First malaria vaccine supply allocations May 2023

Explanation of process and outcomes

Purpose

This document explains the process and rationale for the allocation of the first 18 million malaria vaccine doses currently available for allocation from 2023 to 2025 to countries approved for support from Gavi, the Vaccine Alliance (see Table 1). The allocation is based on the Framework for allocation of limited malaria vaccine supply, which was developed by the World Health Organization (WHO) in 2022 with guidance from expert advisors and inputs from stakeholders during a broad consultation process.

Allocation outcome overview

Table 1: Malaria vaccine allocations for 2023-2025 to countries approved for Gavi support

		Country	Cumulative target population 2024	Allocated doses 2023-2025	Allocated doses **cumulative**
Supply allocations for initial sub-national vaccine roll-out	3 MVIP countries to continue in pilot areas	Ghana Kenya Malawi	953,000	6,900,000	**6,900,000**
	8 countries to receive doses for «Phase 1» areas	Uganda Burundi Burkina Faso Democratic Republic of the Congo Sierra Leone Benin Cameroon Liberia	1,750,000	10,535,000	**17,435,000**
	1 country to be offered partial supply	Niger – partial allocation		565,000	**18,000,000**
Awaiting supply		*Niger gap: 1,065,000*		*Current supply gap to meet requirements for Phase 1: 3,845,000 doses*	
	2 countries without immediate allocation	Mozambique Sudan			

Note: Numbers for target population and allocated doses may be subject to slight adjustments/rounding.

Background

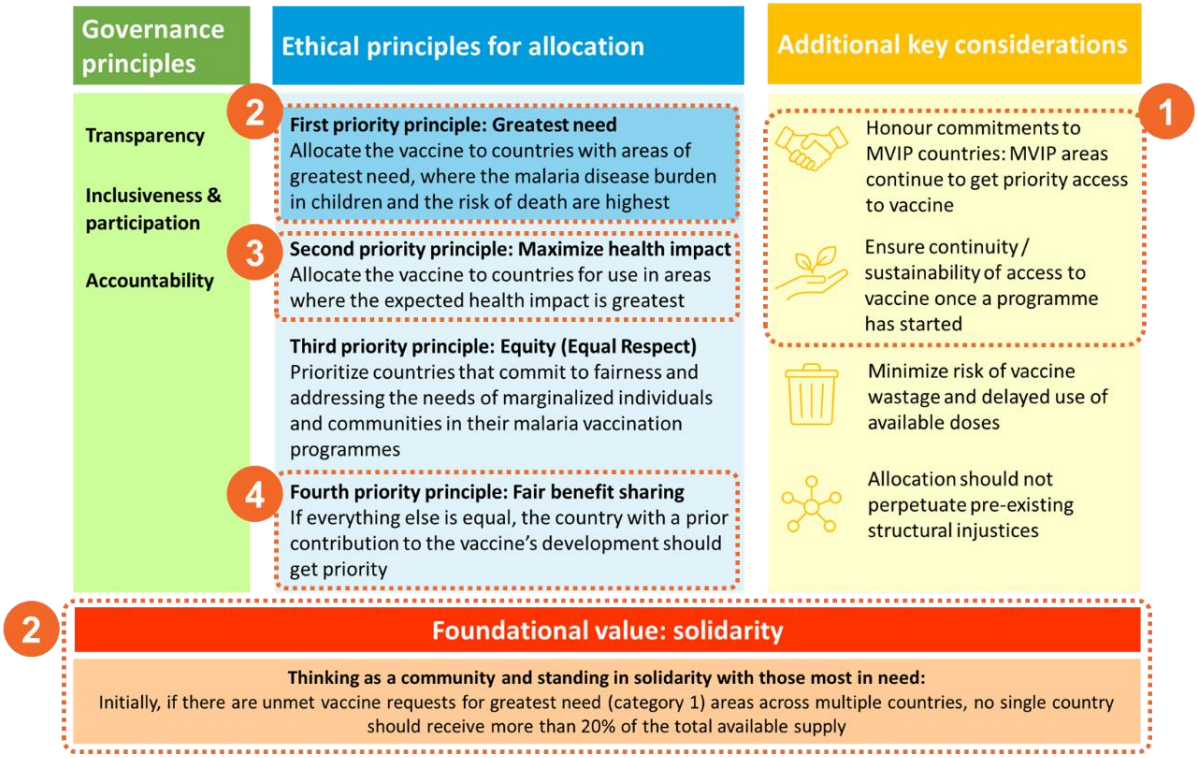
Demand is very high for the first malaria vaccine, RTS,S/AS01, recommended by WHO for the prevention of *Plasmodium falciparum* malaria in children living in regions with moderate to high malaria transmission. In July 2022, Gavi, the Vaccine Alliance, opened a funding window to support Gavi-eligible countries in rolling out this vaccine (and other malaria vaccines as they become available). Since then, over 28 countries expressed interest in introducing the vaccine. Fourteen applications, submitted to Gavi by countries in the first two application opportunities (September 2022 and January 2023), were recommended for approval by Gavi's Independent Review Committee (IRC) following the standard Gavi processes. The available vaccine supply for the period 2023-2025 is currently limited to 18 million doses and falls short of the vaccine dose requirements for the countries recommended by Gavi IRC for approval.

