



Short report on the Workshop on implementation strategies for the introduction of the RTS,S/AS01 malaria vaccine in countries with areas of highly seasonal malaria transmission

**23 - 25 January 2023
Dakar Senegal and online**

**Convened by
TDR (as part of ADP initiative), WHO and the OPT-SMC team**

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Introduction

The World Health Organization (WHO) recommended the use of RTS,S/AS01 (RTS,S) malaria vaccine for the prevention of *P. falciparum* malaria in children living in regions with moderate to high malaria transmission in October 2021. Experience and reflections from the Expanded Programme on Immunization (EPI) and National Malaria Control Programmes (NMCP) in three pilot countries (Malawi, Kenya and Ghana) provide lessons learned for other countries interested in adopting the vaccine as part of their national malaria control strategies and integrating the vaccine into their immunization programmes. However, the pilot studies do not reflect variable EPI coverage nor areas with highly seasonal malaria. Because RTS,S efficacy is short lived, timing of doses in relation to the transmission season is an important consideration.

To address questions about the scheduling and delivering the vaccine in the context of seasonal malaria transmission, this workshop was convened by the OPT-SMC¹ project in collaboration with The Access & Delivery Partnership (ADP)² partners, the WHO Malaria Vaccine Implementation Programme (MVIP) of the Department of Immunization and the Vaccines and Biologicals and the WHO regional office for Africa. The aim was to bring together representatives from EPI and NMCPs, researchers and relevant stakeholders to tackle questions regarding the introduction of the RTS,S vaccine in countries with seasonal malaria transmission and varying levels of EPI coverage in order to optimize malaria control strategies and maximise the reduction of child morbidity and mortality in such settings. The workshop objectives were:

- To review the current evidence on the RTS,S malaria vaccine in terms of evidence on vaccine efficacy and impact, and safety
- To share experiences across countries that have introduced the RTS,S vaccine in routine child vaccination services in Ghana, Kenya, Malawi, and SMC-implementing countries that are considering malaria vaccine introduction, to better understand the practical implementation challenges and lessons learned for vaccine introduction
- To discuss regulatory and supply management issues when introducing the RTS,S vaccine in the health systems
- To discuss implementation strategies and mode of delivery in countries with seasonal transmission and low/moderate EPI coverage during the 1st and 2nd year of life
- To discuss the operational/implementation research needs to document the implementation of RTS,S in terms of effectiveness, acceptability, feasibility, safety and coverage

Workshop participants included: Representatives from the National Malaria Programs (NMCPs) and Expanded programmes of Immunization (EPI) from 13 African countries that are

¹ With funding from the European and Developing Countries Clinical Trials Partnership (EDCTP), the OPT-SMC project supports 14 countries in West and Central Africa to conduct implementation research for optimizing the effectiveness of SMC, working in partnership with the University of Thiès in Senegal, the special programme for Research and Training in Tropical Diseases (TDR), Medicines for Malaria Venture (MMV), and the London School of Hygiene and Tropical Medicine (LSHTM).

² The Access and Delivery Partnership (ADP: consisting of members from UNDP, PATH, WHO regulatory department and TDR) works with low- and middle-income countries to ensure life-saving medicines and health technologies reach the people who need them. ADP is supported by the Government of Japan and led by the UNDP, in collaboration with the WHO, the TDR and PATH. <https://www.adphealth.org/>

currently implementing SMC in West and Central Africa. EPI and NMCP representatives from Kenya, Malawi and Ghana, where the RTS,S vaccine has been piloted [<https://pubmed.ncbi.nlm.nih.gov/35468801/>]. Key stakeholders involved in vaccine implementation and or malaria control strategies included WHO MVIP, WHO Global Malaria Programme, WHO TDR, WHO regional office for Africa, WHO country office Senegal, EDCTP, Gavi, PMI, CRS, MMV, UNDP, PATH, and academics from University of Thiès, LSHTM and the Malaria consortium.

