

4

The Market Shaping Goal

Ensure healthy markets for vaccines and related products

Market Shaping Roadmap

Malaria Vaccines

Public Summary
FINAL

Introduction

Purpose and scope

The purpose of the malaria market shaping roadmap is to articulate the short, medium and long-term market strategy designed to align market-shaping objectives and target outcomes across the Alliance partners, define a set of interventions to reach these objectives and target outcomes, and inform procurement strategies and decisions. This Roadmap primarily covers market shaping objectives for vaccines licensed or being developed / studied that protect against *P. falciparum* malaria in children under the age of five, for use in all Gavi-supported countries / geographies where malaria vaccines are recommended for use. The scope of this Roadmap is 0-15 years, with short term defined as within 3 years, mid-term as 3-6 years and long term as the period beyond 6 years. This Roadmap will be reviewed and updated as required in 2023.

Key background

According to the World Health Organization's (WHO) 2021 World Malaria Report, of the estimated 627,000 deaths caused by malaria in 2020, 77% (479,000) were children under 5-years of age, primarily in sub-Saharan Africa. Malaria is caused by *Plasmodium (P.)* parasites.¹ Of the five *P.* parasite species that cause malaria in humans, *P. falciparum* is most prevalent in sub-Saharan Africa accounting for nearly all estimated malaria cases in the region. Developing a successful vaccine against malaria has been an effort of several decades, given the technical challenges and complexities to develop a vaccine against a parasite. Efforts to develop RTS,S/AS01e, the world's first malaria vaccine have taken over 30 years and extensive public funding in addition to the developer's own substantial investments; the vaccine was prequalified by WHO in July 2022. In October 2021, based on results from the ongoing Malaria Vaccine Implementation Programme (MVIP) piloted in Ghana, Kenya and Malawi, the WHO recommended the RTS,S/AS01e malaria vaccine be used for the prevention of *P. falciparum* malaria in children living in regions with moderate to high transmission as defined by WHO.² The Gavi Board then approved the opening of a funding window for a malaria vaccination programme in December 2021 and the Gavi country application portal opened in July 2022. UNICEF Supply Division (UNICEF SD) has in parallel conducted a tender for supply of malaria vaccines for the period of 2023-2026 (with possible extension of the contracting period through 2028). The tender was open to manufacturers and developers of both licensed and pipeline products. The first award was issued in August 2022 for 18 million doses of RTS,S/AS01e over the period of 2023-2025. Additional awards are expected as additional vaccines receive licensure and WHO prequalification.

Market context

The malaria vaccine market faces considerable supply constraints in the short term and potentially into the medium term, with initial supply expected to fall substantially short of demand. Steady state demand (e.g., by 2030), as per the Gavi Strategic Demand Scenarios (SDS 2021), is estimated in the range of 80-100md (see *Figure 1 below*). As of the publication of this Roadmap, dozens of countries have expressed their intent to the Alliance to apply to introduce the malaria vaccine in the short term. Demand will be reassessed as countries develop formal introduction plans, with an update to the SDS expected in 2023.

On the supply side, as of August 2022, 18 million doses of the first malaria vaccine have been awarded by UNICEF SD for supply during the years 2023-2025.³ Additional supply is expected to be contracted as soon as it is available, largely expected to stem from additional manufacturers

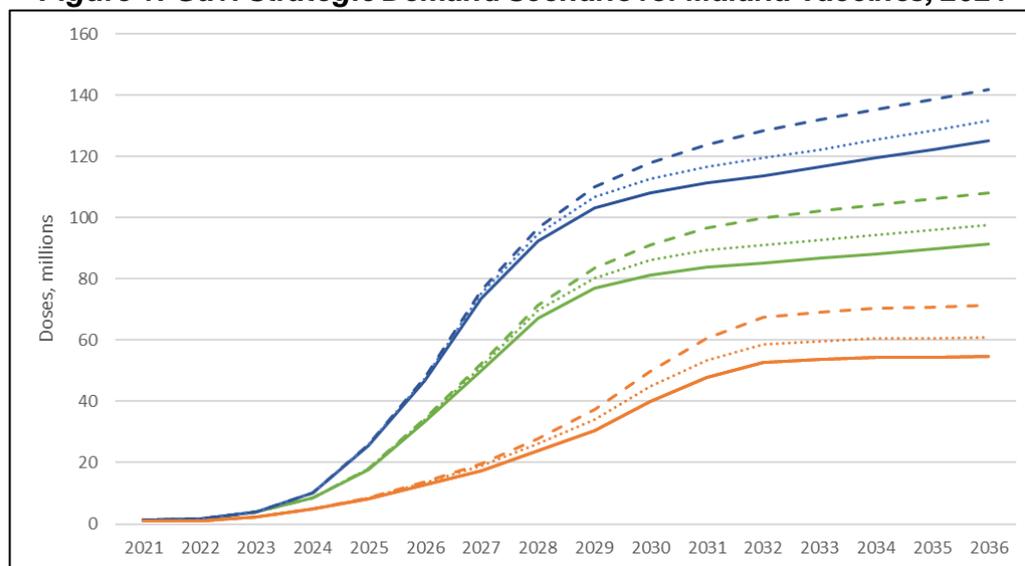
¹ <https://www.who.int/teams/global-malaria-programme/reports/world-malaria-report-2021>

