Meeting on Malaria Vaccines Development and the Decision-Making Framework for the Possible Introduction of a Malaria Vaccine in East and Southern Africa

(August 2nd, 2008)

Lusaka

Meeting Report

East and Southern Africa

MALARIA VACCINE DECISION-MAKING FRAMEWORK

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Meeting on Malaria Vaccines Development and the Decision-Making Framework for the Possible Introduction of a Malaria Vaccine in East and Southern Africa

Lusaka, Zambia (2nd August 2008)

Context

Malaria continues to exert a heavy toll on Africa and almost one million children under five years old continue to die of malaria every year despite the availability of effective malaria control measures.

Over the last decade, the international community has made tremendous progress in accelerating the development of promising malaria vaccines to complement current interventions and to further reduce the burden of malaria. Several African research institutions are contributing to the current vibrant pipeline of malaria vaccine candidates.

Dozens of potential vaccines are being evaluated, and although most are in early development stages, a number of promising candidates are progressing through clinical trials. The leading vaccine candidate, RTS,S, is anticipated to be available as soon as 2012 if remaining clinical trials are successful; other malaria vaccines are likely five or more years behind this timeframe.

Malaria vaccines will likely be delivered through the Expanded Program on Immunization (EPI) as a new intervention to control malaria, building upon and complementing current interventions rather than replacing them. Due to the complexity of the malaria control situation and the anticipated growth of the immunization landscape, decision making about the future role of a malaria vaccine must commence well in advance of actual product availability. Recent experience with new interventions, including insecticide-treated nets (ITNs), artemisinin-based combination therapy (ACTs), and the Haemophilus influenzae type B (Hib) vaccine, has highlighted the importance of early planning.

Background

As research activities continue, there is a need to share information with policy-makers on progress in malaria vaccine development and start to discuss how the decision on the introduction of a malaria vaccine would be made. Experience has shown that there are usually long delays between the availability of a new intervention and its implementation by national health systems due to complex factors involved in policy decisions. Furthermore, a malaria vaccine would complement other malaria control interventions, and the decision as whether to introduce it or not will not be straightforward. In addition, numerous new vaccines

are to be introduced over the next 5 years. The countries and decisionmakers will need to keep abreast of progress and possibilities as they arise in order to be able to expedite the use of an effective malaria vaccine once it is available.

Since January 2006, the World Health Organization's Africa Regional Office and MVI, with support from the US Agency for International Development, have been working in partnership with various multilateral and bilateral stakeholders, researchers, and several Ministries of Health, to develop a framework of information that will help countries to make informed decisions about the potential role of a successful malaria vaccine within their national health systems.

In January 2006, the PATH Malaria Vaccine Initiative (MVI) and the World Health Organization Regional Office for Africa (WHO AFRO) organized a workshop in Cotonou, Benin, hosted by the Ministry of Health of Benin, to develop a draft framework for decision making on the possible use of a malaria vaccine. Health officials from 13 African countries met with multilateral and bilateral partners in Benin to define the processes and data needed for early decisions on the role of a malaria vaccine in national health systems. The group included participants with expertise in malaria, immunization, research and product development, policy, planning, and finance.

The workshop resulted in a generic framework of the information that countries require to make decisions regarding the use of a malaria vaccine in their national health systems. The information is grouped into categories that correspond to those in the WHO's Vaccine Introduction Guidelines. When applying this framework, national decision-makers will have the data to determine, within one to three years of licensure, the appropriate role for a malaria vaccine in their country. Potential decisions might include:

- introducing the vaccine,
- conducting a demonstration project,
- collecting more data before deciding to use a vaccine, or
- not introducing the vaccine.

A malaria vaccine decision-making framework will be a useful tool to countries, given the complexity involved in national decision-making processes. A framework will not provide a "one-size-fits all" perspective on who should use a malaria vaccine. Instead, it will begin an iterative process to help countries structure how to weigh the many factors and begin to fill gaps in information along the path to making such a decision. The framework aims to allow governments and partners at regional, national, and global levels to better align their planning about the role of a malaria vaccine and, eventually, reach a decision regarding its use.

During the second half of 2006, MVI and WHO collaborated with multiple Ministries of Health to adapt the generic framework in six African countries—Gabon, Ghana, Kenya, Mali, Mozambique, and Tanzania—representing diverse health systems and varying needs for and access to malaria and immunization interventions. In each

country, MVI, WHO, and the Ministry of Health convened a two-day meeting that asked key stakeholders to review the generic framework, prioritize their country-specific information requirements, and outline future plans for securing the information. Each country consultation resulted in the development of a country-specific framework for decision making as well as a country-specific near-term and long-term future plan of action.

In early 2007, the country-specific frameworks were synthesized to create a Draft Regional Decision-Making Framework (DMF). MVI's objective is to work with WHO and Roll Back Malaria and other partners to validate this Draft Regional Framework as a common tool for decision-making across Africa by presenting the framework at different regional meetings.

The first validation meeting was held in February, 2008, in Douala during the Central African Roll Back Malaria Network (CARN) meeting. The malaria vaccine decision-making framework meeting for East and Southern Africa, held on 2 August 2008, was the logical follow up to the Douala meeting. A validation meeting with countries in West Africa is currently planned for the last quarter of 2008 in collaboration with WHO, RBM, and the West African Health Organization.

Objectives of the Meeting

The objective of this meeting was to validate the Regional Decision-Making Framework (DMF) as a common decision-making tool for possible introduction of a malaria vaccine in East and Southern Africa.

Specific Objectives

- To review and discuss issues and challenges in the introduction of new malaria control interventions and vaccines and the implications for future malaria vaccines
- To review the Draft Regional Decision-Making Framework
- To agree on the path forward for the implementation of the Draft Regional Decision-Making Framework

Expected Outcomes

- Consensus reached on the use of the Decision-Making Framework (DMF) for malaria vaccine development in East and Southern Africa
- Recommendations made for the DMF in East and Southern Africa

At the meeting, key stakeholders were asked to review the Draft Regional Decision-Making Framework, discuss whether or not the content is appropriate/sufficient, and validate the framework for use as a tool in the East and Southern African region.

