





## Key milestones in the development of the Malaria Vaccine Implementation Programme (MVIP): from pilot recommendation to vaccine introduction



The MVIP was established by WHO to coordinate and support the phased introduction of the RTS,S/AS01 malaria vaccine in selected areas of Africa. The vaccine is being provided to children through the routine immunization services of the Ministries of Health of Ghana, Kenya and Malawi as part of childhood vaccination programmes. Separate from vaccine introduction, independent evaluations are being conducted – household surveys and sentinel hospital and community mortality surveillance. Data from these observational studies (pilot evaluations) will inform policy on how best to introduce the vaccine into routine systems; the effect of the vaccine on child survival; and, the vaccine’s safety profile in routine use. The timeline below shows key milestones in the development and implementation of the programme.

### Legend:

#### Colors:

	Pre-MVIP
	Overall MVIP
	Vaccine implementation
	Pilot evaluations

#### Symbols:

	Global & regional expert engagement
	Country-level engagement

## 2009 – 2014

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**2009-2014:** Phase 3 trial of RTS,S/AS01 conducted across 11 sites in seven countries in sub-Saharan Africa. The final results are published in [The Lancet](#).



**2009-2014:** Regular updates on trial results are shared with WHO expert advisory bodies including the Joint Technical Expert Group on Malaria Vaccines (JTEG), Strategic Advisory Group of Experts on Immunization (SAGE), Malaria Policy Advisory Committee (MPAC), and Global Advisory Committee on Vaccine Safety (GACVS).



**2009:** The Ghana Malaria Vaccine Technical Working Group (TWG) is established with representatives from the Ghana Health Service (including the National Malaria Control Program, NCMP, and the Expanded Program on Immunization, EPI), the Food and Drugs Authority (FDA), research partners, academia, WHO and PATH. As part of the malaria vaccine evidence-based decision-making process, TWGs act as a resource on malaria vaccine development, synthesize and document data to inform recommendations, and provide a forum for stakeholder alignment and discussion.



**2012/3:** Kenya establishes a Malaria Vaccine Technical Working Group (TWG) with representatives from the Kenya Ministry of Health Expanded Programme on Immunization (EPI) and the National Malaria Control Programme (NMCP), the Pharmacy and Poisons Board, the U.S. President’s Malaria Initiative (PMI), UNICEF, National Public Health Laboratory Services, WHO and PATH. The TWG continues as a technical coordinating group through the MVIP.

## 2015

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**July:** the European Medicines Agency (EMA) issues a [positive scientific opinion](#) of the vaccine, concluding that the benefits of the vaccine outweigh the risks.



**October:** WHO expert advisory groups on immunization (SAGE) and malaria (MPAC) recommend pilot implementation of RTS,S/AS01.



**December:** WHO issues a [call for expression of interest](#) to ministries of health (MOH) in sub-Saharan Africa to take part in the MVIP. Key among the criteria for selection were well-functioning national malaria and immunization programmes.



**December:** The [GACVS](#) receives an update on the recommendations made about use of the RTS,S/AS01 vaccine.

## 2016

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**January:** WHO publishes the first [Malaria Vaccine Position Paper](#).



**January:** Ministries of Health from 10 countries express interest to take part in the MVIP.



**January:** WHO convenes a consultation to develop the design of the pilot implementation based on the SAGE/MPAC recommendations.



**March:** [MPAC](#) receives a progress report from WHO on the planning underway to design and mobilize resources to support the pilot implementation. It was agreed that both SAGE and MPAC will be kept informed of the progress of the pilots on a regular basis.



**April:** The Ghana Malaria Vaccine Technical Working Group (TWG) publishes a technical brief on the RTS,S/AS01 vaccine to inform evidenced-based decision-making by national stakeholders on the use of the vaccine in Ghana. The TWG is composed of representatives from the Ghana Health Service (including the National Malaria Control Program, NCMP, and the Expanded Program on Immunization, EPI), the Food and Drugs Authority, research partners, academia, WHO and PATH.



**Q1-Q2:** In Malawi, the MVIP is endorsed by the Malawi Immunization Technical Advisory Group (NITAG). The MOH EPI sub-technical working group and the malaria TWG endorses country participation, and lead development of the vaccine introduction plan, programme objectives and strategies, and oversight of implementation arrangements.



**June:** The MVIP funding proposal developed by WHO is presented to the Board of Gavi, the Vaccine Alliance.



**July:** WHO completes the first draft of the pilot evaluation master protocol with inputs from external experts.



**June-November:** Funding for the MVIP is confirmed: Gavi, the Vaccine Alliance, the Global Fund to Fight AIDS, Tuberculosis and Malaria, and Unitaaid partner to provide \$49.2 million for the first phase of the pilot programme.



