Framework for the allocation of limited malaria vaccine supply

28 June 2022

Preamble

In October 2021, the World Health Organization (WHO) issued a recommendation for the first malaria vaccine, called RTS,S/AS01, 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.[1] The long-awaited malaria vaccine for children is a breakthrough for science, child health and malaria control. It is projected that – at scale – using this vaccine as part of an integrated malaria control programme could save tens of thousands of young lives each year.

This vaccine is the result of several decades of research and development, supported through public-private partnerships and significant contributions by African scientists and communities. Thanks to an innovative financing agreement between Gavi, the Vaccine Alliance, GlaxoSmithKline (GSK) and MedAccess, vaccine doses are available to initiate the Gavi-supported malaria vaccine roll-out.[2] However, current estimates suggest that the initial supply of the vaccine is insufficient to meet the needs of over 25 million children born each year in regions with moderate to high malaria transmission.[3] It is an ethical imperative to address the underlying causes of the current scarcity and to pursue ways to accelerate increased supply to meet demand as soon as possible.

WHO recommends that the RTS,S/AS01 malaria vaccine is provided in a schedule of 4 doses in children from 5 months of age for the reduction of malaria disease and burden.

Countries may consider providing the vaccine seasonally, with a 5-dose strategy in areas with highly seasonal malaria or areas with perennial malaria transmission with seasonal peaks.

More information is available in the WHO malaria vaccine position paper and the WHO Guidelines for malaria

In parallel, until vaccine supply is sufficient to meet the need, a fair and equitable mechanism is needed to guide, in full transparency, how supply is prioritized, based on best available evidence, shared values and appropriate input by key parties. The global immunization community has faced challenges of initial limited supply with other vaccines and lessons learned can be drawn upon to manage the limited supply of this vaccine. This Framework for the allocation of limited malaria vaccine supply outlines the values, allocation principles, governance principles and key considerations for implementation. **The Framework offers guidance on the global allocation of RTS,S/AS01, and other malaria vaccines as they become available, between countries, and guidance on prioritization of areas for vaccination within countries until supply constraints can be fully resolved.** In-country vaccine

[1] WHO News Release, 6 October 2021, accessible from: https://www.who.int/news/item/06-10-2021-who-recommends-groundbreaking-malaria-vaccine-for-children-at-risk

[2] Gavi News Release, 4 August 2021, accessible from: https://www.gavi.org/news/media-room/new-financing-agreement-boost-malaria-vaccine

[3] Current WHO guidance defines moderate to high malaria transmission settings as those with an annual incidence greater than around 250 cases per 1000 population or a prevalence of *P. falciparum* infection in children aged 2–10 years ($PfPR_{2-10}$) of approximately 10% or more.

World Health Organization

deployment should respect sovereign decision-making and align with the High Burden to High Impact (HBHI) approach to sub-national tailoring of malaria interventions.[4] The intended audience of the Framework are policy makers in malaria-endemic countries, the manufacturer(s), Gavi, the Vaccine Alliance and other funding, implementing and technical partners.

This Framework is intended to be dynamic to support prioritization decisions at the start of vaccine roll-out and over the coming years as supply ramps up, until supply constraints are fully resolved. Periodic reviews and updates will ensure that the Framework remains useful and appropriate.

The malaria burden and sub-national tailoring of malaria control

While considerable global progress in malaria control has been achieved over the last two decades, malaria continues to cause unacceptably high levels of disease and death. According to the *World malaria report 2021*, there were an estimated 241 million cases and 627 000 deaths globally in 2020.[5] Almost all malaria deaths are caused by *Plasmodium falciparum*, and approximately 95% occur in sub-Saharan Africa, mostly in children under 5 years of age. With an estimated 479 000 deaths due to malaria in children under 5 years in 2020, malaria remains a major cause of childhood deaths in Africa.[5] The global priority thus continues to be to reduce the burden of disease and death while pursuing the long-term vision of malaria eradication.[5]

To optimize impact, the vaccine should be implemented as part of a comprehensive malaria control plan. Countries should use best available local data and contextual information to target the vaccine sub-nationally as part of a mix of interventions that collectively impact on malaria. Analytical techniques can support country decision making on where the vaccine could be initially prioritized for highest impact, with an understanding that as supplies improve, vaccine access will expand to other areas. Building on lessons from the HBHI approach, the WHO Global Malaria Programme is ready to support countries on the process of subnational tailoring of interventions, including the initially limited supplies of RTS,S/AS01 and of other malaria vaccines as and when they become available.

Why is an allocation framework needed?

In October 2021, following the results of the Malaria Vaccine Implementation Programme (MVIP) in Ghana, Kenya and Malawi showing that RTS,S/AS01 was safe and reduced the burden of malaria, WHO recommended that the vaccine be used as an additional tool for the prevention of *P. falciparum* malaria in children living in regions with moderate to high transmission.[6] This recommendation was followed by an important decision by Gavi, the Vaccine Alliance, to support a malaria vaccine programme for Gavi-eligible countries.[7] Together, these two decisions pave the way for broader roll-out of this new vaccine, with first introductions beyond the MVIP areas expected in 2023.

Demand for the malaria vaccine from endemic countries with moderate to high transmission is expected to be high. Based on most recent data, more than 30 countries have geographic areas with

[4] High burden to high impact. A targeted malaria response. Geneva: World Health Organization; 2019, accessible from: https://www.who.int/publications/i/item/WHO-CDS-GMP-2018.25

[5] World malaria report 2021. Geneva: World Health Organization; 2021, accessible from: https://www.who.int/teams/global-malaria-programme/reports/world-malaria-report-2021

[6] Malaria vaccine: WHO Position Paper. Geneva: World Health Organization; 2022, accessible from: https://www.who.int/publications/i/item/WER9709

[7] Gavi News Release, 2 December 2021, accessible from: https://www.gavi.org/news/media-room/gavi-board-approves-funding-support-malaria-vaccine-roll-out-sub-saharan-africa

moderate to high *P. falciparum* malaria transmission where the vaccine could potentially provide additional protection against malaria to more than 25 million children per year. Demand forecast scenarios suggest that this may translate into a long-term need of more than 100 million doses of malaria vaccine per year (assuming a 4-dose schedule).[8] Most of the affected countries are currently eligible to receive support from Gavi to facilitate vaccine introductions, including the new malaria vaccine.