Key points discussed during the meeting are summarized below and in the next sections.

Introduction and Objectives

— Dr. Paluku, Chair

Dr. Paluku noted that early preparation will be important in considering how future decisions on vaccines will be made.

He noted with pleasure that the meeting consisted of a strong mix of immunization and malaria specialists, certain to ensure a well-rounded discussion drawing upon the experiences of both groups in introducing new interventions.

Dr. Paluku reviewed the objectives and expected outcomes of the meeting.

Update on malaria vaccines development

— A. Brooks, MVI

This presentation provided an overview of the status of malaria vaccine development. Mr. Brooks began by noting the critical importance of scaling up today's intervention efforts as a first priority while also considering how to plan for future interventions. History with other vaccines and malaria interventions has shown that years will pass from the time an intervention is available until it may be implemented if ample planning is not done in advance. Countries, partners, and the international community have the opportunity to also take a long-term view of the implementation of the next generation of malaria interventions, including malaria vaccines.

It is scientifically challenging to create malaria vaccines due to the complex nature of both the parasite and its development stages within the human host. The perception of an unprofitable market has traditionally limited interest from developers; however, recent investments and scientific breakthroughs, including randomized double-blind control trials in Africa showing vaccine efficacy, give reason to believe that malaria vaccines are now coming. MVI and other groups are pursuing a variety of malaria vaccines across a portfolio of candidates, as it is recognized that many in early development will not ultimately be effective. The furthest progressed vaccine, RTS,S/ASO, is anticipated to start phase 3 licensure trials in 11 sites in seven countries across Africa in late 2008 or early 2009. All participants in the trials will receive longlasting insecticide treated bednets and access to other malaria control interventions, according to national policies. If all goes as anticipated, initial phase 3 data could be available in 2011 and submitted for licensure in 2012.

Data to date on RTS,S includes initial efficacy findings of approximately 35% against clinical malaria and 50% against severe malaria in children 1-4 years of age, with little waning over four years. There has been no sign of rebound disease in vaccinated children, suggesting that the vaccine does not increase the risk of a more severe disease later in life.

Swiss Tropical Institute has modeled and published estimates of the impact, cost, and cost-effectiveness of malaria vaccines. A vaccine such as RTS,S in a country like Tanzania could potentially avert 375,000 deaths over 20 years. The cost of fully vaccinating a child, including delivery costs, would range from $4.75 to $35 depending on the cost per dose (ranging from $1 to $10 per dose). Cost-effectiveness could range from $450 to $3,500 per death averted and $12 to $96 per disability adjusted life year (DALY) averted. These early estimates suggest that even a partially efficacious vaccine will be an intervention worthy of consideration by many countries.

However, the introduction of a malaria vaccine will pose challenges, as is usually the case with new interventions. This was highlighted in the following session.

Objective 1: Review and discuss issues and challenges in the introduction of new malaria control interventions and new vaccines; determine implications for future malaria vaccines

From research to policy—challenges of introducing new health interventions: Malaria and Immunization: Malaria

— Dr. Soce Fall, AFRO/Malaria

In his presentation, Dr. Soce pointed out that the introduction of a new intervention for disease prevention and control is always challenging both for the health system and the specific program. The decision-making process is often complex, requiring interaction from and negotiation with various stakeholders; moving from policy to implementation implies many challenges, including determination of inputs, processes, etc.

While the policy decision to introduce a new intervention can sometimes be challenging and sometimes easy, almost every new intervention is certain to encounter problems during implementation. As of 2007, 41 countries have set policies for the use of artemisinin-based combination therapies (ACTs). However, only about 25 (about 60%) of these countries have actually implemented the policy. A similar situation exists with intermittent preventive treatment (IPTp).

Technical and policy issues observed with the introduction of ACTs include:

- Consensus among stakeholders for the introduction of new tools with regards to:
  - Efficacy and effectiveness
  - Ratio of cost to benefit
  - Comparison with existing tools: Is there added value?
- Diversity of epidemiological settings
  - Low-endemic countries versus high-endemic countries

- o Plasmodium species and type of vector
- o Validity of available studies in different settings

• Target groups
- o Under five, pregnant women, or all at-risk groups?

• Revision of drug regulation and Essential Medicines List
• Collaboration with other programs for planning, implementation, monitoring, and evaluation

Once a policy decision is taken, implementation challenges remain. Such challenges include:

• Service delivery approach
• Implementation approach
- o Phased implementation plan, or
- o Nationwide implementation plan

Some implementation efforts, such as those for IPTp, have included pilot districts that have remained pilot programs for years without growing to scale. Several factors which have lead to this include:

• The extensive planning and lead time required to develop guidelines and training and effective communication with communities;
• Planning for basic logistics and supply issues such as transport and storage of high-volume commodities (LLINs, drugs);
• Adequate phramacovigilance system and product quality surveillance to monitor safety and efficacy;
• Monitoring and evaluation systems to track effectiveness; and
• Financial considerations, including direct cost, additional implementation costs, and reliable funding sources.

Dr. Soce Fall concluded on a somber note, stating that the introduction of a malaria vaccine may be even more complex than was the introduction ACTs, which has proven to be a challenge for many countries.

Immunization

— Dr Nestor Shivute, WHO Intercountry Support Team (IST) East and Southern Africa (ESA)/Immunization

In his presentation, Dr Shivute referred to experiences in the Gambia in introducing a Hepatitis B vaccine to illustrate the decision-making process for a new vaccine. In this case, the decision to introduce the vaccine was influenced by the availability of information on the hepatitis disease burden, on the real protective benefits accruing from the vaccine, and by the dissemination of information on the vaccine to the public by credible leaders. In addition, technical and financial support from the Medical Research Council in the Gambia and other partners helped to make for a relatively smooth introduction.

