Gavi Malaria Vaccine Support

Interim Guidelines, initially published in December 2023 and amended in March 2024

Gavi
The Vaccine Alliance

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Updates to the Gavi Interim Malaria Vaccine Funding Guidelines

Since the Gavi Interim Malaria Vaccine Funding Guidelines were published in December 2023, there have been some developments with implications for countries applying for Gavi support. Countries should take these implications - summarised here in this text box - into account when preparing funding applications to Gavi.

Scope of Gavi malaria vaccine funding support
As prioritized in the 2023 WHO recommendation for the use of malaria vaccines, Gavi is currently able to provide support for malaria vaccines for use only in areas with moderate and high P. falciparum malaria transmission. Requests for Gavi support for vaccine introduction in areas of low P. falciparum malaria transmission may be considered once 1) there is clarity from the Gavi Board on the funding available to support the malaria vaccine programme in the Gavi 6.0 (2026 – 2030) strategic period, and 2) robust sub-national tailoring of malaria control interventions have taken place in the respective country(ries).

Gavi's funding support covers introduction of the vaccine into the routine immunisation programme using a four or five-dose schedule. Countries with populations in areas with highly seasonal malaria transmission or perennial malaria transmission with seasonal peaks may apply for Gavi funding support to deliver the vaccine using an age-based, seasonal or hybrid delivery strategy in line with WHO recommendations.

Implication to countries: In developing applications for Gavi vaccine funding support, countries are requested to consider how vaccines will be used at scale in areas of moderate to high malaria transmission in line with 1) WHO guiding principles for prioritizing malaria interventions in resource-constrained country contexts to achieve maximum impact and 2) Gavi's current support in areas with moderate and high transmission only. Countries are required to describe the malaria epidemiology and define the number of eligible children in areas of moderate to high malaria transmission to be targeted. Current WHO guidance defines moderate to high malaria transmission settings as those with:

- **Annual incidence greater than 250 cases per 1000 population; OR**
- **Prevalence of *P. falciparum* infection in children (PfPR) of approximately 10% or more**

To facilitate the review of country applications for malaria vaccine support submitted to Gavi, and determine the extent of Gavi support, it is necessary to ensure uniformity of how countries categorise malaria transmission zones and subsequently quantify target populations for the malaria vaccine introduction. Countries are therefore required to provide the following information to clearly identify the target population that the funding support application relates to as outlined in the table below. If possible, countries are also requested to provide a map of the areas of moderate to high transmission that the funding application relates to.

Administrative area name (e.g. district, LGA, zone de sante etc.)	Total number of age-eligible children in the administrative area (e.g. number of surviving infants	Number of age-eligible children residing in areas of moderate to high malaria transmission in terms of either annual incidence **or** Prevalence of *P. falciparum* infection in children (PfPR)	
		Number of age-eligible children residing in areas of moderate to high malaria transmission (defined based on PfPR in the administrative area (i.e. number of age-eligible children residing in areas where PfPR is 10% or more)	Number of age-eligible children residing in areas of moderate to high malaria transmission (defined based on annual incidence) in the administrative area (i.e. number of age-eligible children residing in areas where annual incidence is greater than 250 cases per 1000 population

Note: While countries are requested to provide data based on annual incidence or PfPR, countries are encouraged to provide both if available.

Further, if countries choose to introduce the malaria vaccine areas of moderate and high *P. falciparum* malaria transmission in a phased manner, countries are required to elaborate on how vaccine introduction will be prioritised (in terms of areas to start introductions) within these areas. Such prioritization will inform Gavi's funding support and can be based on local data, existence of other malaria control interventions, socio-economic nuances and other factors that the country considers important in determining the overall impact of the malaria vaccine.

Introduction

In 2022 and 2023, a number of countries submitted applications for Gavi support for malaria vaccine programme implementation. At that time, due to vaccine supply constraints, countries were advised to focus their application on areas of greatest need, referred to as 'Category 1' of 'Phase 1', as defined by the Framework for allocation of limited malaria vaccine supply. With the evolution of the malaria vaccine supply situation since then, countries, including those that have not yet applied or been approved by the Gavi IRC, may wish to reconsider their malaria vaccine introduction plans. This reconsideration should aim to scale up vaccine introduction beyond the Category 1/Phase 1 areas, prioritising areas with moderate and high transmission, in line with WHO recommendations.