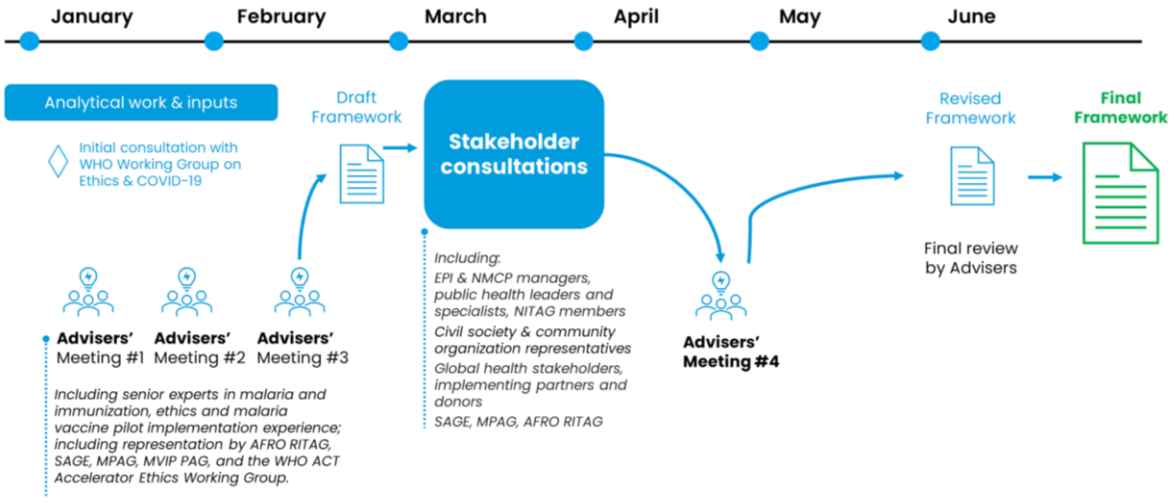
However, supply of the vaccine is expected to be insufficient to meet the need in the initial years. A recent Global Malaria Vaccine Market Study[9], commissioned by WHO, found that vaccine supply might be insufficient through the medium term, with a constrained supply potentially during the first 4-6 years following expected first introductions in 2023. It is difficult to predict when the supply constraints might ease as several factors influence the situation. These include how quickly production of the recommended RTS,S/AS01 vaccine can increase and whether and when a second malaria vaccine might become available for use.

Areas for action have been identified and more are being explored, including through the Gavi Alliance's market shaping work, to increase vaccine supply and facilitate a healthy malaria vaccine market. With the overall goal that all countries with areas of moderate to high malaria transmission have the opportunity to access the vaccine and while efforts to address the supply limitations are ongoing, a prioritization mechanism is required to allocate limited vaccine supply until supply fully meets demand.

Process for developing the Framework

In response to the supply situation, WHO's Strategic Advisory Group of Experts on Immunization (SAGE) and the Malaria Policy Advisory Group (MPAG) recommended that WHO should lead the development of a Framework to guide where the initially limited doses of the malaria vaccine should be deployed, based on best available scientific evidence, an explicit consideration of ethical principles and through a transparent process that incorporates input by key parties, with appropriate representation and consultation. The process, shown in Figure 1, included the convening of a group of temporary advisers to develop a draft proposal and subsequent broad-based consultations.

Figure 1: Allocation Framework development process



[8] Gavi Strategic Demand Scenarios 2021

[9] WHO Malaria Vaccine Global Market Study, accessible from: https://www.who.int/publications/m/item/who-malaria-vaccine-global-market-study-september-2021

The group of temporary advisers to WHO included senior experts (8 female and 8 male) in malaria and immunization, ethics and human rights, malaria vaccine pilot implementation and other relevant fields (see Appendix 1). The group also included representatives of established WHO advisory bodies, including the WHO AFRO Regional Immunization Technical Advisory Group (RITAG), SAGE, MPAG, the MVIP Programme Advisory Group, and the WHO ACT Accelerator Ethics Working Group. Three quarters of the experts are nationals of malaria affected countries in Africa. The group met four times between January and April 2022 to discuss the values and ethical principles that should guide the allocation of limited supply and to review and critically appraise the pros and cons, implications and trade-offs of various allocation options. A draft Framework reflecting the guidance received from the group was finalized in February. Valuable inputs were received through consultations at the beginning of the process with the WHO Access to COVID-19 Tools Accelerator Ethics and Governance Working Group.

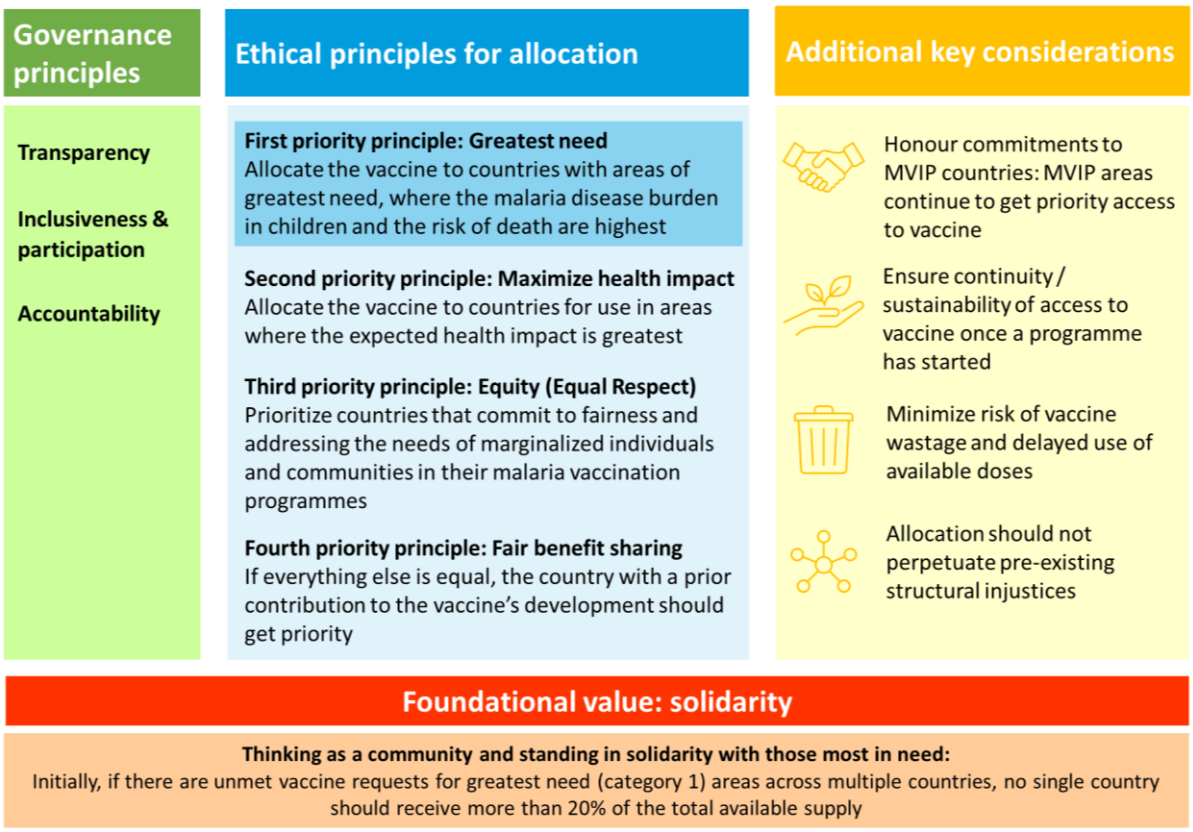
A consultation process organized during the month of March 2022 provided the opportunity for input and feedback on the draft Framework from a wide range of stakeholders. Over 230[10] representatives from endemic countries, civil society and community organizations, global health stakeholders, implementing partners and donors were consulted on the draft Framework. Stakeholders provided feedback in four webinars arranged by the WHO Secretariat and were invited to send additional comments in writing through a standardized form. Comments on the draft Framework were also invited from members of SAGE, MPAG, AFRO-RITAG and staff from the WHO Immunization, Vaccines and Biologicals (IVB) department; and from the WHO COVID-19 Ethics and Governance Working Group. The feedback received during the consultation process was summarized and submitted to the temporary advisers, who considered this input in their process to finalize the Framework.

[10] Total number of unique participants in four consultation webinars. The total excludes advisers, presenters, interpreters, and WHO Secretariat.