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

³ <https://www.unicef.org/press-releases/millions-more-children-benefit-malaria-vaccine-unicef-secures-supply>;
<https://www.unicef.org/supply/media/13396/file/Malaria-Vaccine-Supply-Price-Market-Questions-Answers-August2022.pdf>

licensing and prequalifying their malaria vaccines. Currently, the most advanced malaria vaccines in the pipeline expected to be suitable for the Gavi programme and anticipated to reach licensure and WHO prequalification during the UNICEF SD tender period (including the period of extension) include the technology transfer⁴ of the RTS,S/AS01e vaccine to another manufacturer based in India and another vaccine currently in phase 3 clinical trials (also anticipated to be manufactured in India). Given this pipeline, supply currently is expected to begin increasing between 2024-2026, with full demand anticipated to be met between 2026-2028.

Figure 1: Gavi Strategic Demand Scenario for Malaria Vaccines, 2021



Key: Solid lines = Routine; Dotted lines = Routine + 1 dose seasonal use; Dashed lines = Routine + 3 doses seasonal use

The initial weighted average price (WAP) of malaria vaccines is expected to remain high in the initial years of the Gavi programme, with WAP coming down over time as the cost of vaccine production decreases and reaches economies of scale through higher volumes and as additional vaccines enter the market and achieve WHO prequalification (currently expected sometime between 2024-2026). The manufacturer of RTS,S/AS01e has agreed to price the vaccine at cost plus a margin of no more than 5%; in the first year (2023) of supply to UNICEF SD the vaccine is being supplied at 0% margin, with an initial price of EUR 9.30 per dose. Pipeline manufacturers have indicated they are committed to offering the vaccine at ‘very cost-effective prices’.

The malaria vaccine pipeline is extensive, with more than 100 studies ongoing as of 2021, though the majority of these are in phase 1 and pre-clinical stages.⁵ Promising future pipeline candidates would include those that will meet or surpass the WHO’s Preferred Product Characteristics (PPCs), which are currently under revision, especially with regards to increased vaccine efficacy and reduced number of doses required for a full course. Regional diversification of the supplier base and, given the high burden of *p. falciparum* malaria in Africa, vaccines with a high likelihood of being developed and/or manufactured in Africa, would be of particular interest.

Healthy Market Framework: Assessment of the Malaria Vaccine Market as of Q3 2022

The Alliance’s Healthy Market Framework (HMF) template was updated in 2021 for the new Gavi 5.0 Market Shaping Strategy. The HMF now includes 3 main areas: demand health (new), supply dynamics, and innovations. Using this new HMF, the below assessment of malaria vaccine market

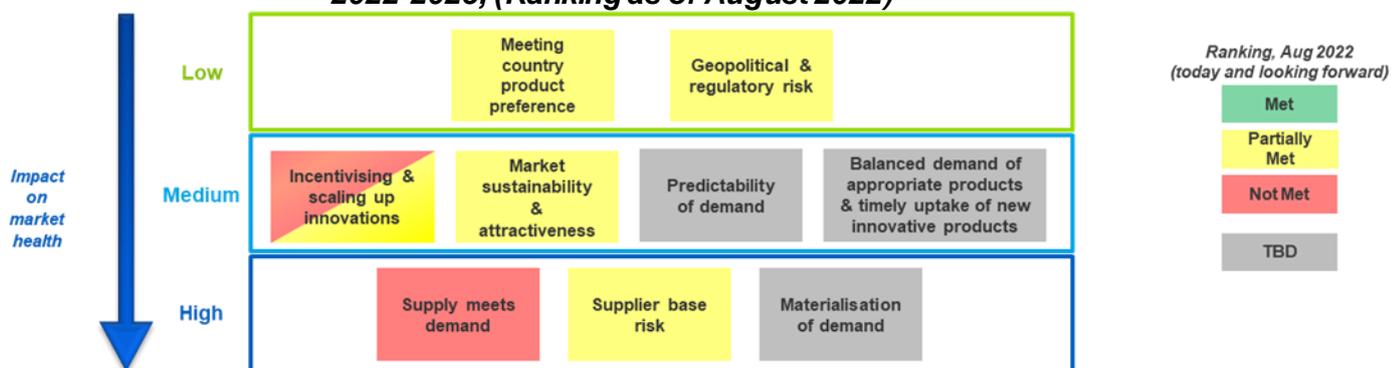
⁴ The manufacturer of RTS,S/AS01e will continue to supply the AS01e adjuvant while the technology transfer recipient will produce the RTS,S bulk and conduct the secondary activities

