SUBJECT:	**UPDATE ON MALARIA VACCINE PROGRAMME**
Agenda item:	08
Category:	For Guidance

Section A: Executive Summary

Context

Malaria remains one of the deadliest diseases for children under five years old, particularly those living in communities facing multiple deprivations and exclusion. In 2020 alone, there were an estimated 241 million malaria cases in 85 malaria endemic countries increasing from 227 million in 2019, with the WHO African Region accounting for most of the increase. Approximately 96% of malaria cases and deaths globally in 2020 were in 29 countries – out of which 28 are Gavi-eligible countries. In December 2021, the Gavi Alliance Board approved support (US$ 155.7 million for the 2022-2025 period) for a malaria vaccine programme to enable the introduction of malaria vaccines as part of a comprehensive approach to malaria control in malaria-endemic countries. The Board also requested the Secretariat and Alliance partners to coordinate with countries, the Global Fund and other malaria stakeholders to design and implement a malaria vaccine programme including key considerations such as country eligibility, optimal mix of malaria interventions, allocation of scarce supply and country financing. Concurrent to the ongoing design of Gavi's malaria vaccine programme, the Malaria Vaccine Implementation Programme (MVIP) continues to evaluate various aspects of programme implementation in Ghana, Malawi and Kenya.

Questions this paper addresses

What progress has been made in the design of the malaria vaccine programme?

Conclusions

The design of Gavi's malaria vaccine programme has advanced: the framework for the allocation of limited vaccine supply is on course to be finalised in June 2022; malaria vaccine funding guidelines are being developed and will be integrated with the new Gavi Application Funding guidelines and launched in July 2022; guidelines for country co-financing of the malaria vaccine are being prepared as part of the Funding Policy Review and will be presented and finalised by the Programme and Policy Committee (PPC) and Board at the end of 2022; and market shaping work progresses with the market shaping roadmap and UNICEF Supply Division tender to both be completed in Q3 2022. Additionally, implementation of the MVIP continues and provides valuable lessons to inform programme design for broader scale-up of the vaccine.

Section B: Content

1. *Plasmodium falciparum* malaria: burden and control

1.1 Malaria (particularly the *Plasmodium falciparum* parasite species) is one of the leading causes of death globally. Malaria case incidence (i.e., cases per 1000 population at risk) reduced from 81 in 2000 to 59 in 2015 and 56 in 2019, before increasing again to 59 in 2020. The increase in 2020 was associated with, although not entirely explained by, a disruption of services during the COVID-19 pandemic. Even prior to the COVID-19 pandemic, slowing of progress and in some cases reversals of gains were observed. This is further complicated by the plateauing of global financing for malaria at approximately US$ 3 billion per year[1] whereas US$ 6.8 billion is estimated to be needed to achieve global malaria control targets. There are growing concerns that the increased burden of disease coupled with the threats of drug and insecticide resistance and climate change will limit the ability to achieve global control and elimination targets with existing tools.

2. WHO recommendation

2.1 In October 2021, the World Health Organization (WHO) issued a recommendation for the first malaria vaccine – RTS,S/AS01.2 (RTS,S) to be used for the prevention of *Plasmodium falciparum* malaria in children living in sub-Saharan Africa and in other regions with moderate to high transmission. This culminated with the Gavi Board decision to open a funding window for use of a licensed, prequalified vaccine, in line with Gavi's parameters for impact and value for money. In March 2022, WHO published an updated malaria vaccine position paper that includes the October 2021 recommendation calling for the wider use of the vaccine among children living in areas of moderate-to-high malaria transmission.[3]

3. Co-ordination

3.1 **Co-ordination with Alliance partners:** In line with the request of the Gavi Board, the Secretariat has adopted a multi-stakeholder and coordinated approach to the design of the malaria vaccine programme. In addition to regular updates provided to the Alliance Coordination Team, the Secretariat has established the Malaria Vaccine Coordination Team (MVCT). The MVCT is co-chaired by Gavi and WHO and convenes stakeholders in the malaria control and immunisation ecosystem at the global, continental and country levels. The core mandate of the MVCT is to advise and assist the Secretariat to design and implement the malaria vaccine programme in line

[1] The Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund) spent approximately US$ 1.4 billion per year; the United States President's Malaria Initiative (PMI) US$ 745 million; endemic countries US$ 0.9 billion. Note, these figures do take into account the cost of adding vaccine to a comprehensive toolkit of effective malaria prevention and control measures.