Purpose of this document

This document outlines the requirements for:

- **Countries whose applications have already been recommended for approval by the IRC** and are seeking additional support from Gavi to scale up their vaccine introduction beyond the scope of their initial approval.
- **Countries that have not yet applied or have not been approved by the IRC yet**, who need to submit applications to request Gavi's support for a malaria vaccine programme.

The requirements described below are relevant to any malaria vaccine programme and are not dependent on the specific vaccine product.

Key resources and references

- Technical resources on malaria vaccine introduction
- World Malaria Report 2023

WHO malaria vaccine recommendations

WHO recommends the use of malaria vaccines for the prevention of P. falciparum malaria in children living in malaria endemic areas, prioritizing areas of moderate and high transmission. Malaria vaccines should be provided in a schedule of four doses[1] in children from around 5 months of age[2] for the reduction of malaria disease and burden.

Countries may consider providing the vaccine using an age-based or seasonal administration, or a hybrid of these approaches in areas with highly seasonal malaria or areas with perennial malaria transmission with seasonal peaks. Countries should prioritize vaccination in areas of moderate and high transmission[3], but may also consider providing the vaccine in low transmission settings.

Product prequalification and performance

The first malaria vaccine, RTS,S/AS01 (RTS,S) was recommended by WHO in October 2021 and received WHO prequalification in July 20224. The second malaria vaccine, R21/Matrix-M (R21), was

[1] A fifth dose, given 1 year after dose 4, may be considered in areas where there is a significant malaria risk remaining for children one year after receiving dose 4.

[2] Vaccination programmes may choose to give the first dose at a later or earlier age based on operational consideration. Studies with RTS,S/AS01 indicated lower efficacy if first dose was given around 6 weeks of age. However, it seems unlikely that efficacy would be substantially reduced if some children received the first dose at 4 rather than 5 months and providing vaccination at an age younger than 5 months may increase coverage or impact.

[3] Moderate to high transmission settings are defined as areas with *P. falciparum* parasite prevalence greater than 10% or an annual parasite incidence greater than 250 per 1000 [WHO guidelines for malaria, 16 October 2023. Geneva: World Health Organization; 2023 (WHO/UCN/GMP/ 2023.01 Rev.1)]. These thresholds are indicative and should not be regarded as absolutes for determining applicability of the malaria vaccine recommendation.

[4] https://extranet.who.int/prequal/vaccines/p/mosquirix

recommended by WHO in October 2023, and is as of December 2023 undergoing pre-qualification review.

Both vaccines are shown to be safe and efficacious in preventing malaria in children and, when implemented broadly, are expected to have high public health impact. Malaria vaccines should be provided as part of a comprehensive malaria control strategy.

The choice of product to be used in a country should be based on product characteristics and programmatic needs, vaccine supply availability and the likelihood of being able to scale up with a single product in the programme, and long-term affordability considerations particularly for countries approaching Gavi transition.

There are no head-to-head trials directly comparing vaccine efficacy between the products, and no evidence that one vaccine has a greater efficacy or duration of protection than the other. While different vaccine administration schedules were evaluated in the clinical trials of R21/Matrix-M or RTS,S/AS01, when given seasonally in areas of highly seasonal transmission, both vaccines demonstrate around 75% reduction of malaria cases one year after receiving 3 doses. There are no data on the vaccine efficacy of R21/Matrix-M in high perennial transmission settings. However, due to the similarities with RTS,S/AS01, it is likely that R21/Matrix-M will also have impact in these settings.

The latest information on the two vaccine products is available on the Gavi website via this link.

