Annex A: WHO background note on operationalisation: supply allocation framework, technical guidance and integration between malaria control and immunisation

1. Development of allocation framework for limited supply

Supply is likely be insufficient in the medium term, with a constraint expected in the first 4-6 years following anticipated first introductions in 2023. This could potentially extend to 9 years should there be demand for additional seasonal doses or if no action is taken to accelerate supply availability. While efforts to address the supply limitations and achieve healthy market goals are expected to intensify if and when a Gavi malaria vaccine programme is approved, a prioritisation process will be required at the onset to allocate limited vaccine supply in the initial years.

Process to develop the allocation framework for limited supply

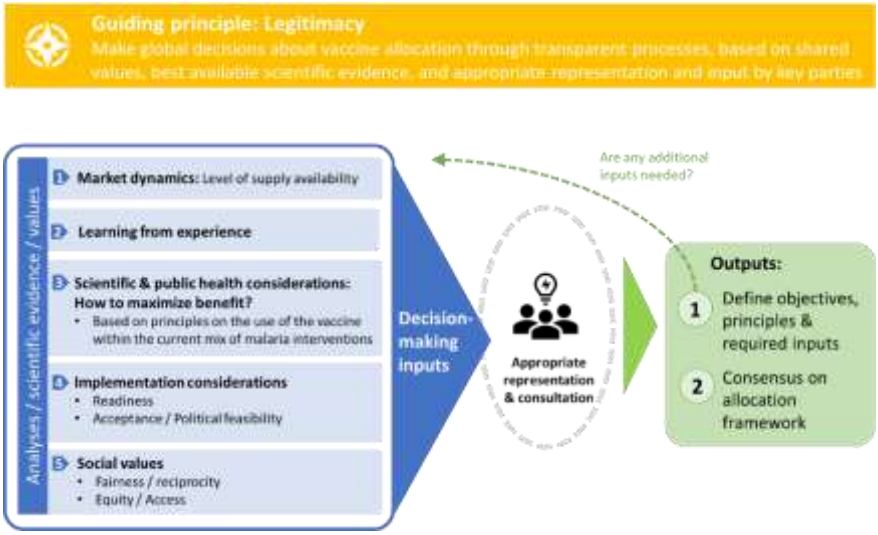
Given the extent and potential duration of the supply-demand imbalance, difficult choices will have to be made by countries and their global partners on how to best use limited resources. The **process,** i.e. ***how*** choices and decisions are made, will be as important as the underlying scientific rationale. **Legitimacy** is proposed as the overarching guiding principle for the *development* of the allocation Framework: global decisions about vaccine allocation should be made through **transparent processes that are based on shared values, best available scientific evidence, and appropriate representation and input by key parties**, drawing heavily on the expertise and views of public health leaders from malaria endemic area.

WHO is coordinating the development of the framework, ensuring appropriate representation and consultation of stakeholders. Ministries of Health in affected countries will be informed of and engaged in the development of the framework. Convenings to establish the principles and objectives of the framework will include leadership from Africa and other affected countries, international funding bodies (e.g. Gavi and Global Fund), key malaria partners (e.g. PMI, RBM regional institutions), civil-society organisations, ethics and human rights specialists, PATH, and others.

The Framework is expected to be in place by Q1 2022, and will guide decision making on vaccine allocation, including where and in which countries limited vaccine doses might best be allocated initially. Once developed, the framework will be used by malaria and EPI stakeholders, as they make decisions on malaria control interventions for a given country or provide support to countries. It will be important for all relevant stakeholders to adhere to the framework, e.g., Gavi in its application guidance and process; partners in their financial, technical and regulatory support to countries; etc.

Inputs to inform decision-making

The graphic below summarises the proposed process. Different work areas provide the scientific / public health, implementation and social value considerations as inputs to decision-making. Stakeholders will be convened to consider the objectives and principles of the Framework and the pros and cons and trade-offs of different options.