WHO, Gavi, Unicef and other Alliance partners consider it an ethical imperative to address the underlying causes of the current supply scarcity and to pursue ways to increase supply and access to meet demand as soon as possible. The supply situation is dynamic and there is reason for optimism for increased supply: a second malaria vaccine, R21/Matrix-M is under review by WHO, and if confirmed to be safe, efficacious and to meet the quality manufacturing standards, it could be recommended for use by WHO and potentially be available for use as early as Q1 2024. Availability of a second malaria vaccine could help close the sizable supply gap. Efforts by Alliance partners to improve the health of the malaria vaccine market are described in Gavi's market shaping roadmap, available here: https://www.gavi.org/news-resources/knowledge-products/malaria-vaccine-market-shaping-roadmap.

Framework for allocation of limited supply

In anticipation of the mismatch between demand and initial supply, WHO coordinated the development of a framework for allocation of limited malaria vaccine supply (herein referred to as the Framework), to guide in a transparent, principles-and evidence-based manner how the initial limited vaccine doses should be allocated. The Framework was developed in early 2022 with guidance from independent expert advisers, the majority of whom are from the Africa region, and inputs from stakeholders during a broad consultation process. The Framework, endorsed by the WHO Director General in July 2022, provides the ethical principles, considerations and methods to determine supply allocations and is available here: https://www.who.int/publications/m/item/framework-for-allocation-of-limited-malaria-vaccine-supply.

Figure 1: Principles and key considerations of the Framework for allocation of limited malaria vaccine supply (highlighted sections are explained below)



Operationalization of the Framework

The operationalization of the Framework , in accordance with the principles and provisions set forth in the document, was performed by the Framework Allocation Implementation Group and the Senior Leadership Endorsement Group.

The Framework Allocation Implementation Group, comprised of technical staff from the WHO, UNICEF, Gavi Secretariat, and Africa Centres for Disease Control and Prevention (Africa CDC) was mandated to recommend the malaria vaccine quantities to be allocated to countries by systematically following the principles, considerations and indicators defined in the Framework. The Group met five times between March and May 2023. Three observers – a representative for civil society organizations (CSOs) from Gavi's CSO Constituency and two of the expert advisors who supported the development of the Framework - were invited to join the meetings to observe the Group's deliberations. The expert advisers helped to ensure that decisions were made in the spirit of the Framework.

The Group's recommendations were reviewed and endorsed by the Senior Leadership Endorsement Group of Gavi, WHO and UNICEF. The deliberations resulted in consensus on the proposed allocation.

