Briefing Document: National decision-making framework for malaria vaccines

Vaccine introduction guidelines

This is one of seven briefing papers produced for a country consultation to develop a decision-making framework for the use of future malaria vaccines. It was developed under the guidance of the consultation steering committee: Alan Brooks, PATH Malaria Vaccine Initiative (MVI); Dr. Carter Diggs, US Agency for International Development; Sarah Ewart, MVI; Dr. Dorothée Kinde-Gazard, Minister of Health, Benin; Annique Lennon, MVI; Dr. Rose Macauley, World Health Organization (WHO) Regional Office for Africa (AFRO); Dr. John Marshall, Consultant to PATH; Dr. Zarifah Reed, WHO; Dr. Magda Robalo, WHO AFRO; and Dr. Rick Steketee, PATH Malaria Control and Evaluation Partnership in Africa.

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1. Purpose

This document summarizes the generic vaccine introduction guidelines recently completed by the World Health Organization (WHO) as part of the Global Immunization Vision and Strategies (GIVS) (see Section 2) that are intended to support:

- Decision-makers to decide whether to add a new vaccine to the national immunization program (NIP).
- NIP managers to implement the operational steps to add the vaccine.

Although these guidelines are primarily focused on the introduction of new and underused pediatric vaccines, they are pertinent to the decision-making process that will be necessary for the introduction of malaria vaccines. The full document is available directly from WHO and must be referred to for any substantial use.[1] Much of the text below is taken directly from the original.

2. GIVS: A renewed global commitment

In response to existing, new, and anticipated challenges to immunization, WHO and the United Nations Children's Fund (UNICEF) have jointly developed a GIVS for 2006 to 2015[2] that aims to increase the use of traditional and new vaccines, as well as contribute significantly to the achievement of Millennium Development Goals.[3]

In view of the marked differences between countries' capacities, priorities, and resources, the GIVS presents a range of immunization strategies from which countries will be able to select those most suited to their needs. It includes goals and strategies under four main areas:

1. Protecting more people in a changing world.
2. Introducing new vaccines and technologies.
3. Positioning immunization, other linked health interventions, and surveillance in the health system context.
4. Immunizing in a context of global interdependence.

In conjunction with the GIVS, countries are encouraged to develop or update comprehensive multi-year immunization plans (MYPs). MYPs provide national goals, objectives, and strategies for up to five years based upon a situational analysis. MYPs also need to be linked to the national

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[1]World Health Organization (WHO). *Vaccine Introduction Guidelines. Adding a Vaccine to the National Immunization Programme: Decision and Implementation*. Geneva: WHO; 2005.

[2]United Nations Children's Fund, World Health Organization (WHO). *Draft Global Immunization Vision and Strategy: Strategic Framework for 2006–2015*. Document in preparation.

[3]United Nations Millennium Declaration. 55th General Assembly, Res. 55/2. Available at http://www.un.org/millennium/declaration/ares552e.pdf, goals and indicators at http://www.who.int/entity/mdg/goals/MDGsList_smartformat.pdf

health and development plans and include a budget consistent with the overall financial planning for health.[4]

New vaccines present numerous issues in prioritizing investments of a national immunization program. The challenge remains to tackle those issues systematically, providing the best available services in a cost-effective way.

3. Deciding on the introduction of a vaccine

3.1. Overview

There are two groups of key issues to be considered before deciding to introduce a vaccine. The first group of issues, referred to as "policy issues," lead high-level decision-makers to agree on whether the introduction of a particular vaccine is acceptable from an immunization policy perspective. The second group of issues, referred to as "programmatic issues," then address the feasibility of the vaccine introduction from a technical perspective. The final decision might be one of two possibilities:

- To introduce the vaccine or
- To wait until more evidence has been obtained (disease burden, cost-effectiveness, etc.) or until the conditions change (price, financial resources, supply, programme strength, etc.) to make the introduction justifiable.