The Framework

Building on and drawing lessons from existing frameworks and mechanisms for prioritizing scarce resources and based on early inputs from the WHO Working Group on Ethics and COVID-19, the temporary advisers assessed various potential principles and options for allocation of the malaria vaccine. Figure 2 presents an overview of the values and principles. Principles explicitly rejected for decision-making are reported in Appendix 2.

Figure 2: Framework principles and key considerations



1. Foundational value: solidarity

The target population for the malaria vaccine are children living in regions with moderate to high malaria transmission, primarily on the African continent. It is thus important that an allocation Framework resonates with ethical values common to African peoples. Communitarian values, such as solidarity, sharing, and harmony, alongside individual rights and duties, occupy a central role in African normative frameworks (see for example, *The African Charter on Human and Peoples' Rights*). In the light of this, a solidaristic approach is required to ensure that the highest priority is accorded to saving the most lives through the administration of the vaccine and prioritizing the needs of children who are at greatest risk of death from malaria. Taking into account that the malaria vaccine is the result of collaborative efforts to address a shared need to fight against the devastating effects of malaria across the continent, and beyond, there is a call to stand with and for those children at highest risk of death who could be saved if access to the malaria vaccine is enabled. The practice of solidarity often requires the abridgment of one's own immediate interests for the interests of others where more good could be done and where needs are more pressing. A request to abrogate

competition between countries for the vaccine – in the spirit of solidarity – and respect for saving the most lives is interwoven throughout the principles and actions suggested in this Framework.

In addition, solidarity as foundational value justifies that initially, if there are unmet vaccine requests from multiple countries for greatest need areas (i.e. category 1 areas, see definition below), no single country should receive more than approximately 20% of the total available supply.[11] This is to enable a larger number of countries with children in areas of highest need to gain access. If following a reasonable period of time during which all countries had an opportunity to request vaccines, there is additional supply available, this restriction should be lifted. Countries that were affected by this 20% cap should get first priority for expansion, starting with additional category 1 areas.

2. Governance principles

The governance principles of transparency, inclusiveness and participation and accountability guide the process for how this Framework has been developed and how allocation decisions should be made and monitored. These governance principles taken together should be seen as advancing legitimate and trustworthy decision-making.

Governance principle 1: Transparency

In a transparent process, the underlying rationale for vaccine allocation decisions and their justifications should be communicated publicly in an honest, straightforward manner and made available for public review. Sufficient information should be provided for countries to understand the practical implications of the supply situation and the allocation Framework, for example that phased sub-national vaccine introduction (rather than full national roll-out) will likely be the norm. Information regarding vaccine supply availability, reasons for scarcity, and actions taken to address them should also be communicated publicly.

Governance principle 2: Inclusiveness and participation

In an inclusive and participatory process, those affected by vaccine allocation decisions – including individuals, communities and countries – should be able to exert some influence over the decision-making process as well as the decision itself.

This Framework has been developed based on guidance received from expert advisers, most of whom either live in or work with malaria affected countries and communities. Guidance has also been sought from established global and regional WHO advisory bodies: SAGE, MPAG, and AFRO RITAG. The consultation process in March 2022 provided the opportunity for verbal and written input from a wide range of stakeholders, including malaria and immunization programme managers and public health leaders in malaria affected countries, representatives of civil society and community organizations and global partners.

The Framework also refers to the need to build capacity over time in communities with currently limited capacity to effectively deliver a vaccine requiring multiple doses to children at risk.

Governance principle 3: Accountability

Decisions should be made with clearly defined objectives, processes, roles and responsibilities, supported by mechanisms to enable decision-makers to be held accountable and mitigate conflicts of interest. A fair process means that global allocation decisions should be made by a legitimate group applying the Framework principles, rather than by individuals, by individual pharmaceutical companies, or, in the case of allocation between countries, by a single country.

[11] Total available supply refers to the total amount of malaria vaccine doses contracted by UNICEF, net of the needs for MVIP areas. 'Approximately' is added to allow for potential rounding of the quantities for operational purposes.

Recipient countries should also be held accountable regarding criteria for internal allocation and actual delivery of vaccines. The Gavi Alliance application process will require countries to detail the rationale for targeting specific subnational geographies for vaccination.

The allocation Framework described below is not static and will require periodic reviews and updates to respond to the changes in supply availability and the epidemiological situations in countries and communities within countries.

3. Ethical principles for allocation

> *Out of the many ways that we might choose to allocate scarce resources, this choice represents the objective that is being **valued** most…Science and/or evidence alone cannot tell us which choice or aim is 'correct' or which aim society should value most. This requires a value judgement, which is the domain of ethics… Consequently, the first step in developing a framework for the allocation of scarce resources requires explicit consideration and clarification of ethical values—values that technical considerations and mechanisms should subsequently operationalize.*
>
> Extract from: Ethical foundations of a global vaccine allocation framework for COVID-19: high-level overview - Considerations from WHO Working Group on Ethics and COVID-19

First priority allocation principle: Greatest need

Among available options, the first priority aim is to allocate the malaria vaccine to countries with **areas of greatest need, that is, areas where the malaria disease burden in children is highest and the risk of death is also highest**. Health system weaknesses, poor access to prevention and prompt treatment, and unjust disparities within the system increase the need for additional protection through the malaria vaccine. Access to other malaria prevention tools does not necessarily negate this need. For example, there are areas of Africa where coverage of insecticide-treated bed nets (ITNs) is relatively high, but malaria burden remains intense, and child mortality remains high. In contrast, there are areas where ITN coverage is low, but malaria burden is moderate or low. All malaria control tools provide only partial protection against malaria, and therefore, are deployed in various combinations for highest impact.

Ultimately, each country must identify the areas of highest burden and need within its own borders based on best available local evidence and the broader context of sub-national tailoring of different malaria interventions. At the global level, to enable across country comparison, the proposed proxy measure for greatest need is a **composite index that combines levels of *P. falciparum* parasite prevalence rate (PfPR) in children and under-five all-cause mortality rate (U5MR) -** see illustration in Appendix 3. The PfPR is a measurement, although imperfect, of malaria transmission intensity and malaria burden, while the U5MR captures system weaknesses or pre-existing structural injustices that increase the risk of a child dying. There are instances where the available PfPR data may not be recent or sufficiently sensitive to inform differences in transmission intensity. In such situations, countries may use their malaria incidence or severe disease data. Where countries have good data on the burden of severe malaria sub-nationally, these data can be very useful in refining the vaccine prioritization process.

Second priority allocation principle: Maximize health impact

The second priority aim 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 expected impact of the vaccine is dependent on a number of factors, including disease burden and ability of the immunization programme to reach and retain children to receive all recommended vaccine doses (currently 4 in perennial malaria transmission settings). The best outcome (health impact) will be achieved where vaccines are most needed and where there is

capacity to deliver the full course to children who need them most, while minimizing sub-optimal vaccine use.

The RTS,S/AS01 vaccine is recommended to be given in a 4-dose schedule for optimal benefit, with the first dose administered from 5 months of age.[12] Little protection is expected, based on the evidence to date, 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 the series will have a lower impact than if the same doses were given to a child who is able to complete the 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 areas where children are likely to complete the full schedule, i.e. where vaccine drop-out rates are low. At the global level, given limitations related to reported subnational immunization coverage data, the proposed proxy measure for a country's ability to use malaria vaccine doses optimally for maximum impact is the national drop-out rate between the third dose of Diphtheria-tetanus-pertussis vaccine (DTP3) and the first dose of Measles-virus containing vaccine (MCV1). MCV1 is proposed because it is typically administered at 9 months of age, i.e. at around the time when the third dose of the RTS,S/AS01 is expected to be given. Preferably, this drop-out rate should be below 10%. The Gavi Alliance application process will require countries to detail the rationale for targeting specific subnational geographies for vaccination, including how drop-out performance was considered.