⁵ <https://www.who.int/publications/m/item/who-malaria-vaccine-global-market-study-september-2021>

health was reached. The market overall was ranked as ‘Unacceptable and requires further intervention’. This ranking was reached primarily because nearly all priority attributes that Alliance partners want to see improve require intervention from the Alliance (e.g., ‘supply meets demand’, ‘supplier base risk’, ‘incentivising and scaling up innovations’, and ‘market sustainability & attractiveness’), while it was deemed too soon to assess the demand-side attributes given that as of Roadmap publication no country has introduced the vaccine (beyond the countries with MVIP pilot programmes). Of the attributes to improve supply-side dynamics, ‘supply meets demand’ and ‘supplier base risk’ are considered the highest priorities given the severe supply constraints facing this market, though in the short to medium term significantly bringing down the cost of malaria vaccines is also a major priority. On the demand health side, ‘materialization of demand’ and particularly the timing of such, is considered the most important attribute to focus on given the urgency to see country interest translate into speedy and high-quality vaccine introductions, which will help ensure as many children as possible are protected with malaria vaccines (particularly those most at risk), and to send a clear signal of the need for additional supply in the market as soon as possible.

The market was also overall assessed as ‘Unacceptable and requires further intervention’ as most of these attributes will require specific interventions and clear coordination and definition of Roles & Responsibilities by Alliance partners to see improvement.

Healthy Market Framework attributes as assessed for the malaria vaccine market for 2022-2025, (Ranking as of August 2022)



Strategy to sustainably improve market health

Gavi Partners defined a long-term strategy for the malaria vaccine market to address these challenges, which translates into the following strategic market objectives and target outcomes:

Objective 1: Supply meets demand in the short to medium term (0-6 years)

- Two malaria vaccines licensed and prequalified in the short term (0-3 years)
- Optimize supply availability in the short term
- Accelerate timelines for scaling up supply capacity and availability

Objective 1 Target Areas	Targets
All suppliers achieve contracted volumes each year	<ul style="list-style-type: none"> • 2023-2025 First awarded tender volumes (18md total) • TBD – other suppliers / vaccines
Total supply availability each year 2023-2028 (cumulative from all suppliers)	<ul style="list-style-type: none"> • Supply target for the entire market equals the unconstrained demand, which is currently estimated at 60-80 million doses at a minimum in 2026

Accelerated timelines for pipeline candidates	<ul style="list-style-type: none"> Accelerate timelines where possible for all pipeline candidates to achieve earliest possible WHO prequalification
Target capacity volumes available from each supplier expected in the medium to longer term + total market	<ul style="list-style-type: none"> Vaccine 1: [Confidential capacity target] by end-2026 Vaccine 2: [Confidential capacity target] by end-2026 <p><i>Note: this target would be revised pending outlook of pipeline vaccines' timelines in the longer term (6-15 years)</i></p>

Summary of Objective 1 action plan (note: several of these activities are already underway as of Roadmap publication):

- Monitoring and follow up to ensure all contracted supply volumes are supplied to countries
- UNICEF SD tender activities to secure supply that meets demand for 2026-2028 and onwards and to secure all available supply from additional suppliers in the short term as and if they enter the market
- Alliance outreach to suppliers on demand forecasts, market updates, and programme updates to ensure suppliers' planned capacity will collectively be able to meet future demand
- Led by WHO, Alliance support to fastest pathway(s) relevant for malaria vaccines for regulatory approvals (national approvals by regulators overseeing the vaccine and WHO prequalification) and new or updated policy recommendations for malaria vaccines
- Identify and implement relevant support to pipeline manufacturers to help reduce timelines to additional vaccine supply, provided candidate vaccines' data and study protocols meet regulatory and policy recommendation requirements

Objective 2: Diversify supplier base for secure, sustainable and competitive supply in the medium to long term (3-15 years)

