Frequently Asked Questions, RTS,S/AS01 Malaria Vaccine (Mosquirix)

1. **What is Mosquirix?**

Mosquirix, also known as RTS,S/AS01, is an injectable malaria vaccine developed by GSK. GSK led the development of RTS,S/AS01 over a 30-year period. In 2001, GSK began a collaboration with the PATH Malaria Vaccine Initiative (MVI) to continue developing RTS,S. An advanced clinical trial (referred to as a Phase 3 trial) to assess the vaccine's efficacy and safety was conducted between 2009 and 2014 through a partnership that involved GSK, MVI (with support from the Bill & Melinda Gates Foundation) and a network of African research centres at 11 sites in 7 countries, including Ghana.

2. **How does Mosquirix Act?**

Mosquirix acts against *Plasmodium falciparum*, the deadliest malaria parasite globally, and the most prevalent in Ghana and the rest of sub-Saharan Africa. Mosquirix offers no protection against *Plasmodium vivax* malaria, a strain of the malaria parasite which predominates in many countries outside of Africa.

3. **Why do we need a malaria vaccine?**

Historically, vaccines have proven to be among the most effective means of preventing disease and saving lives, particularly in the case of infectious diseases. Malaria death rates in sub-Saharan Africa have dropped in recent years with the scale-up of existing tools recommended by the World Health Organization (WHO). These tools include: long-lasting insecticidal nets (LLINs), indoor residual spraying with insecticides, preventive treatment for children and during pregnancy, prompt diagnostic testing, and treatment of confirmed cases with effective antimalarial medicines. However, even with all these interventions in place, people are still getting sick and dying from malaria. Additional tools, including a vaccine could support already existing interventions to help reduce the burden of malaria.

4. **What makes Mosquirix different from other malaria candidate vaccines currently under development?**

Mosquirix is the first and to date the only vaccine to show a protective effect against malaria among young children in phase 3 clinical trials. The vaccine would complement other measures currently used to fight malaria. Mosquirix is also the first malaria vaccine to obtain a positive scientific opinion from a stringent medicines' regulatory authority, the European Medicines Agency (in July 2015). It is also the first malaria vaccine to receive authorization from regulatory authorities in three (3) African countries, Ghana, Kenya and Malawi to be used in the Malaria Vaccine Implementation Programme only.

These three countries were selected by WHO to begin the introduction of Mosquirix in selected areas, as part of a large-scale pilot implementation programme, known as the Malaria Vaccine Implementation Programme (MVIP).

5. What is the Malaria Vaccine Implementation Programme (MVIP)?

The MVIP was established by WHO to coordinate and support the introduction of Mosquirix in selected areas of Africa through country-led routine immunization. The MVIP has been designed to address several outstanding questions related to the public health use of the vaccine.

Specifically, the MVIP will assess:

- the feasibility of administering the required four (4) doses of the vaccine to children.
- the vaccine's role in reducing childhood deaths and
- safety of the vaccine in the context of routine use.

Data and information derived from the MVIP will inform a WHO policy recommendation on the broader use of the vaccine.

6. Which countries are participating in the MVIP?

Ghana, Kenya and Malawi are the three countries participating in the MVIP, with each of the 3 countries selecting the areas to be included in the pilots.

7. Why is the MVIP being rolled out only in Africa, and not in other regions?

The WHO African region bears the greatest burden of malaria worldwide. Most malaria illness and deaths in this region are caused by the parasite targeted by Mosquirix (*P. falciparum*). In recent years, malaria death rates in the region have dropped significantly following a major scale-up of long-lasting insecticidal nets (LLINs), artemisinin-combination therapies (ACTs) and other malaria control measures. However, the disease continues to take a heavy toll: in 2017, the region was home to 93% of all malaria deaths globally (or an estimated 403,000 deaths), mainly among young children. Mosquirix was developed for use in Africa and for African children. Additional studies will be needed before the vaccine can be recommended for use outside Africa.

8. Why is Ghana taking part in the MVIP?

In December 2015, the WHO put out a call for interested countries in Africa to apply to participate in the MVIP. Ghana responded to this call for expressions of interest. Ghana's application was based on the country's malaria burden as well as this country's experience with Mosquirix during the clinical trials.

The existence of robust regulatory, ethical, malaria control and immunization systems and infrastructure in Ghana played a critical role in its selection as one of the three countries on the African continent to participate in this programme.

9. When was the Malaria Vaccine Implementation Programme launched?

The MVIP was launched in Ghana on 30th April 2019 and vaccinations began on 1st May 2019.

10. What was the result from the MVIP?

The MVIP within 24 months after first vaccination (April 2019 – April 2021) from the 3 countries showed the following:

- **Feasibility**: Vaccine introduction is feasible, with good uptake and coverage through the routine systems, no impact on uptake of other vaccines, insecticide-treated bed nets (ITNs), care-seeking behavior.

- **Safety**: Vaccine is safe, with no evidence that the safety signals that were seen in the phase 3 trial were causally related to the RTS,S vaccine and no new safety signals identified.

- **Impact**: Vaccine introduction resulted in a substantial reduction in severe malaria and all cause mortality in children age-eligible to receive the vaccine, even when introduced in areas with good ITN use and access to care, 30% (95% CI 8, 46%) reduction in `hospitalized severe malaria. Preliminary data show reduction in all-cause mortality.