3.2. Policy issues

3.2.1. Public health priority

Each country faces multiple health problems. Addressing those problems requires setting priorities to allocate the limited resources available to the health sector. The NIP may need to present rational arguments for introducing a particular vaccine, in order to convince the decision-makers.

The burden of disease that can be prevented by the vaccine provides the main piece of evidence to set the national health priorities.

The perception of the public and the medical community about the vaccine and the disease is a significant factor used to identify its introduction as a priority. The more important and visible the disease, as well as the more safe and effective the vaccine is perceived to be, the better the acceptance and uptake of the new vaccine will be. Any misperception or opposition to the vaccine should be addressed by advocacy, social mobilization, and communication activities implemented prior to introduction.

When deciding on the priority of a particular vaccine, it is also important to consider:

- Other vaccine presentations against the same disease that would become available in the near future.

[4]World Health Organization (WHO). *Guidelines for Immunization Multi-Year Planning and Costing*. Document in preparation.

- Whether limited financial resources should be preserved because another vaccine against a disease that presents a greater burden is expected to become available in the near future.

3.2.2. Disease burden

National burden of disease studies, including public health surveillance and any special studies if conducted, may provide valuable information on the particular disease and its importance compared to other health conditions. In the absence of such studies, it is generally agreed that the diseases which have the highest incidence or prevalence, which cause the most disability and death occurring early in life or at the productive ages, represent the most significant disease burden in the country.

3.2.3. Vaccine efficacy, effectiveness, and safety

In order for a vaccine to be licensed, it needs to have data on its efficacy in preventing disease in the target populations. These data are obtained from controlled studies where considerable efforts are made to ensure that every aspect of the immunization is delivered under ideal conditions. As efficacy may vary depending on age, nutritional status, co-infections, and other factors, some vaccines may have lower efficacy in developing countries than in industrialized countries. Therefore, in estimating the likely efficacy of the vaccine in the country, careful consideration needs to be given to the range of data available and whether the studies were also performed in countries with similar disease epidemiology to the one considering the vaccine.

On the other hand, vaccine effectiveness describes protection under programmatic implementation and reflects the performance of the vaccine in the actual target population. Programmatic factors like errors in vaccine storage, preparation, or administration, that can impair the vaccine are more likely to occur in the field conditions. Therefore, vaccine effectiveness is usually lower than vaccine efficacy and should be monitored as part of the post-introduction surveillance activities.

In addition it is important that the safety of vaccines, including adverse events, is monitored post-introduction, including any impact on safety and efficacy on other routine vaccines that are given at the same time.

Overall, risks need to be weighed carefully against the benefit of the vaccine, and the risk:benefit ratio may vary between countries. In developing countries where disease morbidity and mortality are high, the expected benefits may far outweigh the risk of adverse events.

3.2.4. Other interventions (including other vaccines)

The new vaccine under consideration needs to be compared with other existing vaccines against the same disease, as well as with other control strategies. Comparisons will be based on relative effectiveness and costs of the different interventions and need to also consider practicality/feasibility, timeliness of effect, changes over time (e.g., emergence of resistance), and any adverse effects of each of the options. If an alternative control strategy or an existing vaccine is more advantageous, then the new vaccine does not need further consideration.

3.2.5. Economic and financial issues

Traditional immunization programs represented one of the best buys in the health sector—significant health impacts could be achieved for pennies per dose. However, new vaccines are much more expensive than the traditional vaccines. Even when the vaccine and non-vaccine costs are considered together, introduction of new vaccines may lead to a considerable increase in the costs of the immunization program. Therefore, it is important to carefully evaluate the costs and benefits of adding new vaccines, as well as to measure their potential impacts on limited national health budgets.

Assessing the economic and financial implications of new vaccines can provide valuable information for decision-making for both governments and their development partners as to:

- Whether a particular vaccine is cost-effective relative to other uses of scarce resources.
- What the long-term resource requirements of the new vaccine will be and how this compares with government budgets.
- The magnitude of the potential funding gap for a new vaccine and whether additional domestic or external funding could be mobilized to fill this gap.
- The potential prospects for financial sustainability of the new vaccine, once introduced.