- Multiple suppliers in this market (*across all time frames*), including at least one vaccine produced in Africa (*medium to long term*)
- Support African continent to enhance supply security, including through transfer of technology and production in the continent (*to be achieved within medium to long term*)
- In the long term, enable sufficiently competitive market dynamics to ensure a sustainable market as countries transition out of Gavi-support

Objective 2 Target Areas	Targets
Price	<ul style="list-style-type: none"> Price goal of [confidential target range] per dose in the medium term resulting from significant decreases to 2023 pricing In the longer term, achieve sustainable further price decreases per full course as compared to the medium-term price target⁶ (e.g., stemming from new or improved products with lower price per dose and/or less doses per course); <i>please also refer to objective 4</i>
Number of suppliers with PQ'd products on LTA with UNICEF SD and on Gavi menu	<ul style="list-style-type: none"> At least 2 suppliers in the market within the short term (0-3 years) that are sustainable over the long-term (6-15 years)

⁶ Longer-term pricing goals will also need to take into account evolving factors, such as if next generation vaccines have significantly improved efficacy and/or if they may be available for expanded populations beyond the current WHO recommendation, thus increasing potential demand and further contributing to economies of scale.

Local manufacturing / diversity in supply chains	<ul style="list-style-type: none"> At least 1 vaccine manufactured in Africa that is PQ'd (including with a national regulatory authority that meets Maturity Level 3⁷ for vaccines), on UNICEF SD LTA and eligible for Gavi support within the long term (6-15 years)
Timelines around product development, regulatory approvals, procurement and programme rollout out	<ul style="list-style-type: none"> Based on lessons learned (including from ongoing activities) from existing malaria vaccines and COVID-19 vaccines, establish new timing targets for development, licensure, procurement and programme rollout of future malaria vaccines

Summary of Objective 2 action plan:

- Speed up access to additional vaccine supply as larger volumes expected to increase economies of scale and pipeline vaccines expected to have lower prices compared to 2023 pricing (*see objective 1 activities*):
 - o This activity includes tender activities aimed at securing additional vaccine(s) supply at best price, with additional activities or mechanisms to be explored as needed to help achieve pricing and supply targets
 - o This activity may also include additional analyses and supplier engagement to help better understand cost drivers of existing and pipeline vaccines.
- Conduct necessary analyses and consultations to arrive at a long-term price target (*to be included as a target in the 2023 Roadmap update*)
- Ensure additional studies conducted that may help reduce cost per full course, noting studies conducted will need to be prioritized as part of the Alliance's Malaria Vaccine Learning Agenda (*to be developed by the Alliance in 2023*)
- Finalize Alliance strategy on local manufacturing in Africa (estimated end-2022) and implement related activities.
 - o Note: These activities will be further expanded upon in the 2023 Roadmap update
 - o Alliance partners are also already implementing some activities related to support of local manufacturing in Africa. These include, for example specialized technical assistance by WHO to vaccine manufacturers in GMP, quality, dossier, etc. to speed up attainment of WHO prequalification / regulatory approvals, and onboarding new manufacturers to global procurement, including those located on African continent, by UNICEF SD. Regional diversification of the supplier base, including manufacturing of a future malaria vaccine in Africa, has also been included as one of the objectives of UNICEF SD's first malaria vaccine tender.
 - o Analysis will also be conducted to understand the landscape of pipeline products and manufacturers in Africa (or suppliers with intent to manufacture in Africa), and plans/progress of national regulators in Africa to achieve Maturity Level 3 for vaccines

Objective 3: Timely demand materialization in the short to medium term (0-6 years) and sustained demand in the long term (6+ years)

- In the short to medium term, ensure operationalization of the Allocation Framework optimizes use of available supply
- Understand full potential of demand (unconstrained) to incentivize increased supply availability
- Predictable and timely demand materialization (across all time periods)
- In the longer term, programmes are sustained, including as countries transition out of Gavi support
- Vaccine prices and co-financing obligations are not a barrier to uptake

⁷ <https://www.who.int/initiatives/who-listed-authority-reg-authorities/maturity-level>

Objective 3 Target Areas	Targets
Timing of demand materialization	<ul style="list-style-type: none"> Alliance partners (and countries) accelerate all steps compared to normal timelines within the application, country readiness and introduction processes to achieve rapid introduction of vaccines All necessary steps between product prequalification and country applications are completed by Alliance partners as quickly as possible to ensure countries are informed and able to access existing and new malaria vaccines
Volumes that materialize	<ul style="list-style-type: none"> All available supply volumes allocated to countries through the WHO Allocation Framework for limited supply of malaria vaccine by the end of each year <i>Note: The Allocation Framework is applicable in the context of demand exceeding available supply</i>
Affordability of (all) malaria vaccines	<ul style="list-style-type: none"> Co-financing approach ensures price is not a barrier to introductions in the short to medium term Co-financing requirements do not lead to low uptake and/or product monopolies within any timeframe and/or de-motivate innovation for new products <p><i>Note: Achieving this target will be dependent upon achieving the objective 2 outcomes related to pricing of malaria vaccines</i></p>
Programme sustainability as countries exit Gavi support	No country that has introduced the malaria vaccine stops their malaria vaccination programme after transitioning out of Gavi support