The workshop allowed the conveners and participants to collate suggested steps going forward in implementing the RTS,S vaccine in countries with seasonal malaria transmission. This short report focuses on the conclusions and outcomes of the workshop. A full report including a summary of all presentations and group work discussions will be published in the Malaria Journal, details will be made available on the TDR website. Also available via the TDR website are the presentations given. A list of illustrative research questions and areas of investigation in this context is provided in appendix 1. Appendix 2 and 3 provide the workshop agenda and list of participants, respectively.

Workshop conclusions and outcomes

The overall conclusions from the workshop summarised below, highlighting more specific areas relating to supply and demand as well as lessons learned to date. Further, open questions and suggested topics for future research were collated (see appendix 1), and proposed steps going forward are included in the below.

This workshop was well received by participants and speakers. It became apparent early on during the meeting that many scientific and implementation questions remain regarding the introduction of this (and potentially other) new malaria vaccine across Africa. Moreover, there are limitations in the lesson learnt from the RTS,S pilot countries as they do not reflect EPI coverage in other settings, nor did they included areas with seasonal malaria. In depth exploration is required to inform implementation of the RTS,S vaccine in countries with low EPI coverage and/or highly seasonal malaria transmission, where greater challenges are likely to be encountered with the implementation of the new malaria vaccine.

Supply and demand

- There is great demand for a malaria vaccine, coupled with high acceptability of RTS,S to date. This has translated into an unprecedented demand with 13 applications submitted to Gavi in early 2023.
- The initial supply for RTS,S cannot meet this demand. Countries therefore may need to take difficult decisions to prioritise areas where the vaccine will be introduced initially.
- Beyond the three pilot countries (Ghana, Kenya, Malawi), it is unlikely that countries will introduce RTS,S before beginning of 2024.

Lessons learned to date from the pilot countries and other research studies

- The community of implementers from vaccine and NMCP programmes would benefit from being informed better regarding the RTS,S vaccine efficacy given different epidemiological contexts.

- Training of personnel administering the vaccine should be carefully timed prior to the introduction of new vaccines, though not too far ahead.
- Community engagement from the outset is key to increase acceptability of the vaccine where it is introduced.
- Dialogue and integration of activities by key national stakeholders, e.g. the expanded programmes of Immunization (EPI) and National Malaria Control Programmes (NMCPs), is mutually beneficial, as evidenced in the RTS,S pilot countries. For countries where EPI coverage is sub-optimal and/or where there is seasonal malaria, joint implementation would likely increase reach for interventions through either programme (e.g. to increase EPI coverage in the 2nd year of life).
- Delivery of 4th dose has been shown to be sub-optimal, even under favourable conditions in pilot countries where EPI coverage overall is good. This suggests the need for additional efforts, or alternative approaches to cover the harder-to-reach and strengthened approaches to increase vaccine coverage during the second year of life.
- Optimal efficacy of RTS,S is achieved with four doses and – where applicable – timing prior to higher malaria transmission periods in highly seasonal areas. Under combined optimal conditions for SMC and RTS,S, the co-efficacy is 92% [<https://www.nejm.org/doi/full/10.1056/NEJMoa2026330>].
- Findings from the pilot countries are extremely valuable towards informing the introduction of RTS,S in other settings.

Open questions and research agenda

- The workshop helped to collate an initial set of questions and more general areas for future investigation (appendix 1) for further consideration and exploration in future. Although it was acknowledged that many implementation research questions remain and will continue to arise as and when countries begin implementation.