Cost-effectiveness. Cost-effectiveness analysis is a tool that is used to evaluate and compare among alternative uses of scarce resources. This approach can help determine whether investment in a new vaccine achieves greater or lesser health outcomes relative to investment in another type of vaccine presentation or public health program.

Fiscal impact. A decision to introduce a new vaccine should include the affordability of the vaccine to the country and the magnitude and timing of future funding gaps. Affordability is a subjective concept and relates to whether a new vaccine can be introduced and absorbed into an immunization budget over the medium to long term without significantly affecting available resources for other public health priorities. Elements to consider should include:

- Analysis of fiscal impact evaluates expected program costs with the new vaccine and estimates of future program resource requirements.
- Interpretation of these indicators is subjective, and ideally these indicators should be compared with those for other public health interventions and programs to have a better sense of relative impacts.

Financial sustainability: Financial sustainability refers to the timely mobilization of needed resources to cover the costs of an intervention into the future. It is only one aspect of sustaining an immunization program, which also requires sufficient human resources and government commitment, among other factors. It is related to sustaining the financing of the entire immunization program after introduction, not just the financing of new vaccines. Elements to consider include:

- Analysis of financial sustainability begins with an evaluation of current and future resource requirements.

- The financial gap (total resource requirements minus expected available funding) can be estimated per year and can include significant under funding of capital and/or recurrent expenditures, excluding new vaccines. Evidence on the expected financing gap can be useful in government budget negotiations, exploration of alternative sources of funding (e.g., local governments, resources from debt relief, development loans, the private sector—foundations and nongovernmental organizations, and social insurance) and in discussions with donor organizations about the need for more resource mobilization.
- Long-term sustainability of vaccine procurement should be a central consideration for any government. Therefore, if there are doubts about the sustainability of introducing a new vaccine, it should not proceed unless it is clear that short-term use of the new vaccine will not have negative consequences.

3.3. Programmatic issues

3.3.1. Vaccine presentation

The presentation of a vaccine includes options like monovalent/combination, single dose/multidose, and liquid/lyophilized. Therefore, it is useful to consider the available presentations of the vaccine, as this may have direct implications on the decision-making. In some cases, the country may be faced with a choice of delaying the introduction until the preferred formulation/presentation is available or vaccine cost reduces, or starting with another option and then moving to the preferred option at a later stage.

3.3.2. Supply availability

As new vaccines take time to reach a level of maturity both in terms of supply and price, it is important to be aware of the current and future supply situation in considering the introduction of such a vaccine; procurement of the vaccines that have a limited global supply can present challenges. For example, in case a country uses a greater quantity of the new vaccine than it had first anticipated (due to high wastage, increased demand, etc.), it might be difficult to obtain additional vaccine in time and there might be a risk of temporary stock-out.

3.3.3. Programmatic strength

The overall NIP performance should be assessed ahead of any new vaccine introduction to identify any areas that need strengthening. Adding a vaccine will provide greater benefits through well-functioning delivery systems. New vaccine introduction can affect the NIP in two opposing ways:

- It may help in strengthening the program through raising demand by adding new resources and increasing public interest.
- It may cause additional burdens and worsen performance in a weak system.

If the infrastructure on which the new vaccine will rely is failing to reach a large proportion of the target population, then the new vaccine will be able to offer only limited benefits to those who most need it. However, if the vaccine is already being used in the private sector, this may have implications on vaccine impact, advocacy, and communication, and even on disease burden, depending on the share of the private sector in overall immunizations.

3.4. Decision-making process

The driving force to consider in the introduction of a vaccine might come from different sources, like the NIP itself, country decision-makers, international organizations, academic community, or the private sector. Although each country has its own mechanisms for an informed decision-making process, it is important to ensure that all interested parties are consulted and the implications of all possible options are discussed.