Summary of Objective 3 action plan:

- Establish and implement an Allocation Framework Committee and a separate Supply Coordination Working Group so that all available supply (*while supply constraints persist*) is allocated and that supply is delivered to countries in a coordinated manner.
- Acceleration of Alliance partner activities to reduce timelines to malaria vaccine introduction; including but not limited to:
 - o Swift rollout of technical assistance to countries to support application submissions and country readiness for introductions.
 - o Speeding up processes related to policy recommendations and guidance to countries issued as quickly as possible to ensure new products can be accessed with minimum lag time after vaccine prequalification completed
 - o Tender activities to ensure that contracting/procurement is not a rate limiting factor in accessing new vaccines, followed by the quick addition of new vaccines to the Gavi menu / application portal and access by countries
 - o Support to country registration of products (existing and new)
 - o Timely sharing of information to countries to ensure awareness of new guidelines and processes for accessing malaria vaccines. This would include support for evidence-based decision making for introduction decisions and programme design within countries
- Updating of relevant Gavi policies, such as the co-financing policy and the Gavi vaccine switch guidelines to help facilitate affordability and access by countries at all stages of Gavi eligibility as market dynamics evolve. Ensure that countries are aware of policy updates and any implications
 - o Additional activities may be defined and implemented to help ensure that Accelerated Transition countries are able to afford and sustain their malaria vaccine programmes as they transition out of Gavi support

- Additional activities may also be implemented through Alliance programme support channels to ensure country preparedness and system readiness are assessed and in place (including through technical assistance activities as required) to facilities effective introduction and scale up of malaria vaccines

Objective 4: Products with critically needed innovations and preferred product characteristics are sufficiently advancing through the pipeline (across all time frames)

- Establish an enabling environment to incentivize (as needed) the following:
 - For licensed or phase 3 trial products, update of these products with improved characteristics to better meet programme needs and reduce costs
 - In the medium to long term, new and improved products prequalified that at a minimum meet the revised WHO PPCs, with strong preference for products that vastly exceed these targets, help reduce overall programme costs, and/or are manufactured in Africa
 - Accelerate product development and access timelines

Objective 4 Target Areas	Targets
Improvements to existing products (licensed / phase 3 trials)	<ul style="list-style-type: none"> • In the short to medium term (0-6 years), product improvements implemented to better meet country programme needs, including multi-dose vials, fully liquid presentation, lower cost/price, etc.
Pipeline products	<p>Within the long term (6-15 years), at least 1 new vaccine licensed that meets at least one of the following conditions:</p> <ul style="list-style-type: none"> • Vastly exceed the forthcoming revised WHO PPC targets • Lower cost vaccine and/or lower cost of total course (e.g., achieved via less doses required, lower production costs, secondary market/broader target population beyond Gavi programme, etc.) • Manufactured in Africa
Timelines around product development, regulatory approvals, procurement and programme rollout out	<ul style="list-style-type: none"> • Based on lessons learned from existing malaria vaccines (including from Roadmap activities) and COVID-19 vaccines, establish new timing targets for development, licensure, procurement and programme rollout of future malaria vaccines

Summary of Objective 4 action plan:

- Identification and communication of priority product updates to existing and late-stage pipeline vaccines that would help first generation vaccines to better meet country product preferences and consideration of potential pathways to help achieve these
- Finalize and publish the updated WHO malaria vaccine Preferred Product Characteristics
- Ongoing monitoring of the malaria vaccine pipeline to identify the most promising candidates, and gain an understanding of potential interdependencies between the malaria vaccine and monoclonal antibody pipelines and markets in the future
- Ensure the evidence and studies needed to help achieve market shaping goals are incorporated and actioned in the Malaria Vaccine Learning Agenda that is being developed by Alliance partners in 2023
- Regular engagement with existing and pipeline manufacturers and developers to provide relevant market information on supply, demand, desired product attributes, programme updates, etc.
- Literature review and mapping of existing product development and access timelines (building on existing understanding) to arrive at potential new product development and introduction timing targets, and communicate findings to wide range of stakeholders