2. Forthcoming WHO guidance

Several WHO malaria vaccine guidance documents are targeted for Q2 2022:

1. **Online guidance for malaria control**
2. **Vaccine position paper** in Weekly Epidemiological Record (WER)
3. **A guide to introducing the RTS,S/AS01 malaria vaccine into national immunisation programmes:** to provide more specific guidance to countries in their decision making and planning around RTS,S use as part of a comprehensive malaria control plan.
4. **Operational manual on malaria interventions:** to provide implementation guidance to countries on tailoring malaria response to subnational contexts, including a malaria vaccine (i.e. approaches for stratification[1], criteria for sub-national tailoring[2] and the identification of the optimal mixes of malaria interventions), as per below.

Operational manual on malaria interventions

Implementation of the operational manual supports the country-led **"High burden high impact (HBHI)"** response, launched in 2018 by WHO and the Roll Back Malaria (RBM) Partnership to End Malaria. HBHI aims to reignite the pace of progress in the global malaria fight. Critical to the response are clear evidence-informed guidance, strategic use of local data, alignment with global technical strategy, and support of national strategic plans that defines the packages of interventions needed to optimise malaria control and elimination in a country.

Under the HBHI approach, countries have undertaken an extensive exercise of tailoring their malaria interventions to subnational context. The **operational manual on subnational tailoring of interventions** recognises the following:

[1] To tailor interventions sub-nationally one must consider the baseline and current risks as well as the various natural and anthropogenic determinants of transmission and burden of malaria. From this perspective, stratification is the process of geographically (and temporally) classifying malaria risk and its determinants into meaningful categories to inform the tailored targeting of the intervention under consideration. Eventually, this process leads to intervention (and strategy) mixes for each subnational unit. Geospatial modeling approaches are useful for stratification.

[2] The use of local data and contextual information to determine the appropriate mixes of interventions, and in some cases delivery strategies, for a given area, such as a district, health facility catchment or village, for optimum impact on transmission and burden of disease.

- Malaria is geographically heterogeneous, with transmission intensity and burden varying sub-nationally, even in high burden countries.
- These variations are not only geographic but also temporal (seasonal and secular trends)
- This heterogeneity is a function of variations in climatic and ecological factors such as temperature, rainfall and humidity but also modulated by anthropogenic factors such as malaria interventions, health system performance, movement and migration, urbanisation, agriculture, mining, etc.
- Current malaria interventions are highly cost-effective but have variable impact on the main burden endpoints (infection, mild disease, severe disease and death). All the prevention interventions have modest efficacies and they are not suitable everywhere and their effectiveness changes over time. A single value of cost-effectiveness is therefore unreliable.
- Therefore, the best pathway to impact (depending on the desired burden endpoint) is through optimised[3] and prioritised[4] combinations (or mixing).
- It redefines universal coverage not to mean everything everywhere, but matching interventions to need driven by a desire to achieve the biggest possible impact with available resources.
- This must be driven by the best possible subnational data, and the evidence informs a nationally owned and governed approach to decision-making, recognising that social justice and equity are not secondary but primary considerations in the decision-making process.

The operational manual on subnational tailoring of malaria interventions to local contexts aims to answer the following questions using aforementioned information and considerations, for each subnational unit:

i) *Where do we intervene?* – this requires an understanding of malaria risk (transmission intensity, burden, age patterns, high risk groups etc) as well as their natural (climate and ecology) and anthropogenic determinants (previous interventions, land use and other human activities).

ii) *Which interventions (or strategies) should we use?* – this requires an understanding of the intervention (and intervention mixes) and strategies (iCCM, SMC, MDA etc)[5] with the biggest impact on malaria risk and burden within a given context, acknowledging that across space and time, context changes and there is a need to tailor choice of tools to context. Effects will vary over time, meaning cost

[3] National malaria strategic plans ought to reflect the ambition of a country in its fight against malaria. These targets are linked to overall national health and development targets. Therefore, the mix of interventions and strategies in these plans focus on what a country needs to do to achieve its targets and not constrained by the resources that are likely to be available at the time of strategy development. Under the HBHI approach, optimisation was the process of ensuring that the interventions and strategies selected for National Strategic Plans are most likely to lead to best possible impact toward national targets. These analyses should ensure that system-wide synergies are considered. This is the basis of National Strategic Plan costing.

