant investments have been made, domestic funding is less than 20% of the total funding contributions to malaria control programmes, and has declined in Cambodia and Viet Nam. An analysis of the economic impact of the interventions in the GMS may be useful to advocate for further investment, comparing the costs of investments in malaria elimination versus the benefits, such as decreases in malaria cases, hospitalization, early deaths, etc. Reaching high-risk populations remains a challenge to project implementation, as does the complex partner landscape. Major issues relating to drug quality assurance and management have been identified, including supply management, national regulatory authority capacity to accelerate introduction, updates and implementation of national guidelines, and quality assurance of drugs. In collaboration with other partners, WHO has developed a response to support the countries on each of the major issues identified. Key areas of work to support improving surveillance in the GMS include data collection and reporting, data use and regular validation of data.

The MME Programme has three areas of work to support GMS countries: the partnership forum, advocacy and communication, and support for cross-country projects. The MME Programme is supporting the Ministerial Call for Action to Eliminate Malaria in the Greater Mekong Subregion before 2030, which was adopted by GMS representatives at a high-level meeting held in December 2017. It is anticipated that the Call for Action will be signed during the World Health Assembly in 2018.

MPAC conclusions: MPAC appreciated the update on malaria elimination in the GMS, noting the granularity of the data presented, as requested in previous MPAC meetings. MPAC noted the overall progress represented by the decrease in the number of cases and deaths in the subregion, but the Committee is concerned about the increase in cases in some areas of the GMS, especially in Cambodia. MPAC emphasized that it is important for GMS countries to ensure that preventive interventions and case management are available to the communities at risk, who often live in remote areas where malaria transmission continues. National programmes supported by WHO and partners should strengthen and focus technical support in these remaining endemic areas. The Committee is hopeful that the upcoming Call for Action to Eliminate Malaria in the GMS by Ministers of Health will enable countries to prioritize strengthening implementation of malaria interventions.

Update on the Malaria Elimination Certification Panel and Oversight Committee

Background: A brief history of the efforts to eradicate malaria, the numbers of countries that have been certified malaria-free and a review of the global targets were presented. WHO launched the E2020 initiative in 2017, including the 21 countries identified in a 2016 WHO report as having the potential to interrupt local malaria transmission by 2020. The objectives of the initiative are: to support countries along their last mile through certification and prevention of re-establishment; to foster networking to share experiences and problem-solving approaches; to strengthen national commitments and political will; and to generate momentum through friendly competition.

To support the E2020 countries, an independent Malaria Elimination Oversight Committee (MEOC) has been established, comprised of 10 members who have a mix of political and technical experience in public health, malaria or disease elimination. The MEOC provides independent operational and programmatic advice and oversight monitoring of global malaria elimination in five primary areas: monitoring and reporting on progress in countries; providing technical advice; identifying risks; sharing observations and recommendations; and questioning the status quo while helping countries to confront difficult issues. The inaugural meeting was held in April 2018 and a key discussion point was the definition of the achievement of the global E2020 target as having zero indigenous malaria cases in 2020.

WHO was given the mandate to certify countries as malaria-free by the World Health Assembly in 1960. Between 1955 and 2017, 28 countries, one subnational region and two territories were certified as malaria-free. The criteria for certification include the interruption of indigenous malaria transmission by *Anopheles* mosquitoes and the demonstration of an adequate and fully functional surveillance and response system for preventing re-establishment of transmission. In 2017, WHO established the Malaria Elimination Certification Panel (MECP), which recommends whether malaria elimination should be certified in applicant countries based on WHO's criteria. The work plan for 2018–19 includes an assessment of four countries that have requested certification, namely, Paraguay, Uzbekistan, Algeria and Argentina. The MECP proposed two recommendations for endorsement by MPAC: 1) that countries reporting zero indigenous malaria cases for 15 or more years be granted certification after a desk review finds no reason to conduct an in-country evaluation mission; and 2) that the MECP annually review the status of certified countries in order to evaluate whether malaria-free status has been maintained. Certified countries reporting indigenous cases will be monitored to determine whether the minimum threshold for re-establishment of transmission has been met. If the minimum threshold (i.e. the occurrence of three or more indigenous malaria cases of the same species per year in the same focus for three consecutive years) appears to have been met, a review will be triggered, which could result in a country evaluation visit and, ultimately, a potential recommendation of withdrawal of certification to the WHO Director General through MPAC.

MPAC conclusions: MPAC was supportive of the newly established Committees, one to support elimination activities and the other to certify malaria elimination when achieved. MPAC highlighted the importance of maintaining independence between the two Committees and that this requirement should be reflected in both the selection of members and the formalization of rules governing the movement of members between the Committees. MPAC noted the development of more sensitive diagnostic methods for detecting submicroscopic infections and the potential future ability to differentiate between introduced and indigenous cases using molecular techniques. MPAC agreed that there should be a future discussion by the MECP on the criteria for certification based on new approaches to the diagnosis of malaria. The current criteria for certification are based on detection by microscopy and RDTs.

MPAC approved the approach of an abbreviated process to certify countries that have reported zero cases and transmission for 15 or more years. This approach would involve a detailed desk review without the need for a site visit. MPAC agreed that it was important to continue monitoring the status of certified countries through the current system of routine reports submitted to WHO, but felt that the MECP should provide more detail on the process that would be used to withdraw certification. It was agreed that the MECP should submit certification recommendations to MPAC rather than directly to the WHO Director General, and that MPAC would rapidly endorse the recommendations of the certification committee unless there was some obvious, major area of concern warranting further review.

Proposed Evidence Review Group on determining non-inferiority of insecticide-treated net (ITN) and indoor residual spraying (IRS) products within an established class

Background: Sponsors of new vector control products that are not covered by an existing policy recommendation need to generate epidemiological data to allow assessment of the product's public health value. The first product in a new class for which public health value has been determined will become 'first-in-class'. Sponsors of second and subsequent products in an established class are not required to generate epidemiological data, but need to demonstrate that the products are 'as good as' the first-in-class product. The term currently used in this context is that of demonstrating "non-inferiority". MPAC has requested that WHO develop guidance to support the implementation of standardized and rigorous study design and analysis to determine non-inferiority. The most pressing need in this area is the comparison of pyrethroid-piperonyl butoxide (PBO) nets, which vary considerably in their design and specifications. The objective of the proposed ERG is to develop methods to assess the non-inferiority of second-in-class ITN and IRS products. For ITNs, the methodology needs to be suitable for the comparison of pyrethroid-PBO nets within their class, but ideally also applicable to the assessment of other ITN products within their respective classes.

The ERG will review data on laboratory and experimental hut studies conducted on pyrethroid-PBO nets, review draft methodologies proposed for the assessment of non-inferiority, and refine the study methodologies to support the generation of high-quality data to inform the development of WHO guidance on the deployment of second-in-class products. Anticipated outputs include: 1) a study protocol developed specifically for determining non-inferiority of pyrethroid-PBO nets; 2) a generic study protocol for determining non-inferiority of ITNs; and 3) a generic study protocol for determining non-inferiority of IRS products.

MPAC conclusions: MPAC supported the proposed ERG and appreciated that this approach to enhancing programmatic guidance on new vector control products faces a number of challenges. A number of questions were raised for the ERG to consider, including:

- What endpoint will be used in the evaluation? Members noted that firm entomological correlates of epidemiological protection have not yet been established, and hence this approach would need to consider non-inferiority criteria in relation to impact on entomological outcomes.
- What margin of non-inferiority in entomological outcomes would be acceptable,