The following steps were followed to arrive at the allocations in Table 1:

1 **Key Framework considerations:** Ensure continuity of access to vaccine once a programme has started & Honouring commitments to MVIP countries

It is a fundamental principle, upheld by national immunization programmes and partners, that once a new vaccine is introduced through routine public health services in a certain area, continuous and sustainable access needs to be maintained. Stopping the provision of a vaccine temporarily or indefinitely while the need is still present' has serious ramifications for the immunization programme as a whole, including a potential loss of trust by communities accessing immunization services.

Since 2019, the RTS,S/AS01 malaria vaccine has been offered by the national Expanded Programme on Immunization (EPI) in selected areas of Ghana, Kenya and Malawi as part of the WHO-coordinated Malaria Vaccine Implementation Programme (MVIP). The MVIP provided the scientific evidence on outstanding questions related to the vaccine's feasibility of delivery, impact and safety, in routine use, which informed the 2021 WHO recommendation for broader use of the vaccine. At the start of the MVIP, the WHO Ethics Review Committee recommended that these pilot areas should be given priority access if the vaccine was recommended for use.

The Framework therefore supports priority access to vaccine supply specifically for the MVIP areas in the three countries, to ensure continuity of services, sustained trust in the EPI, and fairness for communities who have been participating in the pilot evaluation. The cumulative need for all MVIP areas from 2023 to 2025 is approximately 6.9 million doses. This leaves 11.1 million doses to be allocated to additional countries.

2 First priority allocation principle: Greatest need & Foundational value of solidarity

For the distribution of the remaining 11.1 million doses, the first priority aim defined in the Framework is to allocate the vaccine to countries with areas of greatest need, that is, areas where the malaria disease burden in children and the risk of death are highest. The proxy measure for need was defined as a composite index combining measures of malaria burden (either *P. falciparum* parasite prevalence rates (PfPR) in children or malaria incidence rates) and under-five all-cause mortality rates. As part of the application to Gavi, each country presented a sub-national stratification and prioritization of districts into categories of need according to the methods and thresholds described in the Framework (see Table 2 and Figure 2). As all countries followed the same methodology, confirmed by the WHO Global Malaria Programme, a fair comparison was possible to ensure that children living in areas of greatest need across countries are prioritized.

Table 2: Categories of need, based on composite classification of malaria prevalence (or incidence) and all-cause under-five mortality

Category of need	Malaria transmission intensity		All-cause under 5 mortality
	Either: Prevalence	OR: U5 Incidence	
Category 1 Greatest need	>=40%	>=450	>=9.5%
	>=40%	>=450	7.5-9.5%
	20-<40%	350-<450	>=9.5%
Category 2	10-<20%	250-<350	>=9.5%
	20-<40%	350-<450	7.5-<9.5%
	>=40%	>=450	6-<7.5%
Category 3	10-<20%	250-<350	7.5-<9.5%
	20-<40%	350-<450	6-<7.5%
	>=40%	>=450	<6%
Category 4	10-<20%	250-<350	6-7.5%
	20-<40%	350-<450	<6%
Category 5	10-<20%	250-<350	<6%