Possible steps moving forward

- In the context of seasonal malaria, an ‘optimal RTS,S schedule’ resulting in maximum vaccine efficacy balanced against cost-effectiveness and feasibility, would require a **hybrid delivery model** with administration of doses 1-3 through routine EPI (with slight variability in scheduling depending on country), and delivery of dose 4 through a campaign approach before or at the onset of the rainy season, protection under this hybrid model may be as high as 92%. Fourth dose delivery could be coordinated with preparations for SMC delivery (or other mass drug administration programmes), e.g. advanced communications for SMC or using SMC as means to facilitate vaccine referrals. However, there is a great need for exploration of the feasibility, acceptability and cost effectiveness of this model through implementation research.
- Modelling approaches could be explored to provide guidance regarding this hybrid model in meantime particularly with respect to uptake of the vaccine in the 2nd year of life (4th dose) and optimal spacing between the 3rd and 4th dose of RTS,S.
- As recommended by WHO, countries should document lessons learned from seasonal vaccination strategies, especially regarding operational feasibility, vaccine efficacy and safety. The ADP is considering provision of support for countries to develop such documentation.

- Continued information exchange between countries planning to introduce RTS,S should be facilitated, e.g. through future workshops. Further, suitable communication materials should be developed (technical reports may not be accessible) for the community of implementers from vaccine and NMCP programmes to ensure they are well-informed regarding the RTS,S vaccine efficacy given different epidemiological contexts.
- For the development of a comprehensive and vetted research agenda (facilitated by WHO and Gavi) consultation with researchers and other stakeholders on the ground is essential, to capture relevant implementation priorities generated in the global south.

Acknowledgements

The workshop was jointly supported by [OPT-SMC](#) and [TDR](#) under the umbrella of the Access and Delivery Partnership ([ADP](#)) with funding from the Government of Japan.

We thank all participants and presenters who contributed to this workshop. Special thanks go to Jean-Louis Ndiaye and his team for facilitating the smooth running of the meeting on the ground in Dakar, Senegal; and the Chancellor of the university of Thiès Prof Ramatoulaye Diagne Mbengue.

Appendices

Appendix 1: Exemplar research questions and areas for investigation in the context of implementing a malaria vaccine and in settings with seasonal malaria transmission

The primary implementation research question in the context of RTS,S in countries with varying degrees of EPI coverage and seasonality remains: What is the optimal schedule for the delivery of the RTS,S vaccine to achieve highest impact (efficacy) whilst maintaining operational feasibility?

Specific research areas and questions raised during the workshop were collated as follows:

Community engagement and acceptability

- How can vaccine misconceptions be addressed in different settings?
- When and how should engagement with community leaders take place?
- What means could be employed to increase acceptability of RTS,S in areas where SMC is routinely delivered (engagement of health workers, caregivers, wider community)?
- Should RTS,S be subject to parental consent or be considered as for all other routine vaccinations?

Optimisation and feasibility of RTS,S delivery in SMC settings with variable EPI coverage

- Optimizing delivery of child health interventions through integration of services or programmes
 - Can delivery of the RTS,S dose 4 and/or SMC help increase uptake of other child health interventions such as other vaccines, ITN use, Vitamin A, deworming etc. and vice versa?
 - What are the possible assess strategies to reach those with zero EPI doses and under-served populations leveraging community demand for malaria vaccine?
- Piloting models of combined or linked vaccine and SMC delivery through
 - Co-administration via one team covering interventions
 - Parallel administration via EPI and NMCP teams
 - Sequential administration, e.g. through referrals by SMC teams to EPI teams
- What is the cost effectiveness of combined vaccine and SMC delivery models?
- Areas to evaluate in terms of operational feasibility for co-administration
 - logistics
 - programming
 - adverse drug event monitoring
- Evaluation of optimal target age group for a campaign-style delivery of dose 4
 - Context of limited RTS,S supply in the initial phase of the vaccine roll-out
- What is the most feasible delivery strategy given malaria transmission intensity and length of the transmission season?

Vaccine scheduling, efficacy & safety

- What is the level and duration of vaccine efficacy following the 4th dose of RTS,S (vis-à-vis the possible need for subsequent booster doses)?