Since 2000, the implementation of Haemophilus influenzae type B (Hib) has not been as smooth. There have been significant challenges obtaining data and addressing local perceptions of the disease. Additionally, insufficient product information, supply shortages, and financing challenges have manifest as the Global Alliance for Vaccines and Immunization (GAVI) systems evolved. Among the challenges is the need to break the cycle of uncertain demand, which limits supply and raises prices.

Programmatic concerns for Hib were partially addressed by the pentavalent (DTP-HepB+Hib) vaccine, which fit into the existing immunization schedule, becoming the preferred formulation in many countries.

Scientific challenges around the pneumococcal vaccine have been successful addressed. The vaccine has been shown to be efficacious in two African countries, which WHO considers sufficient evidence for all countries in Africa to come to a decision regarding its use. Similarly, the trials planned for a malaria vaccine across multiple settings should prove sufficient for decision making, even for countries in which trials will not occur.

To resolve the logistical issues related to this vaccine, GAVI guaranteed manufacturers that the vaccines would be bought and used. GAVI also pledged USD 1.5 billion of its funds to the financing of the vaccines. The industry, assured of a market, was ready to supply the vaccine, while countries, assured of an affordable and available vaccine, were eager and ready to introduce it. Unfortunately, this success is lessened by several product characteristics (e.g. cold chain and the safe disposal of glass syringes) that are currently limiting introduction.

Reasons for why children in countries with greatest need are the last to get new vaccines include:

- Insufficient understanding about the burden of disease and the potential impact of a vaccine;
- A lack of information and awareness on the part of decision-makers and the public on efficacy and safety;
- Concerns about cost and sustainability;
- National health systems are focused on other health priorities;
- Programmatic issues; such as schedule and number of injections, distribution, handling, etc.
- Inadequate communication package on the product; and
- Supply and demand issues: uncertain demand leads to limited supply which in turn leads to higher prices.

WHO headquarters and one of its subgroups, the Strategic Advisory Group (SAGE) for Immunization, prioritized the diseases for which a vaccine is anticipated to be available by 2012; malaria was determined to be of highest priority.

- As a way forward, countries were called upon to consider not only disease burden when introducing a vaccine, but factors such as national and global goals (e.g. Millennium Development Goals).

- Malaria is a significant public health problem: a vaccine is long overdue, and there is a promising candidate vaccine.
- Introduction of the malaria vaccine should be informed by past experience with other vaccines and should, as much as possible, be integrated within existing immunisation schedules.

Country Experiences in Introducing New Vaccines
— Dr Rachel Seruyange, EPI Uganda

From 1983 through to 2002, the Ugandan EPI largely utilized the same vaccines.

In 2001, the DTP-Hepb+Hib (pentavalent) vaccine was offered by GAVI, which paid for most of the cost. The government of Uganda consulted their Interagency Coordinating Committee (ICC) for Immunization in order to make a decision on introduction. Prior to recommending adoption of the vaccine, it asked for further information on:

- Disease burden;
- Costing and sustainability implications; and
- Cold chain implications.

The MoH also had to present a proposal to the Health Policy Advisory Committee. The country was ready to implement by 2002. Among the challenges faced:

- The difficulty for MoH to pay customs clearing costs for the vaccine, due to high vaccine cost ($3.50/dose);
- Nationwide introduction on a single day in order to avoid suspicions or regional pressures; and
- Smaller vial sizes requiring greatly expanded cold capacity and reconstitution.

Uganda began considering use of a human papilloma virus (HPV) vaccine in 2006. Institutional arrangements within MoH had changed, with all ICCs being replaced by a wider Long-Term Institutional Arrangement (LTIA) Committee. The LTIA experienced a lengthy process of getting all key MoH representatives informed and aligned with respect to this vaccine. A Technical Advisory Committee (TAC) established under the LTIA guided the implementation process. The TAC brings together the key groups; the MoH Reproductive Health Unit chairs the TAC, EPI serves as co-chair, and other government groups such as education participate.

Among the challenges Dr Seruyange reported:

- Determination of which part of MoH would lead policy discussions and introduction;
- Programmatic issues which need to be addressed by formative research:
    - Implementation of the uniquely spaced 0, 1 month, 6 month schedule; and
    - Community awareness of disease burden;

- Vaccine licensure by Ugandan regulatory authority and delays in WHO pre-qualification have been limiting factors in beginning the demonstration project; and
- Limitations in cold chain capacity created by the single-dose presentation and overall changes in EPI policies in vaccine use for target groups aside from children.

Key lessons learned from this experience include:

- There is a need for willingness by national authorities to introduce new vaccines;
- There is a need for adequate planning and involvement of all stakeholders; and
- The introduction process for each new vaccine is different and can experience delays even in countries with recent experience introducing new vaccines.

Country Experiences in Introducing New Malaria Control Interventions — Dr. Charimari, WHO NPO, Zimbabwe

Zimbabwe's experience as described by Dr. Charimari illustrated the long delay often observed from policy decision to implementation:

- The decision to change the first-line treatment from chloroquine was apparent in 2000
- Interim sulfadoxine-pyrimethamine / chloroquine (SP-CQ) policy was adopted in 2002, but not implemented until 2004
- In 2004, the country decided to adopt ACTs and made a proposal to the Global Fund to fight AIDS, Tuberculosis, and Malaria (GFATM).

First arrival of vaccines only arrived in the country in December 2007, some three years after discussion of policy change. Rapid diagnostic tests (RDTs) didn't arrive until February 2008, necessitating the storage of ACTs in the interim.

The government initially decided to phase in ACTs over two years, but changed to nationwide deployment in a single year. Among the challenges:

- The drug arrived prior to the development of a tool to report use, leaving no means to track utilization for some time;
- Two non-governmental organizations (NGOs) implemented ACTs in regions without sufficient MoH coordination; and
- Stakeholders needed to conduct sensitization had not been systematically engaged, only identified.