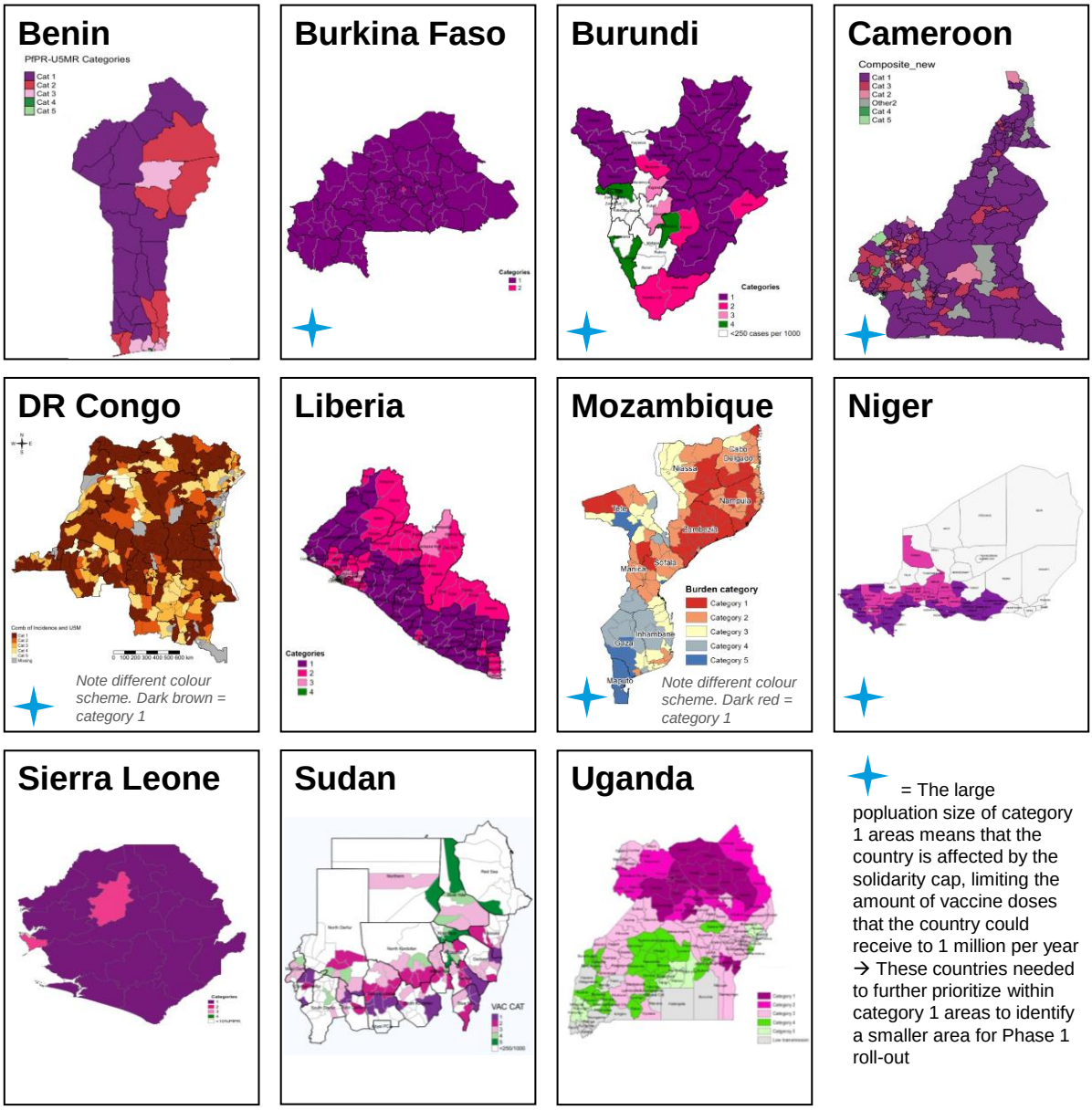
Districts classified as "Category 1" represent the areas in greatest need of additional protection through the malaria vaccine. These areas are characterized by combinations of high malaria transmission and high child mortality. Health system weaknesses, poor access to prevention and treatment, and unjust disparities within the system increase the need for additional protection through the malaria vaccine.

Countries used best available local evidence or modelled estimates for the stratification analysis.

Solidarity is the foundational value interwoven throughout the principles and actions in the Framework. To enable a larger number of countries to access the vaccine for initial roll-out in greatest need (category 1) areas, the maximum quantity (or cap) of malaria vaccine doses a single country can receive at this time is 1 million doses per year. This limit is relevant for countries with large category 1 areas (those with a blue star in Figure 2) and required the concerned countries to further prioritize a sub-set of these greatest need areas for the proposed first phase of roll-out.

The Implementation Group confirmed that all 11 countries had aligned their applications to Gavi with the Framework principles to prioritize doses for children living in areas of greatest need (Category 1) areas and not exceeding the upper limit of 1 million doses per year, where applicable.