**September:** [MPAC](#) receives a progress report on MVIP planning.



**October-November:** A delegation from WHO and PATH makes initial visits to Ghana, Kenya and Malawi to present the proposed MVIP to in-country stakeholders, including the EPI, the NCMP and other representatives from MOH, regulators, ethics committees, researchers and health partners.



**December:** The Ghana TWG recommends options for the geographic areas to be included in the MVIP and determines the district as the appropriate administrative unit for randomized vaccine introduction.

## 2017

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**February:** Regulators from Ghana, Kenya and Malawi agree during African Vaccines Regulatory Forum (AVAREF) meeting on a pathway and strategy for joint regulatory review with support from the EMA, which previously reviewed and provided a positive scientific opinion on the RTS,S/AS01 vaccine under Article 58.



**March:** A delegation from WHO and PATH makes the second round of visits to Ghana, Kenya and Malawi to confirm countries' interest in the MVIP and advance planning.



**March:** [MPAC](#) receives updates on programme design and planning.



**April:** SAGE receives updates on programme design and planning.



**April:** The Malawi National Task Force – comprised of representatives from MOH (EPI, NMCP), Pharmacy Medicines Regulatory Authority (PMRA), research institutions, WHO and PATH – recommends options for geographic areas to be included in the MVIP and determines health facility catchment area as appropriate administrative unit for randomized vaccine introduction.



**April:** Discussions with the WHO Ethics Review Committee (ERC) in advance of the submission of the evaluation master protocol.



**April:** WHO [officially announces](#) Ghana, Kenya and Malawi as the 3 pilot countries to participate in the MVIP.



**Q1/Q2:** The MOHs in all three pilot countries initiate vaccine introduction planning through country-driven processes coordinated by Advocacy, Communications and Social Mobilization (ACSM) committees, which include broad public and private health partner representation. While similar planning approaches are used as for other new vaccine introductions, particular attention is given to the inclusion of relevant stakeholders from the national malaria control programmes. Communications sub-groups develop approaches for: (1) national communications plans and core reference materials; (2) media sensitization and engagement; (3) issues management/crisis communications; (4) district and community stakeholder engagement and information dissemination; (5) national and political advocacy; and, (6) information, education, and communications (IEC)

materials for communities and caregivers. The IEC materials and other community engagement activities follow established community participatory methods that emphasize the reasons for the pilots, the 4-dose schedule, the partial protection provided by the vaccine, and need to continue to use other proven malaria control methods, and why only some communities are getting the vaccine now, among other things.



**June:** The Regional Immunization Technical Advisory Group (RITAG, the principal advisory group to the WHO Regional Office for Africa) and [GACVS](#) receive updates on programme design and regulatory processes.



**July:** After external review by experts in malaria, child survival, epidemiology and statistics the evaluation master protocol is submitted to WHO ERC.



**September:** SAGE receives updates on MVIP progress.



**October:** [MPAC](#) receives updates on MVIP progress.



**October:** At its inaugural meeting, the [MVIP Programme Advisory Group](#) (PAG) reviews and endorses the MVIP design and methodologies.



**October:** Malawi stakeholders convene a malaria vaccine communications strategy workshop to develop a communications plan. Public and private national stakeholders include national MOH Health Education Services, EPI, and NMCP, Pharmacy Medicines Regulatory Authority (PMRA), as well as FHI 360, UNICEF, Village Reach, Zodiak, Malawi Broadcasting Corporation (radio and television broadcasting company), College of Medicine, WHO and PATH. The strategy is presented to ACSM sub-committee, EPI, NMCP, and approved in April 2018.



**October:** Ghana ACSM updates its communications strategies and plans. ACSM membership includes representatives from the MOH Ghana Health Service, civil society organizations (CSOs), local media, health non-profit organizations (NGOs), and the FDA. Meetings are convened at least bi-weekly through the start of vaccination.



**October:** In response to queries about the MVIP from the Catholic community in Kenya, a member of the Catholic community who was also a lead researcher in the prior clinical testing of the RTS,S/AS01 vaccine, speaks at the Catholic community's annual health conference, providing information on the MVIP and responding to the community's questions.



**November:** Training workshop are organized for Malawi's National Safety Review Committee by WHO and PATH as part of a series of activities to strengthen the Malawi national pharmacovigilance system.



**December:** [GACVS](#) receives an update on MVIP progress and countries' pharmacovigilance system.

## 2018

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**January:** The Malawi MOH finalizes its malaria vaccine introduction plan. The MVIP is endorsed by the EPI Sub-Technical Working Group and the Malaria TWG.



**February:** AVAREF facilitates joint regulatory review of the RTS,S/AS01 vaccine by the national regulatory authorities (NRAs) of the pilot countries.