Currently, RDTs for malaria are being implemented, but case management policies are not adequately updated to be compliant with the new drugs. For example, there is no clarity on protocol for case management of RDT negative cases. Furthermore, plans are not yet in place for the withdrawal of current CQ and SP stocks.

Among the programmatic challenges to be addressed:

- The malaria case management policy is not adequately updated for use with the new drug and necessary coordination with the private sector;
- Insufficient training of health workers;
- Plans for the withdrawal of CQ and SP are not yet in place;
- IEC/ community mobilization has not yet fully implemented while demand for ACTs is increasing;
- Pharmacovigilance; and
- Data and information management.

Key lessons from the Zimbabwe experience are that:

- There is a need to plan for physical storage facilities at national and district levels; and
- There is a need for malaria policy to be fully updated and available to stakeholders.

Experience with Change from CQ to SP to ACTs for Case Treatment
— Dr. Rita Njau, WHO NPO/MAL, Tanzania

Tanzania identified five areas to address in changing its malaria treatment policy:

- Epidemiology;
- Characteristics of available alternatives;
- Human behaviors;
- Cost and cost effectiveness; and
- Health system capacity to implement changes in policy.

Ministry of Health and Social Welfare (MoHSW) established a multi-sectoral task force for the policy change for SP to ACT. It reviewed the items identified above, ultimately recommending the switch to ACTs for the MoHSW; WHO recommendations were also instrumental in informing the policy decision. While there were formal meetings with policy-makers during the policy change process, there were also extensive side discussions with policy-makers seeking support for change. Pharmacovigilance was planned through the Tanzania Food and Drug Agency.

Tanzania sought funds from GFATM ($90M over three years), PMI, Italian Cooperation, and a $300k government-commitment through Medium-Term Expenditure Framework. In addition, the government had to make up for $1.4M lost in currency exchange costs when converting dollars from GFATM to shillings, then back to dollars for international procurement.

Tanzania negotiations on policy change to ACTs were initialized in 2001. The final launch of ACTs did not occur until 15 December 2006.

The main challenges included;

- A lack of Home Based Management for Malaria; and
- A lack of definitive diagnosis for malaria.

Key lessons learned are that:

- There is a need for adequate funding to provide for training, material guide development, and advocacy.

Summary of Key Challenges and Lessons Learned

Summary of Key Challenges Reported
• Determination of which part of MoH would lead policy discussions and introduction • Community perception • Implementation of the a new immunization schedule (HPV) • Community awareness of disease burden • Vaccine licensure by Ugandan regulatory authority and delays in WHO pre-qualification to begin the demonstration project • Cold chain capacity, limited due to single dose presentation and overall changes in EPI policies in vaccines use for target groups aside from children • Inadequate planning and coordination for deployment of the new drug • The malaria case management policy is not adequately updated for use with the new drug and necessary coordination with the private sector • Insufficient training of health workers • Plans for the withdrawal of CQ and SP are not yet in place • IEC/community mobilization not yet fully implemented while demand for ACTs is increasing • Pharmacovigilance system not in place • Data and information management • A lack of home based management for malaria • A lack of definitive diagnosis for malaria
Summary of Lessons Learned
• There is a need for willingness by national authorities to introduce new vaccines • There is a need for adequate planning and involvement of all stakeholders • The introduction process for each new vaccine is different • There is a need to plan for physical storage facilities at national and district levels • There is a need for malaria policy to be fully updated and available to stakeholders • There is a need for adequate funding to provide for training, material guide development, and advocacy

Discussion

***Vaccine protective efficacy*:**

Question: Efficacy vs. effectiveness: 50% efficacy is in ideal circumstances, but what is realistic coverage and effectiveness?
Answer: Efficacy is the projection in a perfect environment, and may be quite different from effectiveness. Estimates of effectiveness will come through modeling or demonstration projects.

Question: To what extent can we rely on the shown efficacy outside of Africa and/or other species?
Answer: Clinical trials may need to be done with each vaccine in different parts of the world, given the variability of vaccine. RTS,S will not be trialed nor licensed initially outside of Africa. It will only work for P *falciparum.*

Question: Isn't 30% efficacy against clinical disease too low? Will it be approved by Drug Agencies?

Answer: MVI conducted a market assessment in 2004 prior to committing funds to the RTS,S phase 3 trials. The assessment confirmed that there was significant interest from stakeholders in approximately four African countries for a vaccine with at least 30% efficacy. However, many also indicated that the decision to adopt will be more complex for partially efficacious vaccines. Clinical trials are being overseen by relevant regulatory bodies in Africa, the United States, and Europe, as well as ethics committees. All have endorsed further studies of RTS,S even with partial efficacy.

Question: Confidence intervals (CIs) for efficacy on clinical and severe mortality are very large. Should we not consider the reported efficacy cautiously?
Answer: The CIs do not include zero, plus the P values are significant. The CIs will ultimately be narrowed in the phase 3 trial when we have much larger sample size.

Reasons to expect possible availability of a malaria vaccine:

Question: Can you give an overview of the developmental steps for vaccines and tell us specifically what it is that makes us now believe that a first generation vaccine may eventually be available?
Answer: There are new financial commitments to vaccine development, new collaborations such as those reflected by the Malaria Vaccine Technology Roadmap, new partners including those from the pharmaceutical industry, and, most importantly, new data availably due to findings in recent years from Mozambique of an efficacious vaccine.

Financing:

Question: How will a malaria vaccine be paid for in a manner which allows general access?
Answer: It is anticipated that malaria vaccines could be supported by a mix of international donors currently supporting vaccines and malaria efforts, such as GAVI and GFATM. If the policies of GAVI are used, it would mean that countries would have to provide a co-pay (approximately $0.20 to $0.30 per dose), with the remainder of the price born by the international funders.

MVI will be supporting economic analyses in parallel with the RTS,S clinical trials, including indirect costs.