Figure 2: Countries' sub-national stratification of areas by Framework categories of need



The cumulative vaccine dose requirements for the initial phase of roll-out focussed on greatest need areas, including potential further prioritization to fit within the cap, (i.e. Phase 1 areas) across all approved countries still exceeded the available supply. Therefore, the Framework Allocation Implementation Group applied the second priority allocation principle to inform further prioritization.

3 Second priority allocation principle: Maximize health impact

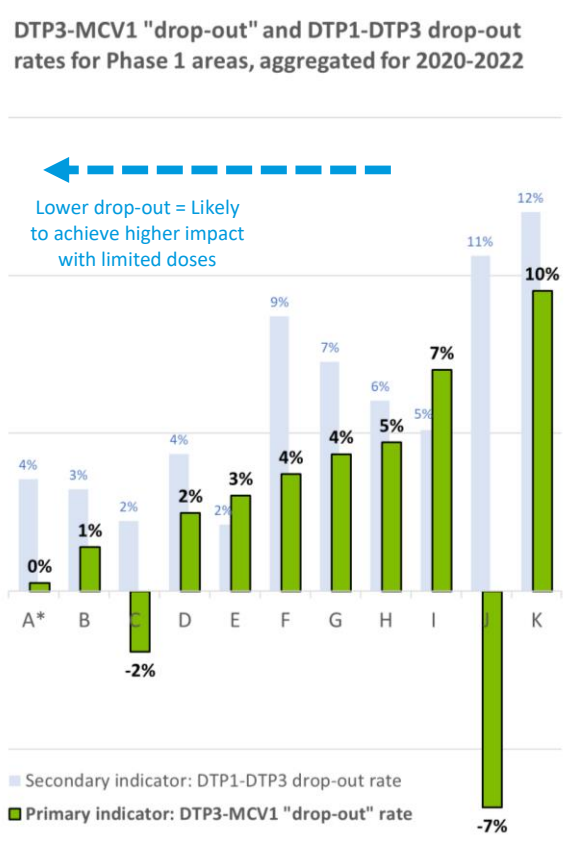
The Framework foresees this second allocation principle to be applied if supply is not sufficient to satisfy all country demands for greatest need areas. The second priority aim defined in the Framework is to allocate the malaria vaccine to countries for use in areas where the expected health impact is greatest, that is where most lives can be saved with the limited available doses. The highest health impact will be achieved where vaccines are most needed and where there is capacity to deliver the full course to children living in areas of greatest need, while minimizing sub-optimal vaccine use. The malaria vaccine is recommended to be given in a 4-dose schedule for optimal benefit, with a 3-dose monthly primary series given from 5 months of age and a 4th dose given in the second year of life to prolong protection. Little protection is expected, based on clinical trial evidence , in a child that receives only 1 or 2 doses; as a result, these first two vaccine doses given to a child that does not complete at a minimum the 3-dose primary series will have a lower impact than if the same doses were given to a child who is able to complete the primary series. In a constrained supply situation, with everything else being held equal, to maximize impact of each available dose, it is therefore preferrable to prioritize the vaccine for greatest need areas where children are likely to complete the primary series, i.e. where vaccine drop-out rates are low.

The Framework's proxy measure for a country's ability to use malaria vaccine doses optimally for maximum impact is the **"drop-out" rate between the number of children reached with the third dose of Diphtheria-tetanus-pertussis vaccine (DTP3) and the first dose of Measles-virus containing vaccine (MCV1) in the districts prioritized to introduce the malaria vaccine**. The drop-out between these two vaccine doses was used for the indicator because the age at which these vaccine doses are given approximates the age when the first and third malaria vaccine doses should be given, thereby indicating the likelihood immunization programmes will be able to reach children at these ages. Countries with a lower vaccination drop-out rate are expected to be better able to reach children with at least 3 malaria vaccine doses, required to achieve impact, and therefore expected to achieve a higher impact with the available doses compared to countries with a larger drop-out in their greatest need areas. Please consult the Framework for more detailed explanation for the choice of this principle and indicator.