There is an inherent tension between the first principle (greatest need) and the second principle (maximize health impact) as those countries or communities in greatest need may also be the ones least able to deliver the vaccine efficiently (that is, as defined above, with low drop-out rates). Allocating vaccines on 'greatest need' principle may entail a higher risk of inefficiencies unless resources are allocated to address capacity and delivery challenges. Relying solely on 'maximizing health impact' for allocation decisions can perpetuate and even exacerbate pre-existing structural injustices. For countries whose children are at high need but where risk of sub-optimal vaccine use is high because of resource and infrastructure constraints, every effort should be made to provide resources and technical assistance to remove these constraints. Availability of health system strengthening support from international partners, such as Gavi, the Global Fund, the World Bank, UNICEF, President's Malaria Initiative, and others, should be explored for this purpose.

Third priority allocation principle: Equity (Equal Respect)

The third priority aim is to allocate the malaria vaccine **to countries that commit in their malaria vaccination programmes to fairness and addressing the needs of marginalized individuals and communities**. The vaccine prioritization within countries should take into account the vulnerabilities, risks and needs of communities who, because of underlying societal or geographic factors, are at risk of experiencing greater burdens from malaria. Proactive steps should be taken to ensure equal access and to address barriers, particularly for socially disadvantaged and vulnerable populations. Any in-country deployment decision that treats the interests of different people or groups of people differently without adequate justification grounded in appropriate moral principles should be rejected.

Consideration should be given regarding the most appropriate delivery channels to effectively reach vulnerable populations in high burden areas. Some Gavi-supported countries may face challenges related to chronic fragility, acute emergencies and/or displaced populations and would qualify for differentiated support and flexible approaches under Gavi's updated Fragility, Emergencies and

[12] A 5-dose strategy might be appropriate in areas with highly seasonal malaria or areas with perennial malaria transmission with seasonal peaks.

Displaced Populations (FED) Policy.[13] In some of these settings, severe malaria and mortality rates could be very high. The policy allows Gavi to channel vaccines and provide additional Health systems and Immunisation strengthening support (HSIS) through Alliance and Expanded partners and Civil Society Organisations, to reach populations, or areas where national government cannot or is unwilling to recognise or provide support. Any support provided through this policy is strongly encouraged to explore opportunities for delivering the full package of vaccines and integrating immunisation within a broader package of essential services by working with cross sector coalitions.

Equity at the global level requires that the allocation of limited supply takes into account and reduces unjust disparities across countries and that the interests of all countries and populations in need are treated fairly. We know that a large number of countries have geographic areas and populations with similarly high needs. The equity principle implies that available supply should be distributed more widely to a larger number of countries with high need, rather than to a few countries (enabling them to cover a larger geographic area). The initial 20% cap (i.e. no single countries should initially receive more than 20% of available supply) further reinforces this principle. The consequence of such an approach is that countries will necessarily have to **roll-out the malaria vaccine in a phased manner**, starting at the sub-national level in areas with highest need – unless they prefer to wait until supply is available to cover all desired medium to high transmission areas at once. The operational feasibility and implications of phased sub-national implementation will have to be considered carefully by national immunization programmes.

Fourth priority allocation principle: Fair benefit sharing

The principle of fair benefit sharing applied to the RTS,S/AS01 vaccine would justify the allocation of vaccines to individuals or groups to whom something is owed because of burdens or risks they have assumed in helping to research and develop this vaccine. Communities from more than 10 countries in Africa have contributed over the past decades to the clinical development of this vaccine.

While these contributions are of tremendous value to all those affected by malaria, it would be inequitable l to allow these contributions in of themselves to be a primary reason for prioritization. A confluence of factors gives this principle less moral weight compared with the aim of reaching those in greatest need or maximizing health impact from limited doses. Among those moral factors are that it favours those with more ability to provide resources (e.g., trial sites, experts) of value to research and development (R&D). By favouring those that might already be better off, it is in direct tension with principles of equity. Nevertheless, the practice of fair benefit sharing in research would recommend engaging with countries that have contributed to the development of the vaccine through supporting them in their malaria control programmes.

As part of the commitment to benefit sharing, if two countries have areas with similar category of need and vaccine drop-out rates, the country that contributed to the vaccine's development should be given priority.

[13] Gavi Alliance Fragility, Emergencies and Displaced Populations Policy, accessible from: https://www.gavi.org/sites/default/files/2022-06/Fragility-Emergencies-and-Displaced-Populations-policy.pdf

4. Additional key considerations

Key consideration 1: Honour commitments to MVIP countries to sustain vaccination for continued implementation in MVIP areas (including expansion to comparator areas)

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 MVIP. The MVIP provides the scientific evidence on outstanding questions related to the vaccine's feasibility, impact and safety in routine use which informed the recent WHO recommendation for widespread use of the vaccine. The three MVIP countries are now considering expansion of vaccination – including, as a priority, to those areas serving as comparator (without vaccine implementation initially) for the purpose of the malaria vaccine pilot evaluation. At the start of the MVIP, the WHO Ethics Review Committee recommended that these pilot areas should be given priority access once the vaccine was recommended for broader use.

The Framework therefore supports priority access to the MVIP areas for future vaccine supply to ensure continuity of services, sustained trust in the EPI, and fairness for communities who are participating in the pilot evaluation. The cumulative need for all MVIP areas (implementing and comparator) is estimated to be approximately 3 – 3.5 million doses per year at full scale. Through the end of the MVIP (expected 31 December 2023) this need will be met with vaccine doses donated by GSK for the purpose of the MVIP. Requests for vaccine supply for expanded implementation in Ghana, Kenya and Malawi *beyond* the MVIP areas will be managed in line with the allocation principles in this Framework.

Key consideration 2: Avoid or minimize the risk of vaccine wastage and delayed use of available doses

While some amount of wastage is unavoidable in the implementation of a vaccine, with even a small multi-dose vial presentation, through the routine immunization programme, unnecessary wastage for a scarce life-saving resource should be minimized. Good cold chain and vaccine management practices, as well as vaccine demand planning and related coordination for demand generation strategies should be reinforced during health worker and other key staff trainings as part of the preparatory activities for new vaccine introduction.

Efforts should be made to minimize the risks of children dropping out from the malaria vaccination programme, as doses given to a child who does not receive at least 3 doses are not an effective use of limited vaccine supply. For countries whose children are at high need but where risk of drop-out or vaccine wastage is relatively high because of resource and infrastructure constraints, every effort should be made to provide resources and technical assistance to remove these constraints.

Countries receiving vaccine doses should aim for timely distribution and effective vaccine administration well before the vaccine expiry date. A maximum allowable time period should be defined between global allocation of quantities of vaccine to a particular country, as per the Framework, and the start of vaccine implementation, which when exceeded, would trigger reallocation (of not yet shipped supply) to another country.