***Indications in other groups or specific populations*:**

Question: Will RTS,S work on children with immune deficiency? On pregnant women?
Answer: The phase 3 studies will include an analysis of safety and immunogencitity in children who are malnourished and HIV+, although it won't necessarily have the power to establish a separate efficacy level in these groups. Pregnant women would require separate studies for RTS,S and none

are planned at this time. Eventually we hope to have a vaccine for pregnant women, but it is many years off.

Question: Will malaria vaccines be used to protect older age groups and adults?
Answer: Work to date is focusing on establishing an efficacious vaccine for the population with the highest mortality: Infants and young children. Future vaccines or trials may consider older age groups.

Possible programmatic implications

Question: Is there a need for a booster dose?
Answer: This is a topic being examined based upon mortality patterns and clinical development plan feasibility.

Question: Will a vaccine be appropriate if all other interventions are fully implemented?
Answer: Clinical trials are done in the context of other interventions for ethical reasons, so the trials will help answer the question of whether or not vaccines will be appropriate when other interventions are widely implemented.

Challenges in introducing new malaria control interventions and new vaccines:

Question: The world is moving from publicly owned to privately owned medical vendors. This will be a challenge as current systems are government dependent, yet bigger forces are moving towards privatization—what will be the implications for new interventions?
Answer: This is a trend and a reality that is still evolving and will need to be managed over time.

Question: Can you explain the difference in time between policy adoption and ACT implementation?
Answer: In the figure, the key problem is now on implementation, not policy adoption. Only Swaziland and Cape Verde have not moved to ACTs. It's a question of having the means to deploy the policy once funds are available.

Discussion on Country Experiences

Uganda

Question: The presentation showed how political commitment cascaded through the system into demand. Where there problems of high demand leading to vaccine shortages?
Answer: Yes, this was a problem. The calculation of required doses underestimated the amount needed. This underestimation, combined with supply shortages from the manufacturer, led to several months without stock, forcing the utilization of DPT for a period of time.

Question: How are new vaccines being reported, through HMIS or another system, given that revamping the system will take a long time? Have you established sentinel sites looking at the impact of these new vaccines?
Answer: The main focus is on the coverage of the third dose of DTP, and thus is reported through HMIS. The impact is more complex: Baseline rates in sentinel sites of Hib meningitis have allowed the MoH to publish a major reduction in Hib meningitis after vaccine introduction. Judging impact will be trickier for HPV, where impact, in terms of cancer cases averted, may take years to manifest.

Question: Are there any particular requirements for health workers to accept the new vaccines?
Answer: Yes, health workers must understand the rationale for introducing the vaccine, administration requirements, and any anticipated adverse events and the proper response.

Zimbabwe

Question: What were the resistance levels of CQ and SP when shift taken?
Answer: SP resistances in 2005, 2006, and 2007 were 7%, 9%, and 33%, respectively.

Objective 2: Review the Draft Decision-Making Framework

Introduction to the Draft Regional Decision-Making Framework for Malaria Vaccines (DMF)
—Dr Antoinette Ba-Nguz PATH MVI

Dr. Ba-Nguz described the historical development of the DMF from 2006, where it began through the collaborative efforts of partners including WHO, PATH, USAID, the Bill and Melinda Gates Foundation, and MVI.

The malaria vaccine is nearer than ever before: By 2015, a malaria vaccine with 50% efficacy is expected to be licensed. Once the malaria vaccine becomes available, policy decision will not be a straight forward process. The DMF takes into account programmatic and policy considerations to arrive at a sound decision-making process, as described in the introduction. The Draft Regional Framework is a synthesis of the outcomes from individual countries, incorporating points included by at least half of the countries consulted.

The framework is split into a set of processes and a set of data points. Identified items are further categorized as critical to reaching a decision or simply beneficial. Finally, the items are differentiated into those which the global community is responsible for generating and those which individual countries or regions are responsible for generating.

The data and processes are grouped along a generic timeline. The timeline begins in the pre-licensure period, up to five years prior to licensing and including a point after which the phase 3 data is available. The second period begins when a product is licensed by the country and lasts until a decision is made regarding introduction. The final period is the post-licensure or follow-up period, given as approximately five years following the introduction of the vaccine. The generic template, once established, gives a country the ability to apply the framework to a specific product—by changing the timeline to match those actually anticipated for each product late in development, if necessary.

Objective 3: Agree on the path forward for the implementation of the Draft Regional Decision-Making Framework

Presentation of the ToRs for Group Discussion on the DMF
—Dr Antoinette Ba-Nguz PATH MVI

Dr. Ba-Nguz split the participants into three groups, each of which tasked with reviewing a portion of the Framework and answering a set of questions. The terms of reference for the groups discussion is attached in Annex 3 of this report.

Objectives of this session were:

- To determine the data and processes necessary to reach a decision on the potential introduction of a malaria vaccine;
- To reach consensus on the use of the DMF for decision making on the future use of a malaria vaccines; and
- To define necessary "next steps" to properly consider implementation of the DMF.

The conclusions of the group discussion are reported below.

A. Review of the data

The 1st group looked at the data from Pre-Licensure through Available Data – Phase 3. They determined that all identified data are relevant for decision making in the subregion and are sufficient; the group felt that all required information is captured by the DMF, and no critical data for decision in the subregion was missing. It provides critical analysis and is a good basis for M&E and BCC frameworks.

The group agreed that, while the DMF is a valid tool to guide the decision on the potential introduction of a malaria vaccine in East and Southern Africa, each country must adapt according to their specific experiences and policies.

A limitation identified was that target group is only children under the age of five; the DMF does not address universal coverage.

The 2nd group examined the data requirements from Licensure & Decision through to Post-Licensure. They determined that all identified data are relevant with the

exception of the national data point under "Programmatic Considerations at the Time of Licensure," which reads: "Defined targeted groups and a communication plan." The group felt that the communication plan was not relevant as data as it addresses a process.

The group did not find the data sufficient. It added or modified several items, which are reflected in the graphic by boxes with an orange background.