***Note**: the link downloads an excel-based file with the product information*

Co-financing implications for countries

Gavi's exceptional, time-limited co-financing approach for malaria vaccine will apply to both RTS,S and R21. Summarised below are the co-financing implications for countries in different co-financing transition phase[5]:

- **For Initial Self Financing countries**, country contributes US$ 0.20 per dose, with no annual increase. **This is applicable for both RTS,S and R21**- i.e. country will pay US$ 0.20 per dose irrespective of the vaccine used by the country.
- **For Preparatory Transition countries**, country contributes US$ 0.20 per dose in the first year of introduction. This amount increases by 15% annually (for example, US$ 0.23 per dose in the second year, and so on). **This is applicable for both RTS,S and R21**- i.e. country will pay US$ 0.20 per dose in the first year irrespective of the vaccine used by the country. The following year, the country will US$ 0.23 per dose and so on, with contribution increasing 15% annually.
- **For Accelerated Transition countries**, country contributes 20% co-financing of vaccine price in the first year of introduction. This co-financing increases by 10 percentage points annually (i.e. 20% first year, 30% second year and so on). Country should reach 100% co-financing after 8 years. At currently awarded prices, Countries in Accelerated Transition would pay less for R21, as co-financing share is directly linked to vaccine price. Higher priced vaccine results in higher co-financing.

[5] For further details and support to calculate the exact co-financing implications, please reach out to your SCM.

Available financial support: Vaccine Introduction Grants (VIGs)

Gavi provides Vaccine Introduction Grants (VIGs) to facilitate the timely and effective introduction of a vaccine into the routine vaccination programme. Considering the expected phased roll-out of the malaria vaccine, the VIG amount will be calculated and provided as follows:

Vaccine Introduction Grants (VIGs)	
Roll-out phase	**VIG amounts**
Phase one The first introduction of the malaria vaccine into a country's routine immunisation programme, which is occurring at a subnational level	Lump sum of US$ 100,000 or an amount calculated on the targeted subnational birth cohort, whichever is higher. The calculated VIG amount is, depending on the country's transition status, US$ 0.80/0.70/0.60 per infant in the birth cohort of the subnational area covered in phase one. For example, for a country in the initial transition phase, it is US$ 0.80 per infant in the birth cohort (live births in the year of introduction) of the subnational area covered.
Subsequent phases Expanding provision of the malaria vaccine into additional areas, including the expansion of immunisation beyond the MVIP areas (implementation and comparator areas) in MVIP countries	Calculated VIG amount is, depending on the country's transition status, US$ 0.80/0.70/0.60 per infant in the birth cohort of the subnational area covered in the phase.

Guidance, considerations and requirements

Countries must pay attention to the guidance and considerations outlined to apply for the introduction of malaria vaccine through Gavi support.

Overarching requirements

Applications need to demonstrate:

- Confirmation of the country's decision to introduce the malaria vaccine, for example Ministry of Health signoff, as well as NITAG meeting minutes, immunisation inter-agency coordination committee (ICC) minutes;
- Existence or plans to establish a joint immunisation-malaria coordination mechanism that brings together national immunization and malaria control programmes;
- Details of plans that appropriately prioritize vaccines within broader malaria prevention and control efforts and prioritize interventions based on local data, context and considerations;
- Integrated and multi-sectoral approaches where, as much as possible, the deployment of the malaria vaccine uses existing health systems, including the existing routine immunisation systems;
- Strong community engagement to ensure vaccine acceptance and resilient demand;
- Country readiness and commitment to meet co-financing obligations by having their applications signed off by the Minister of Health (or their delegated authority); and Minister of Finance (or their delegated authority)
- Where feasible, countries are encouraged to provide information on the status of regulatory registration of RTS,S/AS01 and R21/Matrix-M by the national drug authority

Malaria vaccine supply and epidemiological considerations

<u>Note:</u> Please refer to the content in this chapter in the context of the 'Updates to Gavi Interim Malaria Vaccine Funding Guidelines' (outlined in page 2 of this document)

With the WHO recommendation and pre-qualification of R21, the overall supply of malaria vaccines is anticipated to be sufficient to meet country demand[6]. Countries are therefore encouraged to consider how vaccines will be used at scale in coordination with other malaria prevention and control interventions prioritizing areas of moderate to high malaria transmission in line with WHO recommendation. Countries are required to describe the malaria epidemiology, use of other malaria prevention and control measures and define the number of eligible children in areas of moderate to high malaria transmission to be targeted.