All countries provided data on the number of DTP1, DTP3 and MCV1 doses administered in 2020, 2021 and 2022 in the districts prioritized to introduce the malaria vaccine, based on their administrative immunization data systems. The numbers were aggregated across districts and years to derive a single DTP3 to MCV1 "drop-out" rate per country as the primary indicator for this second allocation principle. Country reported data were used, rather than WHO/UNICEF estimates of national immunization coverage (WUENIC) for a number of reasons.[1]

[1] Reasons include: The need for an estimate relevant to the sub-national areas where the vaccine will be rolled-out first (WUENIC estimates are only available at national level); WUENIC estimates are released once a year in mid-July, i.e. 2022 WUENIC estimates were not yet available while administrative data was. While *coverage* rates based on administrative data have recognized limitations that are often due to the unreliable denominator, the calculation of drop-out uses the number of administered doses, without requiring a denominator. Therefore, country-reported administrative data showing the number of doses administered in the Category1/Phase 1 areas was considered the most appropriate source for the indicator on drop-out.

Figure 3: Countries' drop-out rates in the districts prioritized to introduce the malaria vaccine as proxy measure for likelihood of maximizing health impact with limited malaria vaccine doses



Country reported data was used to calculate the primary indicator for the second allocation principle, i.e. the DTP3 to MVC1 "drop-out" rate in the areas where the malaria vaccine will be introduced first.

The lower the drop-out rate, the higher the likelihood that a child will be able to complete the primary 3-dose series of the malaria vaccine, thereby maximizing the impact of the administered doses.

A large negative value means that fewer DTP3 doses were administered than MCV1 doses, which could be an indication of challenges with delivery of the DTP series and/or weaknesses in supply chain / vaccine management systems (among potential reasons).

Given the difficulty in interpreting a large negative value for the DTP3 to MVC1 "drop-out" (country J), the DTP1 to DTP3 drop-out rate for the same time period in the same priority areas was used as secondary indicator to help inform the appropriate place in the ranking for this country.

The Implementation Group used **the ranking of countries based on the drop-out rate indicator in the targeted areas, to allocate vaccine supply for the approved Phase 1 areas (i.e. greatest need areas)**, starting with countries with the lowest drop-out rate (left side of Figure 3) until available supply was exhausted. **Supply was sufficient to cover the vaccine dose requirements for the pilot areas of the 3 MVIP countries and the initial phase of roll-out for 8 countries. One country (Niger) straddled the line of supply availability and will be offered a partial supply allocation. Two countries, Mozambique and Sudan, were last in the ranking, and could therefore not be allocated supply at this point in time.**

4 Final priority allocation principle: Fair benefit sharing

Mozambique and Sudan were found to have similar levels of performance in relation to the second allocation principle (i.e. the vaccine drop-out rates). In order to establish the rank order between the two, the Framework's final priority principle, i.e., fair benefit sharing, was applied. Mozambique participated in the clinical development of the RTS,S/AS01 vaccine as a Phase 2 and 3 trial site and would therefore be prioritized among the two.

Next steps

Countries with a confirmed supply allocation will be informed and will be able to start planning for initial vaccine implementation in the proposed greatest need areas.

Niger, as the country that straddled the line of supply availability, will be offered a partial supply allocation. If the offer is accepted, the country will be able to start planning for introduction in a smaller sub-set of category 1 areas. Should vaccine doses become available or be freed up, for example through delayed introductions or recalibration of vaccine dose requirements after introduction (based on actual programme performance) in other countries, Niger would be offered the additional doses until its Phase 1 allocation needs are met.

Due to insufficient supply to meet initial allocation requests, Mozambique and Sudan will not receive a supply allocation at this point in time. Gavi and WHO are committed to supporting these two countries to address the underlying issues so that higher impact can be achieved when additional supply becomes available.

The supply situation is dynamic and there is reason for optimism for increased supply. Additional quantities of malaria vaccine could become available next year, for example through the WHO recommendation and prequalification of a second malaria vaccine and UNICEF's ability to secure timely access to supply. If so, more countries will be able to access malaria vaccine doses and expand vaccination with the ultimate goal of reaching all children who would benefit from additional protection.