This group also concluded that the DMF is a valid tool to guide the decision on the potential introduction of a malaria vaccine in East and Southern Africa, but suggested that several terms such as "licensure" be clarified, that the DMF be given a title, and that the position of the legend be simplified.

B. Review of processes

The 3rd group examined the processes. The group concluded that all processes are all relevant for decision making in the sub-region, but they are not sufficient. The group made suggestions which are reflected in the graphic in the orange background boxes, as above.

The group found the DMF to be a valid tool to guide the decision on the potential introduction of a malaria vaccine in East and Southern Africa, but gave several comments. The group noted that the DMF has critical elements which guide decision making in a systematic way and, while it is relatively simple and user friendly, there is room for improvement. The DMF will require explanatory notes on its use. Lastly, the group felt that the DMF requires a title.

Consensus: Recommended Next Steps

The findings from the groups were endorsed by all participants. The following were agreed upon:

- The development of a malaria vaccine is now inevitable. The Decision-Making Framework is a tool that should be understood at the country level by policy makers, regardless of whether they intend to introduce the malaria vaccine. The DMF needs to be disseminated to partners, governments, and at the global level to inform all affected parties of the process for decision making;
- There is a need to develop an advocacy plan targeting all stakeholders;
- Countries should seek assistance from partners to generate the required information;
- Technical assistance to countries regarding malaria vaccine development will be available to countries as required, upon request;
- The development of a strategy document for the implementation of the DMF must take place;
- Support must be provided to countries to start implementing the DMF; and

• Information on the developmental progress of malaria vaccines must be shared.

Conclusion

During this meeting, the most recent results from the trials on the malaria vaccine candidate RTS,S were disseminated to regional stakeholders. Information was also shared on the status of research on other malaria vaccines.

The draft Decision making Framework was presented to EPI and NMCP managers from eleven countries in the East and Southern Africa subregion. Participants have reviewed the data and processes identified and made suggestion to make it a valid common tool for decision on the introduction of malaria vaccines in East and Southern Africa.

Next Steps

In 2008 and beyond, MVI and its partners anticipate similar consultation with other sub-regions in Africa for the revision and validation of the DMF.

With guidance from the Steering Committee, MVI will continue to work with WHO, RBM and other stakeholders in African countries to gain insight into the Regional Decision-Making Framework, as well as develop plans for its implementation.

Appendices

Annex 1: Agenda
2nd August 2008

Time	Topic	Facilitator/Speaker
8h00	Introduction to the meeting	Chair
8h30	Update on malaria vaccines development	A. Brooks PATH- MVI
Objective 1: Review and discuss issues and challenges in the introduction of new malaria control interventions and new vaccines. Determine implications for future malaria vaccines		
9h00	**Key note presentation** ***From research to policy: challenges of introducing new health interventions***	Dr Soce Fall AFRO/ MAL Dr Nestor Shivute IST ESA/EPI
9h30	Country Experiences in introducing new vaccines	Dr Rachel Seruyange EPI Uganda
9h45	Country Experiences in introducing new malaria control interventions	Dr R. Njau NPO/MALTanzania, Dr. Charimari NPO/MAL Zimbabwe
10h00	Discussion	
10h30	**Tea break**	participants
Objective 2: Review the Draft Regional Decision-Making Framework		
11h00	Introduction to the draft regional decision making framework for malaria vaccines (DMF)	Dr A. Ba-Nguz PATH MVI
11h15	Presentation of the ToRs for group discussion on the DMF	Dr A. Ba-Nguz PATH MVI
11h20	Group discussion on the draft DMF Groups 1 (a-b): Data Group 2: Processes	Facilitators: WHO-RBM-MVI
13h30	**Lunch**	
Objective: Agree on the way forward for the implementation of the Draft Regional Decision-Making Framework for countries and partners		
14h30	Report from group discussion	Participants
16h00	Consensus on Recommendations and next steps	Chair
16h30	**Closure**	

Annex 2: List of Participants

Country/Organization	Name	Position
Angola	Elsa Gabriel	Malaria Manager/ MHS Angola
Burundi	Niyunoeko Deo	Director of Research/ National Institute of Health/ Burundi
	Baza Dismas	Transmissible &Deficiency Diseases Control Program Director/ Burundi
	Diane Ndayiragije	Project manager PSI/Burundi
Comoros	N. Ahamada	NPO MAL WHO Comoros
	Affane Bazor	NMCP Coordinator/ Comoros
Djibouti	Hawa Hassan Guessod	Malaria Prevention Programme/ Djibouti
	Abdura Amhed Hade	EPI Djibouti
	Mouna Osman	NMCP /Djibouti
Eritrea	Ayob Yohaness	NPO Malaria WHO Eritrea
Ethiopia	Worku Bekele	NPO Malaria WHO Ethiopia
	Daddi Jima Wayessa	NMCP Ethiopia
Kenya	Tatu Kamau	Head of the Division of Vaccines & Immunization, Ministry of Public Health & Sanitation /Kenya
Madagascar	Tuseo Luciao	NPO Malaria WHO/Madagascar
Malawi	Wilfred Dodoli	NPO Malaria WHO Malawi
	Edward Soko	EPI Malawi
Mozambique	Eva D. Carvalho	NPO Malaria WHO/Mozambique
South Africa	J. A. Urbech	Director Africa Fighting Malaria/ South Africa
Sudan	M. Wais	NPO Mal Sudan, Khartoum
Tanzania	Mary Kitambi	EPI programme Manager/Tanzania
	Ritha Njau	NPO Malaria WHO/Tanzania
Uganda	Kaggwa Mugagga	NPO Malaria WHO Uganda
	Rachel Sernyange	EPI Uganda
Zambia	Prof. B. Baboo	Chair IRS/ University of Zambia
	Fred Masaninga	NPO Malaria WHO /Zambia
	Major Tenson Mbale	Environmental Health Technologist/ Zambia Army
	C.J. Shinondo	University of Zambia,