[4] Often, the resources required to fully implement national malaria strategic plans are not available. The subnational tailoring prioritisation process aims to provide the right evidence to inform the hard decisions countries need to make to prioritise investments for impact, social justice and equity. The difference between the National Strategic Plan costing and the prioritised plan is the resource gap. As new resources become available and context changes, the prioritisation analysis will require revisions even with the lifespan of the National Strategic Plan.

[5] iCCM= integrated community case management; SMC = seasonal malaria chemoprevention; MDA = mass drug administration

effectiveness also varies. Over reliance on existing single estimates of cost effectiveness should be avoided as they are not applicable in most places most of the time.

iii) *Which interventions can we afford and how do we prioritise?* This prioritisation process aims to achieve maximum impact with available resources (domestic and external). Ideally, it will require that decisions are based on the intervention and strategic mixes defined in the National Strategic Plan. However, current funding processes can lead to considerable mismatches between national priorities and donor priorities, even when the latter may be less impactful. This is a governance issue that should not be delinked from the subnational tailoring process. Mathematical transmission dynamic modelling[6] (with a cost-effectiveness component) provides unique advantages in answering these questions.

iv) *How and when do we deliver them?* – these discussions usually happen during the optimisation and prioritisation processes but may require their own unique consideration, as the same interventions can be delivered through different mechanisms at different costs / effectiveness.

v) *How do we design systems to monitor their impact?* – attributing impact is a complex process, as intervention and non-intervention determinants occur at the same time in the same place. This is made even more difficult with weak health information systems in most high burden countries. The subnational tailoring process builds on available data but investment in the design and implementation of the appropriate surveillance, information and monitoring and evaluation systems must be considered as part of the process, and not as an afterthought.

3. Opportunities for integrating the malaria vaccine into national immunisation and malaria programmes based on pilot country experience

Key findings of the pilots were based on data and insights generated from two years of vaccination in child health clinics in the three pilot countries, implemented under the leadership of the Ministries of Health (MOH) of Ghana, Kenya and Malawi. Within the MOH, the malaria vaccine pilot introduction has been led by the Expanded Programmes on Immunization (EPI), in close coordination with the National Malaria Control Programmes (NMCP) among other key stakeholders.

Malaria vaccine introduction is feasible, improves health and saves lives, with good and equitable coverage of RTS,S reached through routine immunisation services using routine systems. RTS,S introduction increases access to malaria prevention tools by children at risk - with data from the pilot programme showing that more than two-thirds of children in the 3 countries who are not sleeping under a bednet have received at least their first dose of the RTS,S vaccine. Layering the tools (insectide treated bednets and RTS,S) results in over 90% of children benefitting from at least one preventive intervention (insecticide treated bednets or the malaria vaccine). In areas where the vaccine has been introduced, there has been no decrease in the use of insecticide-treated nets, uptake of other childhood vaccinations or health seeking behavior for febrile illness. Within the pilot programme's qualitative study, primary

[6] Malaria transmission is complex with the human-parasite-vector relationship continuously modified by multidimensional factors such as climate, interventions and other factors. Mathematical modeling of transmission dynamics offers effective mechanisms to capture this complexity, simulating real-world settings and providing operationally useful information, including linking impact on malaria to cost-effectiveness.

caregivers and health workers expressed understanding and acceptance of the partial protection of the malaria vaccine.

The pilots have provided lessons learned and insights into the potential coordination required between the EPI and NMCP for successful implementation of a malaria vaccine. Despite the traditionally vertical nature of the EPI and NMCP and the complicated nature of a pilot introduction, the malaria vaccine implementation has benefitted from good cooperation and engagement between these programmes.

- ***Coordination*:** The pilot countries have malaria vaccine technical working groups (TWGs) with joint participation from the EPI and NMCP to provide technical guidance for decision making, planning and implementation. Ghana and Kenya had TWGs that pre-dated the pilot—established between 2009 and 2013—that acted a resource on malaria vaccine development and synthesised and documented data to inform recommendations for evidence-based decision-making. Malawi did not have an active TWG prior to the pilot and convened a temporary Malaria Vaccine Task Force to guide malaria vaccine preparations; from 2019 onward, the Malaria Vaccine Programme Coordination Group was established as a TWG. In all pilot countries, TWGs have continued to meet at least semi-annually since the start of vaccinations.