Finally, while equal opportunities should be created for all interested countries to submit a request for access to vaccine doses (either via the Gavi application process for Gavi eligible countries, or through communication to UNICEF or WHO for countries not eligible for Gavi support), available doses should not remain unallocated for an extended period of time. Timeliness in implementation of the available vaccine supply will increase the manufacturers' confidence that continued and projected higher demand will materialize.

Key consideration 3: Ensure continuity and sustainability of access to vaccine once a programme started

It is a fundamental principle, upheld by national immunization programmes and global partners (including UNICEF and Gavi), that once a new vaccine programme is started through public health services in a certain area, continuity and sustainability over time need to be guaranteed. Stopping the provision of a vaccine while the need is still present has serious ramifications for the immunization programme as a whole, including a potential loss of trust by communities in immunization services. Erratic or unpredictable supply make it more difficult for country programmes to achieve optimal performance. Moreover, vaccine introduction has been shown through the pilots to reduce paediatric hospitalizations for severe malaria and is likely to reduce all-cause child mortality. Withdrawal of the malaria vaccine in the setting of ongoing stable transmission would likely precipitate an increase in the malaria burden similar to that seen before vaccine introduction. It is recognized that the recurring vaccine needs to immunize newly age-eligible children in prioritized areas will have to be deducted from the globally available supply each year.

Key consideration 4: Vaccine allocation should not perpetuate pre-existing structural injustices

Structural injustices can result in disparate health care services between or within a country. When allocating limited vaccine supply, and especially when aiming to maximizing health impact or to reduce suboptimal vaccine use or vaccine wastage, care must be taken not to perpetuate or exacerbate pre-existing structural injustices. By prioritizing malaria vaccine allocations to populations at greatest need as a first principle, the Allocation Framework reduces the probability of propagating structural injustices.

5. Framework implementation

This section describes in some more detail how the Framework will be operationalized.

Who is responsible for the implementation of the Framework?

Implementation is a shared responsibility. To achieve its objectives, this Framework should, as far as possible, be adhered to by all relevant stakeholders. This includes WHO member states, the Gavi Alliance in its prioritization of support and vaccine procurement, manufacturer(s) and other partners as they consider their financial and technical support. As the principal global funding partner supporting eligible countries to roll-out the malaria vaccine, Gavi will have a particularly important role in implementing the Framework.

When will the Framework be applied?

Decision-makers in malaria endemic countries are encouraged to use the Framework principles when developing their malaria vaccine introduction plan. Countries applying for malaria vaccine support from Gavi will be invited to present the full scope of desired vaccine roll-out (i.e. supply-unconstrained) alongside the stratification of sub-national areas according to the categories of need in the Framework (including number of children in the target population of each category). As part of this comprehensive application, the country should provide more details on the proposed scope of the first phase of vaccine roll-out that would be implemented in greatest need areas while there is limited supply. Table 2 of Appendix 3 provides an overview of global estimates of the number of new annual births in each “need” category across Sub-Saharan African countries with moderate to high malaria transmission. This table can be used to assess at a high level the indicative number of children who might be covered in each phase of prioritization. Of note though, these global estimates are illustrative: countries are encouraged to use their best available local evidence to

assess the annual target population falling into the different categories of need in line with the definitions provided in the Framework.

In order not to delay vaccine implementation in countries that have successfully completed the Gavi application process, it is suggested that supply allocation decisions are made in line with the Allocation Framework principles **following the conclusion of each Gavi application round** (typically three times a year). An allocation working group including WHO, UNICEF and the Gavi Secretariat will be responsible for applying the Framework principles in light of available supply to all country applications that are recommended for approval by Gavi's Independent Review Committee (IRC). This group would also consider vaccine requests from countries that are not eligible for Gavi support but that communicated their vaccine requirements to UNICEF or WHO.

In order to prevent first-come-first-serve decisions during the initial Gavi application windows, firm allocation decisions should initially be limited to requests for category 1 areas for each country and implement the solidarity principle that no single country should receive more than 20% of the total available supply, if needed.

To avoid delays in use of available vaccine (a key consideration in the Framework), if following a reasonable period of time during which all countries had an opportunity to apply for Gavi support (and/or to address outstanding issues highlighted by the IRC), there is additional supply available, countries with successful applications may be provided with additional supply (starting with category 1 areas, followed by category 2 areas and so on).

How will the allocation principles be used to inform actual global allocation decisions? What is the hierarchy between the principles?

The first order principle is to allocate all available vaccine where the need is greatest (principle 1). Principles 2 and 4 would be invoked for allocation decisions if multiple countries have requests for the same 'need' category that cannot be matched with supply. Principle 3 will be assessed as part of the application review by Gavi's IRC. Table 1 below provides more details on each principle.

Table 1: Allocation principles – indicators and operationalization

Allocation principle	Indicator	Operationalization: How is it applied in practice?
Principle 1: Greatest need	Proxy measure: Composite index that combines sub-national levels of *P. falciparum* parasite prevalence rate (PfPR) in children and under-five all-cause mortality rate (U5MR) – using best available local data (see Appendix 3 regarding the composite index) 5 categories of need	This is the primary principle for supply allocation. The vaccine requirements of category 1 areas should be satisfied first, before moving to category 2 areas then category 3, 4, then 5. If supply is not sufficient to satisfy all country demands (expressed in successful Gavi applications or to Unicef or WHO, for interested countries that are not Gavi eligible) within the same category of need, the second allocation principle (Maximize health impact) would be applied to establish the order of priority.
Principle 2: Maximize health impact	Proxy measure: WHO-UNICEF estimates of the national drop-out rate between the third dose of Diphtheria-tetanus-pertussis vaccine (DTP3) and the first dose of Measles-virus containing	This principle will be applied if vaccine requests from multiple countries for areas within the same category of need cannot be fully satisfied. The country with the lower drop-out rate would get priority.

	vaccine (MCV1) for the latest available year	
Principle 3: Equity (Equal Respect)	Measurement and monitoring through the Gavi IRC in line with the established Gavi processes, requirements and suggested analyses related to coverage & equity	Equity is a key organising principle of Gavi's support. This entails a focus on ensuring that priority is put on extending services to communities that are currently missed including refugees, displaced, and other vulnerable populations. All countries should describe in their application to Gavi how they implement an equity approach in their planning for and implementation of the malaria vaccine. Countries will be required to detail the rationale for targeting specific subnational geographies for malaria vaccination. The IRC may request clarifications or modifications if the requirements in the Gavi guidelines are not met. Countries should monitor and report on this aspect as part of their regular reporting to Gavi
Principle 4: Fair benefit sharing	Countries with participation in clinical development of the vaccine (Phase 2 or phase 3) – yes or no.	If two countries are equal in terms of allocation principles 1 and 2, the country with a prior contribution to the vaccine's development should get priority. In MVIP countries, this applies to use of the vaccine outside of the MVIP areas.
Foundational value: initial 20% solidarity cap	Maximum share of total available supply that each country can initially receive (not more than 20% of the total available supply, net of the needs for MVIP areas)	Initially, if there are unmet vaccine requests for greatest need (category 1) areas across multiple countries, no single country should receive more than 20% of the total available supply. After a reasonable period of time during which all countries would have had an opportunity to request access to malaria vaccine, this restriction should be lifted. Countries that were affected by this cap should get first priority for expansion, starting with additional category 1 areas.

How is 'greatest need' defined and measured?