- What is the optimal age range for vaccination efficacy (consideration of vaccine efficacy in younger children <5 months and older children > 17 months)?
- What is the best schedule to maximise efficacy depending on malaria transmission intensity and length of the transmission season?
- Could fractional dosing be considered vis-à-vis vaccine efficacy and dose sparing?
- What are the potential benefits of clearing malaria parasitaemia prior to vaccination to increase vaccine efficacy?
- With introduction of RTS,S, can SMC be reduced over time?
- What is the optimal interval in terms of efficacy and safety between dose 3 and 4 (modelling studies might be informative)?
- Do additional annual doses need to be considered after the initial vaccine course (i.e safety and efficacy of >4 doses)?
- Is there a need for a 'coverage target' for vaccination campaigns (context: No herd immunity with the malaria vaccine)?
- How can vaccine effectiveness and safety be monitored, where RTS,S may be introduced seasonally (in view of possible adaptation of schedule)?
- What is the safety of co-administration of RTS,S and SMC through a campaign strategy?
- Are there added/synergistic effects of the malaria vaccine with Perennial Malaria Chemoprevention (PMC)?

Monitoring & evaluation; Digital technology

- Post-introduction Evaluation (PIE) – methods for evaluation of RTS,S delivery in SMC settings
- Implementation research on opportunities for digitalisation of vaccination / adverse drug event monitoring

General

- Documentation and sharing of best practices from (sub-)national implementation of RTS,S (e.g. in high priority areas)
- Interchangeability of RTS,S and candidate malaria vaccine R21

Appendix 2: Workshop resources

A dedicated website about [TDR's malaria vaccine implementation research activities](#) provides further detail about this workshop, including a short workshop report in English and French, as well as links to the workshop presentations.

The workshop was convened by [TDR](#) under the umbrella of the Access and Delivery Partnership ([ADP](#)), with WHO and the [OPT-SMC](#) team. This short report written by Jean-Louis Ndiaye, Ibrahima Mbaye, Fatimata Bintou Sall, Paul Milligan and Susana Scott (OPT-SMC), Corinne Merle and Branwen J Hennig (TDR), with input from the workshop presenters.

Appendix 3: Workshop agenda

Note: The agenda was slightly adapted during the meeting to accommodate discussion time and technical issues.

Time (GMT)	Topic	Speakers
Day 1 Monday 23rd January 2023		
Setting the scene		
Chairperson: Dr Mahamat Saleh Issakha Diar		
9:00-9:10	Welcome and opening of the meeting	Chancellor of university of Thiès Prof Ramatoulaye Diagne Mbengue
9:10-9:20	Meeting objectives and introduction of participants	Jean Louis Ndiaye (Univ Thiés) & Corinne Merle (TDR)
9:20-9:40	Introduction to OPT-SMC (5min) Introduction to ADP (5min) Q&A (10min)	Jean Louis Ndiaye (Univ Thiés) Cecilia Oh (UNDP, remote)
9:40-10:10	RTS, S malaria vaccine current evidence, including efficacy, safety, feasibility and impact and update on R21 (20+10 min Q&A)	Mary Hamel (WHO MVIP, IVB, remote)
10:10-10:25	Vaccine efficacy and seasonality of malaria (10+5min Q&A)	Paul Milligan (LSHTM)
10:25-10:40	Update on supply of RTS,S with allocation framework (10+5min Q&A)	Eliane Furrer (WHO MVIP, remote)
10:40-10:55	GAVI malaria vaccine programme update (10+5min Q&A)	Stephen Sosler (GAVI, remote)
10:55-11:30	Break	
11:30-11:50	Practical considerations for RTS, S malaria vaccine supply chain and limited supply management at country level (10+10min Q&A)	Betsy Wilskie (PATH)
11:50-12:00	Regulatory consideration for introduction of RTS, S in countries with seasonal malaria (10+10min Q&A)	Lydia Tuitai (WHO AFRO)
12:00-13:00	Round table on plans for RTS, S roll-out in countries who applied in January 2023 for RTS, S vaccine procurement	Countries
13:00-14:30	Lunch	
Chairperson: Dr Olimatou Kolley		