The key steps in this process can be suggested as follows:

- Identify stakeholders of the immunization programme and other disease control programs.
- Identify funding sources (government agencies or donors).
- Establish a task force to bring together all parties; existing committees such as an Interagency Coordinating Committee (ICC) or Advisory Committee on Immunization could be used as a forum for this purpose.
- Elaborate policy and programmatic issues by reviewing existing evidence, identifying the need for additional information, and assessing the possible options.

For countries that do not already have one or more advisory committees that provide technical and programmatic advice for the NIP, establishing one should be considered to aid with the assessment process for adding a vaccine. The committee members are usually selected from the scientific community, immunization partners, and program implementers. They may also have knowledge of future developments and thus help with the current decision-making.

Appendix 1: Criteria for assessing the national immunization program readiness for new vaccine introduction

From World Health Organization (WHO). *Vaccine Introduction Guidelines. Adding a Vaccine to the National Immunization Programme: Decision and Implementation*. Geneva: WHO; 2005.

1. Obtaining full benefit from existing vaccines

- An immunization multi-year plan (MYP) and annual work plans are in place, with regular updating of policies.
- Immunization coverage reflects satisfactory access and limited drop-out. Each NIP should set its own coverage targets in the MYP, considering the regional targets and global targets in GIVS.
- Specific objectives are met or well underway for already existing vaccines. For example timely (i.e. within 24 hours) coverage with hepatitis B birth dose is achieved where relevant, catch-up measles vaccination has been conducted, or two-dose measles strategy has been established.

2. Financially sustainable programme

- The NIP is able to mobilize and use resources for existing program strategies with secure current and future financing.
- MYPs include a budget linked with the national health budget to secure vaccine supply and other costs.
- There is a capacity to expand the program without threatening financial sustainability.

3. Functional cold chain

- National cold chain policy and vaccine management systems include an updated cold chain inventory as well as plans for the maintenance and replacement of equipment.
- The cold chain has adequate volume capacity and performance for existing vaccines at all levels.
- Cold space is able to meet any additional demands of the new vaccine, with an adequate spare capacity to meet campaign or unforeseen needs.

4. Well managed vaccine stock

- There are two-year to five-year forecasts for all existing vaccines (including planned/likely campaigns) and the new vaccines, including the transition period when existing vaccines are being replaced.
- There is effective monitoring of wastage for all vaccines, with acceptable levels of wastage compared to coverage.
- Vaccine stock-outs at national or sub-national level are infrequent.

5. Safe immunizations and monitoring of adverse events

- All vaccines are given with auto-disable syringes.
- Proper diluents and reconstitution methods are used for lyophilized vaccines.
- There is capacity to procure, distribute, and dispose of additional injection materials for new vaccine.
- There is capacity to investigate and respond to adverse events following immunization.

6. High quality disease surveillance

- There is timely, reliable, and comprehensive surveillance for major vaccine-preventable diseases.
- There is surveillance with pre-introduction baseline data to monitor impact of new vaccine.

Appendix 2: Examples of country decision-making processes for paediatric vaccines

From World Health Organization (WHO). *Vaccine Introduction Guidelines. Adding a Vaccine to the National Immunization Programme: Decision and Implementation*. Geneva: WHO; 2005.

Country example 1: South Africa

South Africa introduced Haemophilus Influenzae type b (Hib) vaccine in 1995 with its own resources. Several local studies had documented the importance of Hib disease burden, including non-meningitis Hib. In addition, data were available from the Gambia, Finland, and the United States showing impact of Hib vaccination. There was a strong lobby of pediatricians supporting Hib vaccine introduction. South Africa therefore developed an extensive process outlining financial implications and long-term prospects for Hib vaccine introduction. This was accompanied by political lobbying and the case was presented to national and provincial decision-makers. Hib vaccine was introduced in June 1999 as a combination with diphtheria, tetanus, and pertussis vaccine (DTP), following an open tender system and supported by domestic funding.

The successful introduction process in South Africa resulted from a comprehensive approach and the unquestioned availability of the vaccine of choice. The availability of clear disease burden data was critical to convince decision-makers. The data from other countries on the effectiveness and impact of the vaccine was helpful because they demonstrated the potential disease control that could be achieved by the programme. The availability of internal financing resources ensured the long-term viability of the approach.