At the global level, to enable across country comparison, the proxy measure for greatest need is defined by a composite index that combines sub-national levels of *P. falciparum* parasite prevalence rate (PfPR) in children and under-five all-cause mortality rate (U5MR) – see illustration in Appendix 3. The areas with highest need are those where PfPR and U5MR are greatest (see thresholds in Appendix 3); these areas, where the need for additional protection is highest, form "Category 1". Countries will use best available local data to determine areas of greatest need according to the categories of the Framework, and may use other indicators of malaria risk, such as malaria incidence or severe malaria data. However, lack of local data should not prevent a country from accessing vaccine support; modelled estimates available at a global level can be leveraged to help guide in-country decisions.

What is the most important implication of the Framework for countries considering introduction of the malaria vaccine?

Solidarity as a foundational value and the allocation principles (including equity) imply that available supply will be distributed more widely to a larger number of interested countries with high need,

rather than to a few select countries. Therefore, as long as demand exceeds globally available supply, most if not all countries will have to consider a ***phased*** **approach to vaccine roll-out, starting at sub-national level in areas of highest need**. It is recognized that this may represent a novel approach to vaccine introduction for some countries that comes with specific challenges and opportunities. Countries can use the subnational tailoring process, developed under the HBHI approach, and outlined in the WHO GMP guidance, to identify where the vaccine should be initially prioritized for highest impact (and to categorize areas of need for subsequent phases of implementation as additional supply becomes available). Some countries may consider a phased approach as an opportunity to gain experience with vaccine implementation to help inform future expansion. Other countries may prefer to wait until more vaccine supply becomes available.

How are other aspects that are not explicitly mentioned in the Framework, for example a country's readiness, being assessed?

The Framework has been designed within the context of the existing global support mechanisms for immunization, most importantly, the vaccine support provided by Gavi to eligible countries. The usual Gavi policies, processes and requirements (with a few additions) are expected to apply for the malaria vaccine.[14] This includes the review of a country's request for new support by Gavi's Independent Review Committee (IRC) who makes a recommendation as to whether to fund the programme. The aim of the IRC review is to assess whether a country's plan will likely achieve the proposed results and contribute to Gavi achieving its mission and strategy, considering the country's justification, soundness of approach, country readiness, feasibility of plans, system strengthening and sustainability, economic and financial considerations, and public health benefit of the investment in line with Gavi's mission. Among other issues, a successful request is expected to articulate how zero-dose children and missed communities are identified and reached and demonstrate broad participation in planning, design, and implementation across diverse country partners and stakeholders, including local partners and civil society. Pro-active involvement of civil society in planning and implementation should be particularly encouraged in light of the constrained supply to ensure that populations in high need are identified and reached.

Will the malaria vaccine be affordable for countries?

Affordability of a new vaccine depends on a number of factors, including the vaccine price, the co-financing payments required by Gavi, and country-specific parameters such as per capita income and government spending for immunization. This Framework cannot address any of these factors directly. However, noting that many of the high need areas are located in countries least able to pay, a plea is made to partners able to influence these factors, including:

- Current and future manufacturers of malaria vaccines in the prices they charge
- Partners in the Gavi Alliance as they revise the Gavi Co-financing Policy (review currently ongoing)
- Partners in the Gavi Alliance and others in their efforts to ensure sustainable, healthy market dynamics for malaria vaccines at affordable prices
- Governments and partners as they make investment decisions

What if a country is not eligible to apply for Gavi support?

The majority of malaria endemic countries are currently eligible to apply for Gavi support.[15] There are, however, a few countries that have never been Gavi eligible or that can no longer apply for new support given their income level. These countries, should they wish to introduce the malaria vaccine, are encouraged to express their vaccine requirements to UNICEF Supply Division or to WHO so that

[14] Gavi Support Guidelines, accessible from: https://www.gavi.org/our-support/guidelines

[15] Eligibility for Gavi support, accessible from: https://www.gavi.org/types-support/sustainability/eligibility

the vaccine needs can be assessed based on the Framework principles, alongside the needs expressed by Gavi eligible countries.

How will the implementation of the Framework be monitored?

Periodic reviews will take place to assess the Framework implementation and whether it is achieving the intended objectives. Revisions to the approach or its operationalization might be needed based on the findings and the evolving supply situation, including the potential availability of a second malaria vaccine. It is proposed that the first formal review takes place following the first two Gavi application rounds. A monitoring plan will be developed to guide the review.

Appendix 1: List of advisers

Professor Helen Rees (Co-Chair)	Chair of AFRO Regional Immunization Technical Advisory Group (RITAG) & Executive Director, Wits RHI, University of the Witwatersrand, Johannesburg, South Africa
Professor Rose Leke (Co-Chair)	Emeritus Professor of Immunology and Parasitology and Fellow of the Cameroon Academy of Sciences CAS, the African Academy of Science (AAS) and The World Academy of Science, (TWAS), Université de Yaoundé, Cameroon
Professor William Brieger	Member of AFRO RITAG & Professor, Health Systems Program, Department of International Health, The Johns Hopkins Bloomberg School of Public Health
Dr Folake Olayinka	Member of AFRO RITAG & Immunization Team Leader, U.S Agency for International Development
Professor Richard Adegbola	Member of AFRO RITAG & Research Professor & Consultant, Nigerian Institute of Medical Research
Professor Alejandro Cravioto	Chair of the Strategic Advisory Group of Experts on Immunization (SAGE) & Affiliated with the Faculty of Medicine of the Universidad Nacional Autónoma de México (UNAM)
Professor Dyann Wirth	Chair of the Malaria Policy Advisory Group (MPAG) & Director, Defeating Malaria: From the Genes to the Globe, Harvard University and Faculty Director, Harvard Integrated Life Sciences Ph.D. Programs
Dr Fredros Okumu	Member of MPAG & Public Health Researcher and Director of Science at Ifakara Health Institute, Tanzania
Professor Evelyn Korkor Ansah	Member of MPAG & Director, Center for Malaria Research, University of Health and Allied Sciences, Ghana
Dr Bvudzai Magadzire	Senior Technical Advisor, Research & Advocacy at VillageReach, South Africa; Gavi Alliance Alternate Board member representing Civil Society Organizations
Dr Caesar Atuire	Senior Lecturer, Department of Philosophy and Classics, University of Ghana, Accra, Ghana & Member of the WHO ACT Accelerator Ethics Working Group
Professor Fred Binka	Expert from MVIP country (Ghana) & Professor of Epidemiology and the Vice Chancellor of the University of Health and Allied Sciences Ho, Ghana
Dr Rose Jalang'o	Expert from MVIP country (Kenya) & Strategic Information Management and Communications Officer in the National Vaccines and Immunization Program, within the Kenya Ministry of Health
Professor Peter Smith	Chair of MVIP Programme Advisory Group (PAG) & Professor of Tropical Epidemiology, London School of Hygiene and Tropical Medicine (LSHTM), UK
Dr Eusebio Macete	Co-Chair of MIVP Programme Advisory Group (PAG) & Director, Farmácias de Moçambique SA, Mozambique
Prof Keymanthri Moodley	Distinguished Professor in Department of Medicine and Director of the Centre for Medical Ethics and Law, Stellenbosch University, South Africa and Adjunct Professor, Department of Social Medicine, University of North Carolina- Chapel Hill, USA

Appendix 2: Principles explicitly NOT proposed to be used to allocate limited supply

Other potential principles for allocation of scarce resources were reviewed and explicitly rejected for the purpose of the malaria vaccine, the reasons of which are described here:

- **Lottery-based (i.e. random) allocation**

Allocating the malaria vaccine randomly to countries would imply an excessively arbitrary allocation approach, going against the principles of greatest need and maximizing impact.