Programmatic requirements

Applications need to demonstrate/provide the following, which is typically articulated in the new vaccine introduction plan:

- A detailed introduction strategy that outlines the scope of vaccine introduction with a prioritization of areas with moderate to high malaria transmission in line with the WHO recommendation
- Description of preparatory activities required to enable vaccine introduction, e.g., training, social mobilisation, etc.
- Explanation of schedule choice and delivery modalities. Countries need to specifically demonstrate what plans and systems they have (or will develop) to deliver the vaccine, given that the vaccination time points for the four (or five) doses of the malaria vaccine may fall outside of the time points provided in the existing EPI schedule.
- Strategies that will be implemented to minimise suboptimal vaccine use and wastage and reduce drop-out rates with a particular focus on minimizing drop-out between the third and fourth dose.
- Description of the country's technical assistance needs for vaccine introduction and implementation.
- Confirmation of cold chain readiness. Countries need to provide analysis of their cold chain capacity and describe how that capacity will (or will be enhanced to) accommodate the malaria vaccine introduction.
- Description of how the routine immunisation programme and health system will be strengthened to accommodate the additional work that malaria vaccine introduction will create, including the need to provide the malaria vaccine at touch points (time points) not currently used in routine immunisation. Description of how the potential impact of the vaccine introduction and additional vaccination time points on the workload of the human resources for health will be managed.
- Description of the country's risk communication and community engagement (RCCE) strategy to ensure vaccine acceptance and resilient demand. The country's community engagement strategy should include community education on the vaccine, including the need to continue using other malaria control interventions even after the roll-out of the vaccine. If vaccine introduction is subnational or phased, the RCCE strategy should outline measures to manager perceptions of selective and inequitable access.
- Description of country plans on development of training materials for health workers and information, education and communication materials; adaptation, printing and distribution of revised routine monitoring and reporting tools for use in facilities; distribution method of vaccines and injection supplies; training of health officials and health care workers; and information, communication and social mobilisation of malaria vaccination activities.
- A post-introduction monitoring and learning plan. This needs to describe how the introduction of the malaria vaccine will be monitored, including estimated coverage and vaccine stock levels

[6] Given differences in product-specific availability, countries' first product preference may not always be met.

and how lessons from the introduction will be curated and used to inform the future implementation of the vaccine.

- How the malaria vaccine will be used as a complementary tool to existing malaria control interventions and as part of the country's national immunisation strategy and national malaria strategic plan. In demonstrating this integration, countries may provide an updated comprehensive multi-year plan for immunisation, national immunisation strategy or national malaria strategy or addenda to these documents if these exist and are updated to demonstrate this integration. Countries that do not have these documents must describe how the malaria vaccine is integrated as a complementary tool to existing malaria control interventions and as part of the country's immunisation strategy and national malaria strategic plan.

Zero-dose and missed communities considerations

Applications need to reflect the following:

- Consideration of differentiated delivery strategies to reach missed communities and zero-dose children. Countries need to describe how they plan to introduce the malaria vaccine to reach zero-dose children with vaccines available through EPI;
- Reference the identify, reach, monitor, measure and advocate (IRMMA) framework to reach missed communities and zero-dose children;
- Identify gender-related barriers to immunisation and demonstrate gender-responsive interventions to address these barriers; and
- Role of the vaccine in extending the reach of current health services (e.g. using the demand for malaria vaccine to offer other health services and support catch-up vaccination).

The support covers vaccines, i.e. vaccine dose procurement and associated supplies (e.g. injection safety devices) and financial support to facilitate the introduction (VIG).

Documents to submit

Entirely new Vaccine introduction application	**Vaccine introduction scale up** i.e countries amending a malaria application previously reviewed and recommended for approval by Gavi IRC
To be submitted via the country portal	**To be submitted by email to: proposals@gavi.org**
• Application form (Country Portal)	• Scale up request form (Annex 3)
• New Vaccine Introduction Plan	• Addendum to the New Vaccine Introduction Plan
• Gavi 5.0 budget template	• Updated Gavi 5.0 budget template
• Workplan	• Updated Workplan
• NITAG meeting minutes and/or Immunisation Inter-agency Coordination Committee (ICC) minutes	• NITAG meeting minutes and/or Immunisation Inter-agency Coordination Committee (ICC) minutes
• Minister of Health signature (or delegated authority)	• Minister of Health signature (or delegated authority)
• Minister of Finance signature (or delegated authority)	• Minister of Finance signature (or delegated authority)