14:30-14:45	Overview of SMC (target population, eligible geographic area, model of delivery, integration with other preventive measures, etc.) (10+5min Q&A)	André Tchouatieu (MMV)
14:45-15:15	Lessons learned and practical experience from pilot introduction of the RTS, S malaria vaccine: implementation in routine child immunization programmes (incl PIE) and possible implications for implementation through SMC or other MDA programmes Kenya (10min) Malawi (10min) Ghana (10min)	Rose Jalang'o (EPI, Kenya) John Sande (EPI, Malawi) and Brenda Lupafya Mhone (NMCP) Mohamed Naziru Tanko (EPI, Ghana) and Muniratu Venu (NMCP, Ghana)
15:15-15:30	Qualitative findings and lessons learned from the pilot countries: perceptions of malaria, the vaccine and other interventions	Scott Gordon (PATH)
15:30-16:00	Discussion on country lessons learned and qualitative findings	All
16:00-16:30	Break	
16:30-16:45	Considerations and possible modalities for introduction of RTS,S malaria vaccine in countries with seasonal malaria	Rafiq Okine (WHO MVIP, remote)
16:45-17:15	Brainstorming - collating questions to be addressed in break-out groups on day 2 under different modalities of RTS,S malaria vaccine introduction in countries with seasonal malaria.	All
17:15-17:30	Wrap-up of Day 1	
18:30	Dinner	Venue to be confirmed
Day 2 Tuesday 24th January 2023		
Implementation strategies and mode of delivery for combined RTS, S and SMC programmes		
Parallel sessions		
9:00-13:00	Groupwork on implementation strategies depending of model delivery defined on day 1 (Break out groups)	All
13:00-14:30	Lunch	
Chairperson: Dr Marcellin Ateba		
14:30- 17:00	Feedback from breakout groups & discussion	All
17:00-17:15	Wrap-up of Day 2	
Day 3 Wednesday 25th January 2023		
Implementation research needs and evaluation strategies to document the implementation of RTS, S in terms of effectiveness, acceptability, feasibility, safety and coverage		
Chairperson: Scott Gordon		
9:00-9:45	New vaccine post-introduction Evaluation (PIE) as tool WHO IVB 10.03 eng.pdf (20 min presentation & 25 min discussion)	Jenny Walldorf (WHO MVIP, remote) and Mohamed Naziru TANKO
9:45 – 10:30	Case Control studies to evaluate vaccine strategy efficacy	Thomas Gyan & Kwaku Poku Asante
10:30-11:00	Break	
11:00-11:15	Implementation questions and funding for evaluation and implementation research questions (15min)	Stephen Sosler (Gavi, remote) & Mary Hamel (WHO MVIP, IVB, remote)

11:15–12:30	General discussion on the research agenda, potential additional implementation research questions to be considered and funding opportunities	All
12:30-13:15	Overall conclusions & next steps	All
13:15-14:30	Lunch	
END OF MEETING		

Appendix 3: Workshop participants

First Name	Last Name	Affiliation
IN-PERSON PARTICIPANTS		
Cyriaque Dossou	AFFOUKOU	NMCP Benin
Souliatou Yolande	AFFO	EPI Benin
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Issa	OUEDRAOGO	EPI Burkina Faso
Marcellin Joel	ATEBA	NMCP Cameroon
Andreas Ateke	NJOH	EPI Cameroon
Olimatou	KOLLEY	NMCP Gambia
Sidat	FOFANA	EPI Gambia
Mohamed Binné	CAMARA	NMCP Guinea
Gassim	CISSE	EPI Guinea
Jose Ernesto	NANTE	NMCP Guinea Bissau
Humberto	IMBUNDA INTCHALA	EPI Guinea Bissau
Muniratu	VENU	NMEP Ghana
Mohamed Naziru	TANKO	EPI Ghana
Aissata	KONE	NMCP Mali
Yacouba	COULIBALY	EPI Mali
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Fatou	CAMARA	CRS
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