- **Purely population-based / proportional allocation, if not justified by need or impact**

Allocating a fixed proportion of available supply to each malaria endemic country based on population size alone would go against the principles of greatest need and achieving most health impact while supply is severely constrained. Given the severity of supply shortage and the high number of countries in need, the amount of vaccine that most countries would get through a purely proportional allocation would be very small - likely not allowing for a successful implementation. It is recognized, however, that population size may indirectly feature in the principles of 'impact' and 'need', as larger populations may have larger numbers of children in need, and would therefore, benefit more from greater supply.

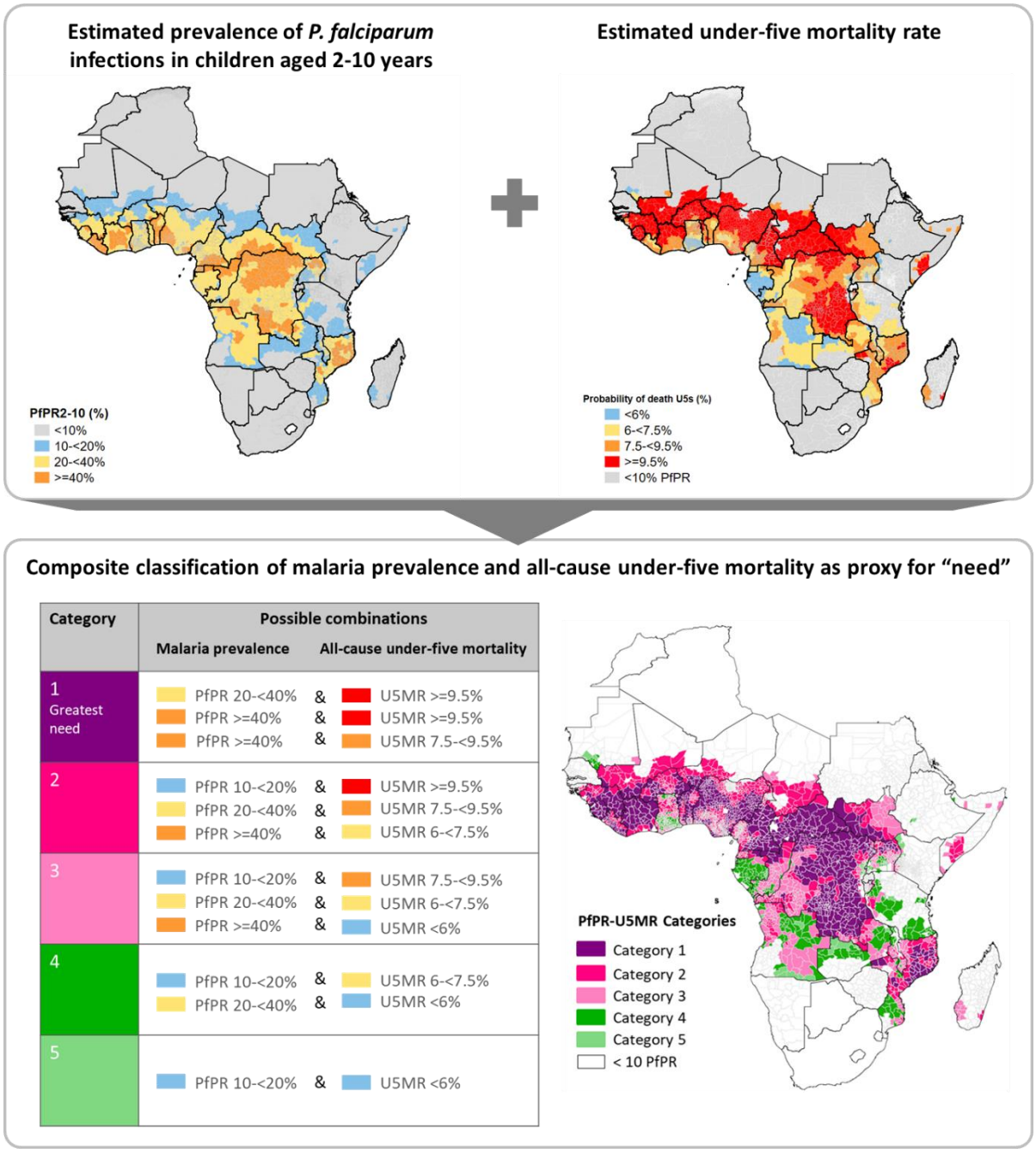
- **Purely first-come-first-served**

In a severely supply constrained situation, as we are facing initially with the malaria vaccine, allocating the vaccine at the desired quantity (that is, to allow a national roll-out, for example) to the first countries that apply would likely be in conflict with the principles of greatest need and maximizing impact. While some sub-national areas within these countries would likely indeed be at greatest need, other areas may face a considerably lower burden when compared with other countries in the region. It would also favour countries that are better prepared to submit a high-quality application to Gavi rapidly. However, an early application to Gavi is likely an indication of high commitment and (potentially) readiness to implement the vaccine swiftly. A reasonable balance will therefore have to be reached.

Appendix 3: Illustration of "need" classification

The maps shown below are for the purpose of illustrative cross-country comparisons for considerations in global discussions on the allocation framework. It is not a formal analysis of the impact of the malaria vaccine. They should not be seen as the eventual sub-national tailoring of the vaccine that countries will include in their national strategic plans. A small number of countries outside Africa may have areas with moderate to high malaria transmission - these are not shown here.

Figure 1: Combining measures of malaria prevalence and under-five mortality



Category	Possible combinations	
	Malaria prevalence	All-cause under-five mortality
1 Greatest need	PfPR 20-<40%	& U5MR >=9.5%
	PfPR >=40%	& U5MR >=9.5%
	PfPR >=40%	& U5MR 7.5-<9.5%
2	PfPR 10-<20%	& U5MR >=9.5%
	PfPR 20-<40%	& U5MR 7.5-<9.5%
	PfPR >=40%	& U5MR 6-<7.5%
3	PfPR 10-<20%	& U5MR 7.5-<9.5%
	PfPR 20-<40%	& U5MR 6-<7.5%
	PfPR >=40%	& U5MR <6%
4	PfPR 10-<20%	& U5MR 6-<7.5%
	PfPR 20-<40%	& U5MR <6%
5	PfPR 10-<20%	& U5MR <6%

At the global level, the proxy measure for **need** is a composite index that combines sub-national levels of *P. falciparum* parasite prevalence rate (PfPR) in children and under-five all-cause mortality rate (U5MR), estimated here at district level (Figure 1). To establish the composite index, the range of estimated malaria prevalence levels and the estimated under-five mortality rates (expressed here as the probability of dying, i.e. as a percentage) were divided in approximate quartiles. The possible combinations of the two indicators were regrouped to form five categories of need (with category 1 representing the "highest need" areas).

The following data sources were used for the estimates presented in this Appendix:

- District level mean estimates of *Pf*PR in 2-10 year old children in 2019 (Malaria Atlas Project)
- District level mean estimates probabilities of death from all-causes before the age of 5 in 2015 (IHME)
- District estimated population (UN population projections, crude birth rates & Worldpop population estimates). District-level population distributions obtained from Worldpop are applied to national UN population projections to estimate population at district level

Initially, malaria vaccine supply will be prioritized for use in areas that meet category 1 definition. As supply constraints ease, implementation can be expanded in a phased manner to areas meeting the definitions of subsequent categories (see Figure 2 and Table 1).