  Based on pilot country experience, malaria vaccine introduction in further countries should consider TWGs as beneficial forums for decision making and alignment between the EPI and NMCP, among other key stakeholders.

- ***Decision making*:** final decision by the Minister of Health on a vaccine introduction considers the advice from the National Immunization Technical Advisory Group (NITAG). For decision making on participation in the pilot, the malaria vaccine TWGs (see *Coordination)* compiled evidence for the NITAG and included representation from the EPI and NMCP.

- ***Planning & preparation*:** WHO is developing a guide for introducing a malaria vaccine as well as operational guidance for sub-national tailoring of malaria interventions. Country consideration and planning on vaccine introduction will rely on data-driven decisions and upon NMCP expertise on parasite prevalence, disease burden, and existing malaria interventions, among other factors. The EPI would lead the logistics of vaccine roll-out and delivery to the relevant health facilities.

  In the WHO-coordinated pilot introductions, the new vaccine introduction plan and budget were developed by an EPI sub-committee that included the NMCP. The malaria vaccine TWG (see *Coordination)* facilitated preparations and provided guidance with EPI and NMCP focal points as key members. Vaccine introduction activities (i.e. training, M&E tools, communication materials) were led by the EPI with active participation from the NMCP. For example, the NMCP supported the sub-national trainings, emphasizing the complementarity of the vaccine to the existing malaria control interventions.

  Malaria vaccine introduction timing and resources would be considered in context of other planned new vaccine introductions, campaigns for immunisation or malaria interventions, among other priorities.

- ***Strategies and guidance*:** The malaria vaccine will be integrated into relevant malaria control and immunisation strategies and guidance. This did not occur for

the pilot implementation, but is appropriate for a WHO-recommended intervention. For the NMCP, national strategic plans—aligned with global technical strategy—define the packages of interventions needed to optimise malaria control and elimination in a country. For the EPI, national immunisation strategies and comprehensive multi-year plans (cMYP) can be aligned with the "Immunization Agenda 2030: A Global Strategy to Leave No One Behind."

- ***Communication and stakeholder engagement*:** Prior to the malaria vaccine introduction, all pilot countries had developed and/or updated malaria vaccine communications strategies along with stakeholder engagement and crisis communications plans. For the pilot introductions, key stakeholders from EPI and NMCP were involved to ensure agreement and effective communications. Technical discussions were held with malaria and immunisation partners, and health management teams, at national, district, and sub-district levels to disseminate information about the pilot.
- ***Information, education, and communications (IEC) materials*:** The EPI and NMCP perspectives should be incorporated in the development of key messages, as was done in the pilot implementations (i.e. 4-dose regimen, partial protection provided by the vaccine, need to continue to use other proven malaria control methods).
- ***Monitoring, evaluation, surveillance*:** for the pilot, the EPI updated monitoring tools for deployment in health facilities in the implementing areas, integrated the malaria vaccine into routine administrative data reporting, and conducted post-introduction evaluations (PIE) following vaccine introduction. The malaria vaccine has been integrated into District Health Information Systems 2 (DHIS2)—alongside malaria and EPI indicators. The NMCP has integrated pilot district coverage data into quarterly and annual reports. Supportive supervision by the EPI have included the NMCP.
- ***Leveraging opportunities for integration:*** In addition to integrating key messages and taking advantage of additional health visits to deliver important health messages about malaria or other child health messages, there may be other opportunities for integration between the EPI and NMCP related to increasing malaria vaccine uptake – including the 4th dose, successful seasonal deployment of the vaccine alongside seasonal malaria chemoprevention (SMC) via campaigns, improving impact of outreach by community health workers to increase insecticide treated net use and vaccine uptake or coverage – and/or monitor for both, and/or other health interventions. The continuation of the pilot programmes through 2023 could provide further opportunities to learn and explore synergies for broader health system benefit from malaria vaccine implementation. For example, the Ghana EPI has in the past leveraged long-lasting insecticide-treated net (LLIN) distribution to improve the uptake of the MR2 and MenA doses.

For more information, please access the "Key milestones in the development of the Malaria Vaccine Implementation Programme" on the WHO website