Country/Organization	Name	Position
		Lusaka
Zimbabwe	Lincon Charimari	NPO Malaria Zimbabwe
	Mary Kamupota	EPI Manager Zimbabwe
World Health Organization	Nathan Bakyaita	M&E officer Malaria Unit WHO AFRO
	Soce-Fall	Malaria WHO AFRO
	K. Gausi	Malaria IST ESA/WHO
	John Govere	Malaria IST ESA/ WHO
	Samson Katikit	Malaria IST ESA/WHO
	Namboze Josephine	Malaria IST ESA/ WHO
	Mrs N Ngwenya	Malaria IST ESA WHO
	Charles Paluku	Malaria IST ESA/ WHO
	N. Shivute	EPI IST ESA/WHO
	Muziki Sam	WHO IST East and Southern Africa, Harare
Roll Back Malaria	Udom Boi- Betty	RBM secretariat Geneva
PATH MVI and MACEPA	Antoinette Ba-Nguz	Programme Officer PATH MVI
	Alan Brooks	Director Policy And Access PATH MVI
	Asefaw Getachen	Consultant PATH MACEPA Ethiopia

Annex 3: Terms of Reference for Group Discussion on the DMF

A. Review of the data and processes

1. Data:
Objective: Determine the data necessary to reach a decision on the potential introduction of a malaria vaccine

Review the data outlined in the DMF and discuss if:

a. They are relevant for decision making in the sub-region?
b. There is any which is not and why?
c. They are sufficient?
d. If not what are the most critical data for decision in the sub-region which are missing

2. Processes:
Objective: Determine the processes necessary to reach a decision on the potential introduction of a malaria vaccine

Review the processes outlined in the DMF and discuss if

a. They are relevant for decision making in the sub-region?

b. There is any which is not and why?
c. They are sufficient?
d. If not what are the most critical processes for decision in the subregion which are missing

B. Draw a conclusion:

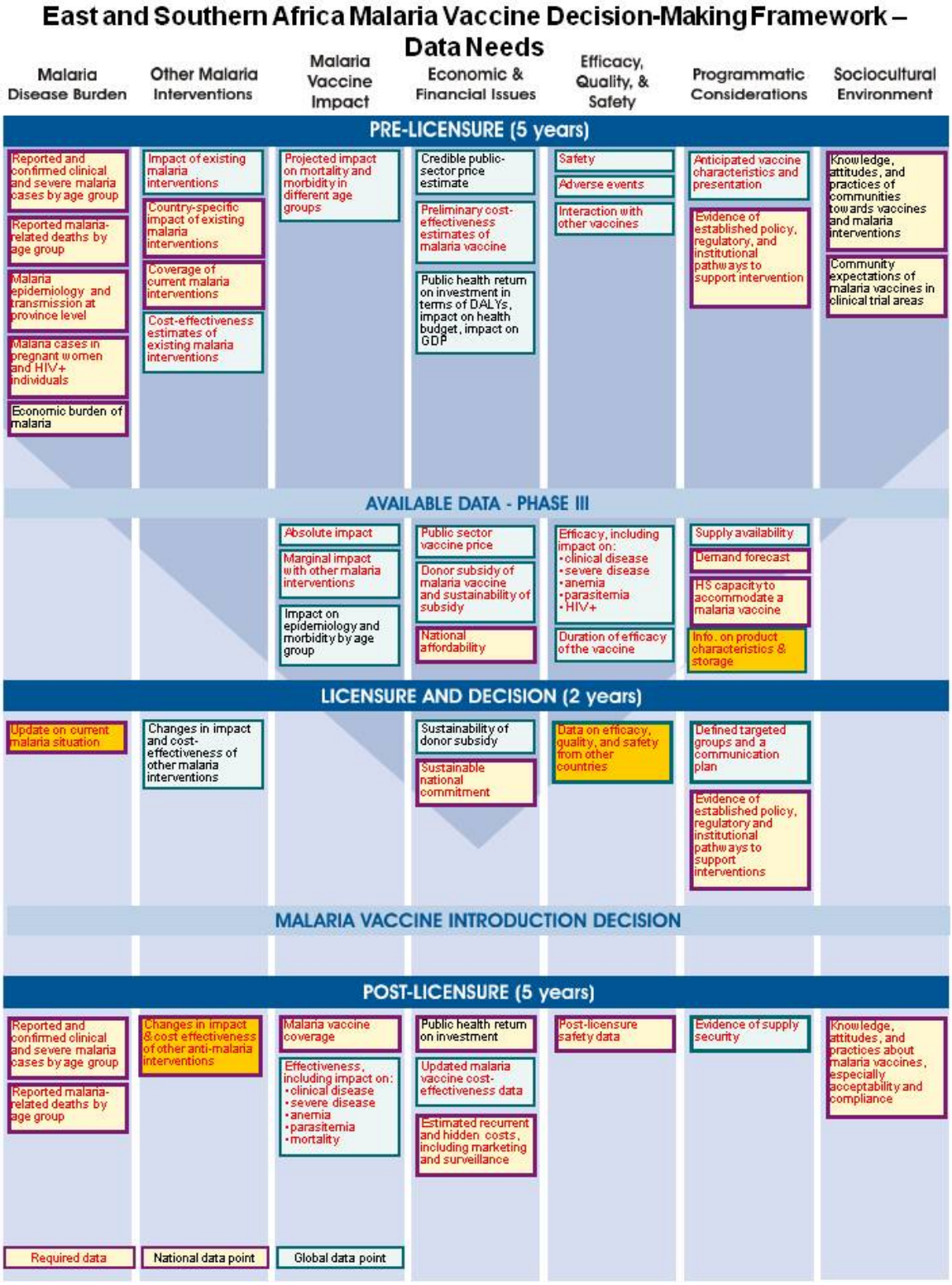
Objective: Report and reach consensus on the use of the DMF for decision making about the future use of a malaria vaccines.