Figure 2: Categories of need: Composite classification of malaria prevalence and under-five mortality

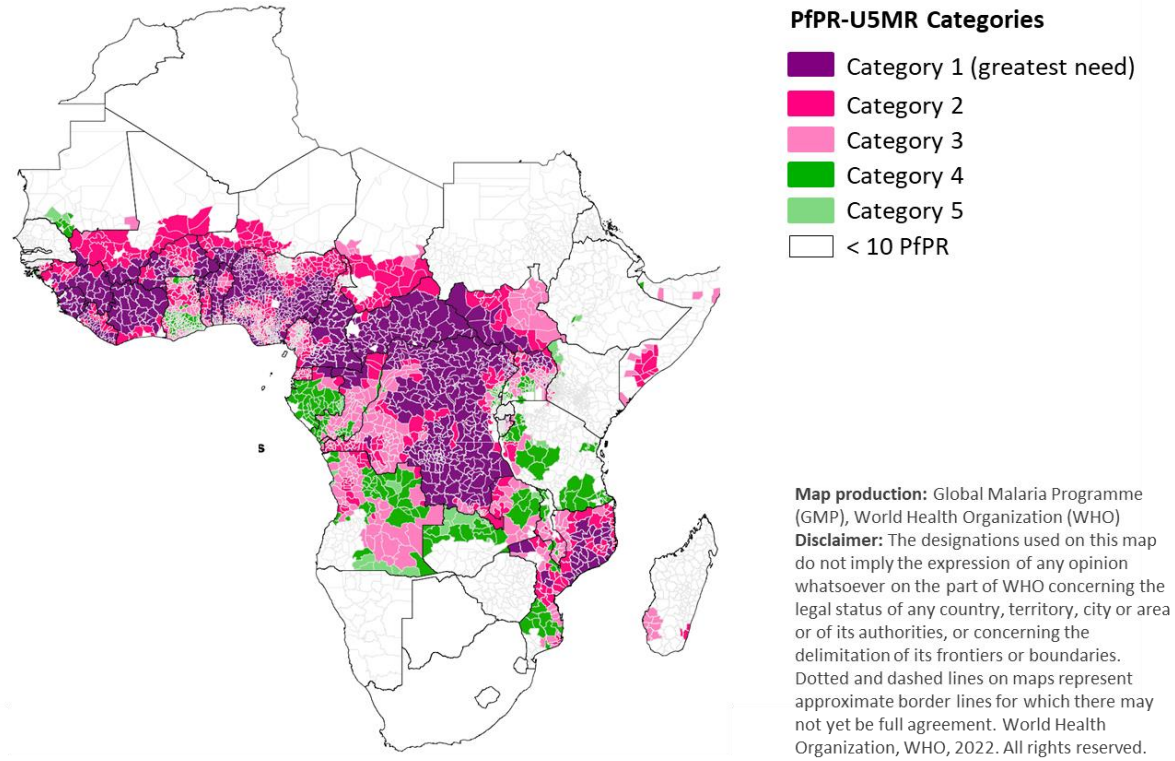


Table 1: Target children and vaccine doses required for categories of need (illustrative)

Supply availability	**Category of need** (order of prioritization)	**Target children per year** (births in 2023)	**Vaccine doses per year**[1] (if 100% coverage, 4 dose schedule, 0% wastage)
	MVIP areas in Ghana, Kenya & Malawi	**~900,000**	**~3,600,000**
	Category 1 Greatest need, highest priority	**7,900,000**	**31,700,000**
	Category 2	**7,800,000**	**31,100,000**
	Category 3	**4,500,000**	**17,800,000**
More supply	**Category 4**	**2,300,000**	**9,400,000**
	Category 5	**1,600,000**	**6,500,000**
	TOTAL	**25,000,000**	**100,100,000**

[1] Vaccine dose calculation for illustrative purposes only. Actual number of doses required will vary by country based on programmatic realities, including target population, vaccine coverage, and wastage rates. Some countries may choose a 5-dose strategy in areas with highly seasonal malaria or areas with perennial malaria transmission with seasonal peaks.

Table 2: New births estimated for 2023 by need category in sub-Saharan African countries with moderate to high malaria transmission

Numbers in the table reflect indicative estimates based on globally available modelled estimates (see data sources above). Countries are encouraged to use their best available local evidence to assess the annual target population falling into the different categories of need in line with the definitions provided above. Estimates of new births by need category using country level data are likely to differ from global estimates.

	Cat 1	Cat 2	Cat 3	Cat 4	Cat 5	Total Cat 1-5	<10% PfPR
Angola	-	86,000	255,000	224,000	351,000	916,000	297,000
Benin	205,000	102,000	108,000	43,000	-	458,000	-
Burkina Faso	266,000	385,000	163,000	-	-	814,000	-
Burundi	111,000	80,000	100,000	24,000	-	315,000	208,000
Cameroon	190,000	213,000	318,000	104,000	32,000	857,000	91,000
Central African Republic	168,000	11,000	-	-	-	179,000	-
Chad	-	376,000	78,000	-	-	454,000	263,000
Congo	4,000	4,000	48,000	66,000	55,000	177,000	-
Côte d'Ivoire	567,000	328,000	-	-	-	895,000	-
Democratic Republic of the Congo	1,987,000	535,000	641,000	130,000	369,000	3,662,000	180,000
Equatorial Guinea	-	20,000	5,000	-	-	25,000	-
Ethiopia	-	-	-	7,000	19,000	26,000	3,620,000
Gabon	1,000	5,000	2,000	49,000	1,000	58,000	-
Ghana	10,000	75,000	70,000	247,000	147,000	549,000	96,000
Guinea	291,000	141,000	17,000	-	77,000	526,000	-
Guinea-Bissau	-	9,000	5,000	3,000	-	17,000	54,000
Kenya	-	4,000	4,000	11,000	93,000	112,000	1,097,000
Liberia	48,000	75,000	49,000	-	-	172,000	-
Madagascar	-	32,000	32,000	12,000	-	76,000	827,000
Malawi	-	19,000	240,000	136,000	-	395,000	13,000
Mali	171,000	458,000	11,000	-	-	640,000	244,000
Mauritania	-	-	3,000	26,000	44,000	73,000	86,000
Mozambique	337,000	406,000	183,000	77,000	-	1,003,000	237,000
Niger	192,000	628,000	100,000	-	-	920,000	281,000
Nigeria	2,830,000	3,188,000	890,000	301,000	-	7,209,000	788,000
Sierra Leone	178,000	-	37,000	-	-	215,000	-
Somalia	-	80,000	30,000	16,000	-	126,000	412,000
South Sudan	129,000	199,000	164,000	-	-	492,000	13,000
Togo	61,000	73,000	78,000	-	67,000	279,000	-
Uganda	181,000	192,000	650,000	327,000	243,000	1,593,000	163,000
United Republic of Tanzania	-	33,000	77,000	385,000	41,000	536,000	1,783,000
Zambia	15,000	33,000	113,000	160,000	88,000	409,000	312,000
TOTAL	**7,942,000**	**7,790,000**	**4,471,000**	**2,348,000**	**1,627,000**	**24,178,000**	**11,065,000**