Country example 2: Finland

Finland has been administering the Hib vaccine to infants in monovalent form since 1987. The country decided to switch to a combination product in 2005, while assessing the possibility of introducing pneumococcal conjugate vaccine. Finland has taken a four-step approach in the process of decision-making for all new vaccines:

1. Expected public health benefit.
2. Safety of vaccine individually.
3. Safety effects on population level.
4. Cost-effectiveness.

Using the well established technical working groups and advisory committees within the government structure, the two vaccines were evaluated according to those factors.

The impact of Hib immunization on the disease was dramatic. The high incidence which was documented by studies in the pre-vaccination era showed a sharp decrease in a few years and stayed very low, enforced by consistently high (96 percent) immunization coverage. Moreover, the vaccine impact was greater than estimated due to the herd effect. According to the National Registry, adverse events associated with Hib vaccine were minimal. Although the decision to

introduce Hib vaccine had been made without an economic evaluation, a later study showed that the vaccination cost per child was low enough compared with the associated treatment costs.

The evaluation for pneumococcal conjugate vaccine exposed a different picture. The estimated impact of the vaccine in the country could be documented based on the existing evidence on disease burden and vaccine efficacy. Pneumococcal vaccine was feasible in terms of public benefits, safety, and effects on the population. However, introduction of the vaccine in routine immunization was not found cost effective in the economic analysis. Therefore the country decided not to introduce pneumococcal conjugate under these circumstances.

Country example 3: United Republic of Tanzania

The United Republic of Tanzania indicated its intention to the World Health Organization (WHO) to introduce hepatitis B (HepB) vaccine in the mid-1990s already, because serological data suggested that the prevalence of the carriage of HepB surface antigen (a marker for the high risk of liver cancer) was high. However, the country could not introduce the vaccine due to lack of financial resources. In 1999, the United Republic of Tanzania and Zanzibar signed a memorandum of understanding with a WHO Collaborative Centre in Naples to introduce HepB vaccine. By the time GAVI became available as a resource for HepB vaccination there was already strong conviction that this vaccine was needed. In the case of Hib, a rapid assessment was conducted in 2001 to establish the disease burden. No Hib cases were identified in laboratory records, indicating how invisible the disease was in the country. Based on hospital data of pneumonia and meningitis and on data from a reproductive and child health survey, the rapid assessment indicated that between 3,300 and 3,450 deaths caused by Hib meningitis could occur every year among children aged less than five years of age. The consensus meeting held in December 2001 led to the decision not to apply for Hib vaccine introduction because the burden of Hib disease compared to the cost of vaccination was not convincing. As a result, DTP-HepB combination vaccine was introduced in January 2002. Although Tanzania has not introduced Hib vaccine, the Expanded Programme on Immunization remains interested in introducing it. To do so, its main challenge will be to convince senior Ministry of Health officials about the long-term prospects for financial sustainability.

Appendix 3: Implementing the decision

This is a summary of the different categories of considerations and actions that are required for implementation once a decision has been taken to introduce a specific vaccine; some can have a long lead time, others can be addressed close to, or at, the time of vaccine introduction.

Major categories for consideration	Sub-components of the major categories
1. Updating the immunization multi-year plan	
2. Choosing the vaccine formulation and presentation	
3. Introduction strategy: phased vs. countrywide introduction	
4. Procuring the vaccine and safe injection supplies	Forecasting supply needs Ensuring vaccine quality
5. Immunization strategy	Routine infant immunization schedule Catch-up immunization
6. Cold chain readiness and vaccine management	Estimating additional cold chain requirements Ensuring adequate functional cold chain capacity Wastage optimization
7. Immunization safety	Safe injection supplies and waste disposal Adverse events following immunization
8. Staff training	
9. Advocacy, social mobilization, and communication	
10. Supportive supervision	
11. Information systems	