1. Is the DMF a valid tool to guide the decision on malaria vaccine in East and Southern Africa ?
2. What are the strengths of such a tool
3. What are the limitations

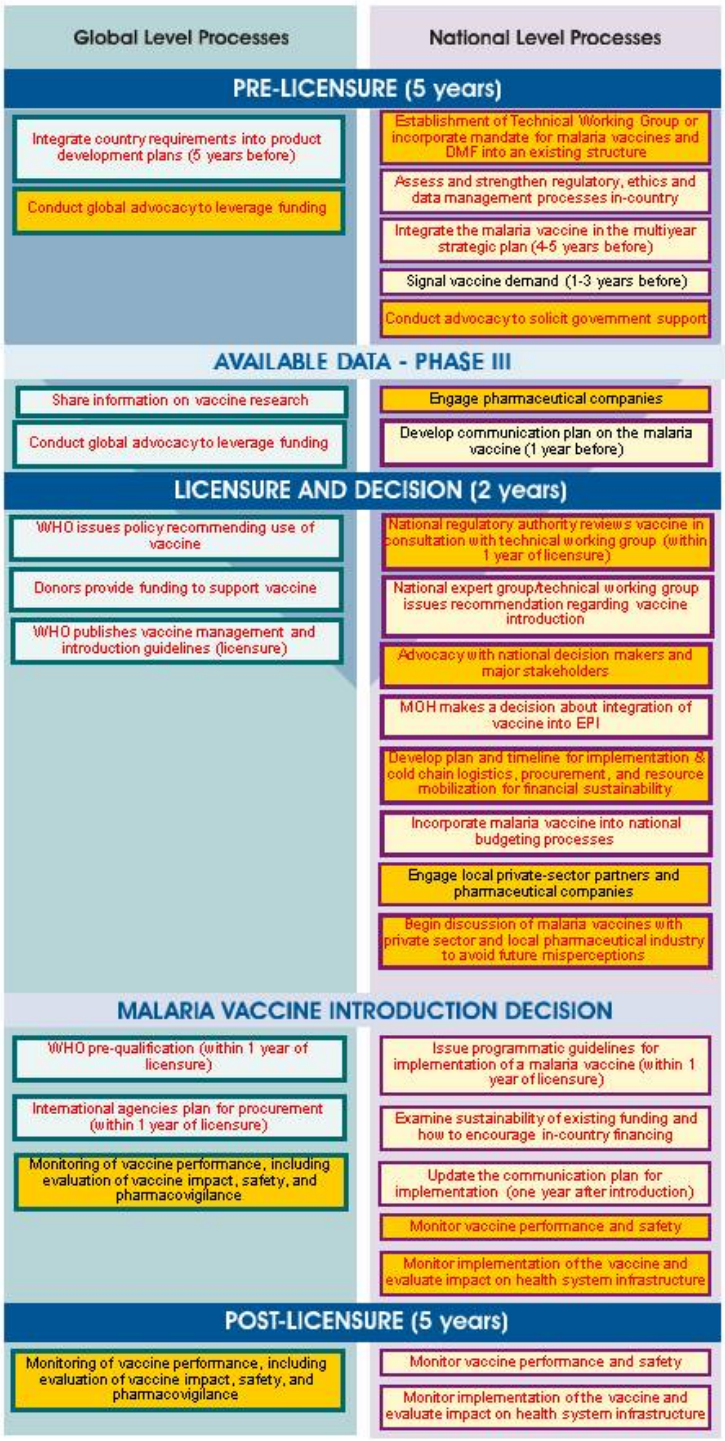
C. Make recommendations to countries and partners for the use of the DMF

Objective: Define next steps necessary to properly consider implementation of the DMF.

Annex 4: Revised version of the draft Regional DMF for East and Southern Africa



East and Southern Africa Malaria Vaccine Decision-Making Framework – Process Needs



Steering Committee

A steering committee of experts provided technical input into content development for the Malaria Vaccine Decision-Making Framework. The members of the 2009 Steering Committee include:

- Dr. Antoinette Ba-Nguz, Program Officer for Africa, MVI
- Mr. Alan Brooks, Director Policy and Access, MVI
- Dr. Carter Diggs, Senior Technical Advisor, USAID
- Professor Dorothée Kinde-Gazard, University of Benin
- Dr. Georges Ki-Zerbo, Malaria Regional Advisor, WHO AFRO, Malaria Control Programme
- Dr. Rose Macauley, WHO AFRO, Vaccine Preventable Diseases
- Dr. Eusebio Macete, WHO Initiative for Vaccine Research (IVR) and Centro de Investigación en Salud de Manhiça (CISM)
- Dr. John Marshall, Consultant to PATH
- Dr. Kamini Mendis, WHO Global Malaria Programme
- Dr. Vasee Moorthy, WHO IVR
- Mr. Gerard Cunningham, Bill & Melinda Gates Foundation

Briefing Paper Summary

Members of the Steering Committee produced seven briefing papers to provide input into the Workshop on a Malaria Vaccine Decision-Making Framework held in Cotonou, Benin in January 2006. These papers summarize current knowledge that is likely to inform future malaria vaccine decision making. The topics of the briefing papers are as follows:

- Analysis of the Demand for a Malaria Vaccine: Outcome of a Consultative Study in Eight Countries
- The Return on Investment for Malaria Vaccines: Preliminary Estimates of Public Health Impact in Africa
- Vaccine Introduction Guidelines from WHO
- Malaria Control Policies: Pathways for Decision Making
- Landscape of Other Vaccines and Malaria Control Options on the Horizon Over the Next Decade
- Status of Malaria Vaccines: Development Process and the Product Pipeline
- Moving from Development to Policy to Implementation of New Products in Countries where Malaria is Endemic: Historical Context for a Malaria Vaccine

Copies of these papers are available at www.malvacdecision.net.

Contact Information

For further information the Malaria Vaccine Decision-Making Framework process, please see www.malvacdecision.net or contact:

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