[2] https://www.who.int/news/item/06-10-2021-who-recommends-groundbreaking-malaria-vaccine-for-children-at-risk

[3] Updated WHO position paper: https://www.who.int/publications/i/item/WHO-UCN-GMP-2022.01-Rev.1

with experiences and evidence from the MVIP including programme sustainability and effective coordination between national immunisation and malaria control programmes. The MVCT will comprise working groups that engage on specific topics that are critical to the malaria vaccine programme's success including sustainability and integration. Considering there are a number of other existing fora already addressing related topics, the MVCT will also play a coordinating role across these different work areas.

3.2 **Co-ordination with the Global Fund:** Gavi is working with the Global Fund to look at means of harmonising the funding application process for countries that are applying for funding for malaria vaccine support from both organisations. The approach aims to identify opportunities between the application processes of both organisations for enhanced efficiency and optimal use of resources to alleviate the application burden on countries. This harmonisation is timely as both organisations are developing funding application guidelines expected to be launched by July 2022. Additionally, Gavi and the Global Fund are working to identify country-level support synergies across malaria and immunisation programmes, including technical assistance to determine the optimal mix of malaria control interventions (including the vaccine), communication and advocacy, monitoring and supervision.

4. Allocation framework

4.1 Supplies of the RTS,S vaccine are expected to be limited in the short to medium term while demand is expected to be high. WHO has convened a group of temporary advisors comprising malaria and immunisation experts at the global, Africa regional and country levels to develop an approach to allocate limited malaria vaccine supplies in a fair, equitable and transparent manner, drawing on the lessons of other vaccine programmes including COVID-19 vaccine supply prioritisation as well as inputs from key stakeholders.

4.2 The Malaria Vaccines Allocation Framework aims to provide global guidance on the allocation of malaria vaccines between and within countries until supply constraints can be resolved. While acknowledging countries' sovereign decision-making, the framework also intends to guide country-level decisions on targeting priority geographies for vaccination. Gavi is expected to play a key role in implementation of the framework as most malaria endemic countries in sub-Saharan Africa are still Gavi-eligible.

4.3 The draft allocation framework prioritises areas of countries with the highest malaria burden. A number of countries with this category of malaria burden also have weaker health systems and poorer health outcomes, including coverage of public health interventions such as conventional malaria prevention and control strategies and Expanded Programme on Immunization (EPI) vaccines. The Secretariat is working with Alliance and expanded partners through the MVCT to ensure adequate and timely technical assistance to countries in support the development of quality new vaccine introduction applications to effectively introduce the vaccine.

5. Vaccine programme design

5.1 Gavi's new Application Funding Guidelines will launch in July 2022 and include support for malaria vaccine. This will permit countries to apply for malaria vaccine support for the first time during the September 2022 application window. Per the Board's request that the malaria vaccine programme design be consultative, the malaria-specific guidelines are being developed in collaboration with partners through the MVCT.

5.2 Malaria-specific guidelines will be framed within the overarching principles of Gavi's funding for vaccines as part of comprehensive portfolio support and the centrality of equity and gender equality in new vaccine introductions. Additionally, countries will be required to align with the Allocation Framework principles of targeting the areas with highest need, consider the implementation of malaria vaccine vis-à-vis other malaria interventions, as well as programmatic implications on the wider routine immunisation programme, including leveraging Gavi systems strengthening investments.

5.3 Co-financing is central to Gavi's catalytic funding model. Specific co-financing considerations for newer and more expensive vaccines such as malaria are being developed through the ongoing comprehensive funding policy review and expected to be presented to the Gavi Board at the end of 2022. The updated policy is intended, in part, to account for risks associated with high-priced vaccines such as RTS,S. The specific implications of the updated co-financing policy and effect on individual country affordability will not be known to countries applying in the September 2022 funding application window.

5.4 With MVIP set to conclude at the end of 2023, MVIP countries planning to continue their malaria vaccine programme will need to apply for Gavi support in the initial September 2022 application window to ensure seamless transition from study donated doses to Gavi-country supported doses. Given longer-term co-financing commitments would only be finalised in late 2022, MVIP countries will need to review the new co-financing implications and confirm their interest before the issuance of decision letters. Other eligible countries will be supported to develop and submit new vaccine applications in subsequent application windows beginning in January 2023 when countries will have full visibility of the revised co-financing arrangements, available vaccine supplies and vaccine price.