- **Equity**: the vaccine is reaching children who are not using other forms of prevention such as insecticide-treated nets, increasing access to malaria prevention interventions to > 90%

The WHO on 6th October 2021 recommended the widespread use of Mosquirix among children in sub-Saharan Africa and in other regions with moderate to high *P. falciparum* malaria transmission following the above results.
In Ghana, a phased approach has been used for the introduction of Mosqirix. The 1st phase in 42 districts was initiated on 1st May 2019. The 1st phase of the MVIP was expected to continue through 2023 to help understand better, the added value of the 4th vaccine dose, and to measure the impact of vaccine introduction on lives saved.

The 2nd phase commenced on 1st December 2022 in additional 51 districts (40 comparator districts and 11 additional districts in the Upper East region).

A 3rd phase of nationwide scale-up to the remaining 168 districts or areas of greatest need based on the malaria burden and epidemiology outside the pilot areas is anticipated to be initiated in January 2024, depending on global vaccine availability of Mosquirix.

11. What are the known side effects of Mosquirix

Known side effects include pain and fever as well as swelling in area of the limb where the vaccine is injected. These side effects are similar to reactions observed with other vaccines given to children. Occasionally, children with fevers have seizures. An increased risk of febrile seizures was seen within 7 days of the administration with any of the four doses of Mosquirix.

As with other new vaccines, and in line with national regulations, the safety profile for Mosquirix will continue to be monitored during the MVIP.

12. What role could Mosquirix potentially play in Ghana's malaria control programme?

The vaccine is a complementary malaria control tool in Ghana **and will not replace** – the core package of proven malaria preventive, diagnostic and treatment interventions, such as long-lasting insecticidal nets and indoor residual spraying with insecticides.

13. Which districts will participate in the 2nd phase of the MVIP?

The 2nd phase will include a total of 93 districts, involving all districts already involved in Phase 1and 51 districts made up of the 40 comparator districts and 11 districts from the Upper East Region.

14. Which partners are involved in MVIP?

The MVIP is coordinated by WHO in close collaboration with the Ministry of Health and a range of in-country and international partners.

The Ministry of Health delivers the Mosquirix through the Ghana Health Service/Expanded Programme on Immunization in the selected districts.

The National Malaria Elimination Programme will ensure that existing WHO-recommended prevention tools, such as LLINs and artemisinin-based combination therapies (ACTs), will continue to be deployed.

In-country research partners were identified to lead a rigorous evaluation of the MVIP.

WHO and PATH worked and are still working together across a number of areas, including on economic assessments, and in the qualitative assessment of behavioural change that may occur during the introduction of the vaccine.

GSK plays a key role in manufacturing and supplying the vaccine free of charge for the MVIP.

The Food and Drugs Authority continues to work closely with the Ghana Health Service, GSK and in-country research partners to ensure safety of children who receive Mosquirix during the MVIP.

15. How will the vaccine be given?

The vaccine is recommended to be given as an injection in four doses to children, with the first dose given as soon as possible after the age of 5 months. In Ghana, it will be given at 6 months, 7 months, 9 months and 18 months of age.

16. Why is Mosquirix not for adults?

The vaccine was developed with children in mind since they are at highest risk of being infected with malaria and eventually dying. Adults living in malaria-endemic areas such as Ghana usually acquire partial immunity against malaria and are less likely to die from malaria compared to children below 5 years of age.

17. What is the position of WHO on Mosquirix?

The WHO recommends that the RTS,S/AS01 malaria vaccine is provided in a schedule of 4 doses in children from 5 months of age. The vaccine should be administered in a 3-dose primary schedule, with a fourth dose provided 12 – 18 months after the third dose to prolong the duration of protection.

Countries may also 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.

18. Recommendation by the National Immunization Technical Advisory Group, Ghana

Following the recommendation by the WHO, the National Immunization Technical Advisory Group (NITAG) reviewed the evidence and adopted WHO's recommendation for a nationwide scale-up of the RTS,S vaccine in Ghana using a phased sub-national approach. The expansion will commence from the comparator districts where MVIP was initiated including all districts in the Upper East region. A scale up of the programme will be considered based on availability of the vaccine and stratification of malaria burden based on epidemiology.

19. Malaria Control Measures-What other interventions exist for malaria control?

There are effective interventions available that can be used to reduce the burden of malaria in Africa. These include: prevention through mosquito vector control using long-lasting insecticidal bed-nets; indoor residual spraying with insecticides; seasonal malaria chemoprevention in specific settings; intermittent preventive treatment for pregnant women; prompt diagnostic testing; and treatment of confirmed cases with effective anti-malarial medicines. All the interventions are implemented nationwide with the exception of indoor residual spraying and seasonal malaria chemoprevention, which are targeted to some regions. These measures have dramatically lowered malaria disease burden in many African settings over the years. The malaria disease burden can be lowered further by continuing to scale up existing WHO-recommended control measures. Available malaria control interventions represent some of the most cost-effective measures for public health.

Mosquirix is being considered as a **complementary** intervention. This means that any use of Mosquirix would be in addition to the existing malaria preventive measures described. The use of high quality, safe and effective drugs to treat malaria will continue regardless of any deployment of a first-generation malaria vaccine.

20. Will Vaccination with the Mosquirix be optional or compulsory?

Vaccination with Mosquirix in the selected implementation areas is not compulsory, but the Ghana Health Service and partners expect that community engagement will provide sufficient information to allow parents and caretakers to make informed decisions on vaccinating their children so that they can benefit from the potential protection against malaria disease and death.

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