6. Market shaping

6.1 Alliance market shaping activities for malaria vaccines fully commenced in December 2021, with several activities begun at-risk even before then in anticipation of a positive Board decision and in view of the urgency to address expected supply constraints against high country demand.

6.2 Production of the RTS,S bulk antigen by GSK continues under the Gavi Antigen Production De-risk Agreement with GSK, which was backstopped by MedAccess to reduce Gavi's risk exposure prior to the Board's programme funding decision (after which MedAccess's involvement

concluded). Financing to GSK (up to a maximum US$ 56.6 million) will be applied toward procurement of finished doses for the Gavi programme.

6.3 UNICEF Supply Division (SD) launched a tender for malaria vaccine supply in December 2021 which is currently in the tender negotiation stage. The tender is expected to conclude with supply agreements for prequalified products established in early Q3 2022. This tender aims to secure all available supply in the short to medium term (4-6 years). All suppliers anticipating having a WHO prequalified product during this timeframe were invited to submit bids.

6.4 An accelerated market shaping roadmap development process was formally launched in December 2021, in parallel with, and taking into consideration, the tender process and its eventual outcomes. Partners engaged in this collaborative and consultative process include Gavi Secretariat teams, UNICEF SD, WHO, Bill & Melinda Gates Foundation and other partners who are consulted based on their areas of expertise. One of the immediate and highest priority objectives of the tender and roadmap process is to address the expected short term supply constraint. The roadmap will be published in Q3 2022, though partners are beginning to implement an action plan in support of this goal. The roadmap also examines key dimensions around long-term supply, a competitive, secure and sustainable supplier base (including options for manufacturing in Africa), timely demand materialisation, and product innovations, while also addressing ongoing affordability of the vaccine.

6.5 There are two vaccines expected on the market with WHO prequalification in the short to medium term: RTS,S/AS01 and R21/Matrix M[4].

6.5.1 GSK, producer of the RTS,S/AS01 vaccine, has recently submitted the vaccine for WHO prequalification (outcome expected by end Q2 2022). A product technology transfer to Bharat Biotech India Ltd (BBIL) is expected to be completed within the medium term (e.g. by 2028), with GSK retaining production of the AS01 adjuvant and BBIL producing the antigen and finished doses. Options to accelerate these timelines are being actively explored. GSK has publicly committed to making available at least 15 million doses per year (including of the adjuvant post-tech transfer) at a price of no more than cost +5%. BBIL has not publicly indicated their expected pricing, but it is expected to be lower than the price of GSK-produced RTS,S.

6.5.2 The R21/Matrix-M vaccine will be produced by Serum Institute of India (SII) and involve a technology transfer for the Matrix-M adjuvant, meaning SII will produce both the R21 antigen and adjuvant. The vaccine is in Phase 3 trials, with potential market entry within 2-5 years (note: timelines dependent upon on final regulatory and WHO prequalification requirements and pathways, with an expedited pathway being explored to first license the vaccine for use

[4] R21 is still undergoing Phase 3 clinical trials.

in areas with seasonal transmission of malaria). SII has publicly stated they will be able to supply from 120-250 million doses per year at cost effective prices.

6.6 The current expected capacity for RTS,S and product licensure timelines for R21 mean that supply is likely to be significantly lower than country demand in the initial years of the programme. Market shaping efforts aim to lessen this situation by exploring and implementing options to accelerate timelines and/or increase production capacity for both vaccines.

7. Gavi support for Nigeria

7.1 As part of the Malaria Vaccine Programme Investment Case discussed by the PPC in October 2021, the Secretariat presented considerations for supporting the introduction of the malaria vaccine in Nigeria. These included the high burden of malaria in the country and the Gavi Board approved support with a fixed financial envelope until 2028. Further engagement with the Government of Nigeria and alignment with partners and stakeholders is required to determine the future scope of Nigeria's malaria vaccine programme.

Section C: Actions requested of the Board

The Gavi Alliance Board is requested to **provide guidance** on progress to date to design a malaria vaccine programme taking into consideration the current limited supply.