**February:** The WHO ERC approves the evaluation master protocol.



**March:** PAG quarterly progress review meeting.



**March:** The Kenya Paediatrics Association is briefed on the MVIP by the Kenya National Vaccines and Immunization Programme (NVIP) manager at the Association's annual scientific conference. The Paediatrics Association resolves to continue to support the phased introduction of the new vaccine.



**March:** At its inaugural meeting, the MVIP Data Safety and Monitoring Board (DSMB) reviews the MVIP objectives and design.



**April:** The Ghana MOH finalizes its malaria vaccine introduction plan. The decision to introduce the malaria vaccine in a pilot implementation receives approval from the national Inter-Agency Coordinating Committee (ICC).



**April:** [MPAC](#) and [SAGE](#) receive updates on MVIP progress and plans to develop a Framework for Policy Decision on RTS,S/AS01.



**April:** MVIP presentation at the Multilateral Initiative on Malaria (MIM) Pan African Malaria Conference in Dakar, Senegal, one of the world's foremost gatherings of malaria specialists.



**April/May:** The NRAs of Ghana, Kenya and Malawi issue regulatory authorization for use of RTS,S/AS01 in the MVIP areas following internal reviews in each of the countries.



**May:** The Secretary for Health in Malawi approves the formation of a multi-sectoral national task force to oversee the introductions of several new vaccines, including the malaria vaccine. The task force is chaired by the Chief of Health Services and includes over 60 members, including: representatives of MOH (EPI, NMCP, health education, community health and zonal offices); other ministries; research and health teaching institutions; public and private health partners (WHO, UNICEF, JSI, PATH and others); and, mass media and civil society organizations. Five sub-committees are responsible for different aspects of the introduction and report to the national task force.



**May:** Kenya sub-national county stakeholder forums take place to review the rationale for malaria vaccine pilot implementation and for randomization of vaccine introduction areas.



**May:** Information, Education and Communication (IEC) messages and materials are adapted and pre-tested in MVIP areas by MOH in Malawi and Ghana. They include a community information flip chart, flyer, handbook sticker, poster and vaccine key facts booklet, which emphasize the reasons for the pilots, the 4-dose schedule, the partial protection provided by the vaccine, and need to continue to use other proven malaria control methods, and why only some communities are getting the vaccine now, among other things.



**June:** DSMB quarterly progress review meeting.



**June:** [GACVS](#) is updated by the 3 countries on pharmacovigilance readiness.



**June:** The MVIP is presented by WHO at an event hosted by the UK All-Party Parliamentary Group on Malaria and Neglected Tropical Diseases (APPMG). The MVIP overview is part of a broader dialogue among Parliamentary and development public officials, malaria scientists, global health advocacy groups and non-profit organizations on advances in malaria research and control tools.



**August:** PAG quarterly progress review meeting.



**August:** An update on the status of MVIP preparations is provided to the Malawi National Immunization Technical Advisory Group (MITAG).



**September:** DSMB quarterly progress review meeting.



**September:** The country-specific protocols for pilot evaluations in Ghana and Malawi are submitted for ethics review:

- The Ghana-specific protocol is submitted to the Ghana Health Service Ethics Review Committee (GHS-ERC). There was simultaneous submission to the WHO Ethics Review Committee (ERC).
- The Malawi-specific evaluation protocol is submitted to the University of Malawi's College of Medicine Research Ethics Committee and the University of North Carolina at Chapel Hill institutional review board. There was later submission to the WHO ERC in November.



**October:** [MPAC](#) receives an update on MVIP and the Framework for Policy Decision.



**October:** Following in-country expert recommendations from both NMCP and NVIP, eight counties in western Kenya are included in the MVIP, and sub-counties are determined as the appropriate unit for randomized vaccine introduction.



**October/November:** Ghana's Adverse Events Following Immunization (AEFI) committee is established and refresher trainings to strengthen the pharmacovigilance system are conducted with regional investigation teams with support from WHO and PATH.



**November:** Vaccine implementation areas are selected in Ghana through a random process during a meeting of the national TWG. The event – convened by the Ghana Health Service – is attended by the regional directors of health of the MVIP regions and TWG members (which include representatives from EPI, NMCP, national ethics and regulatory agencies, evaluation partners, academia, and health partners such as PATH and WHO.)



**November:** The Kenya country-specific protocol for the pilot evaluation is submitted for ethics review to the Scientific and Ethics Review unit of the Kenya Medical Research Institute (KEMRI), Oxford Tropical Research Ethics Committee (OxTREC) and institutional review boards at the U.S. Centers for Disease Control and Prevention (US CDC). There was later submission to the WHO ERC in December.



**November:** PAG quarterly progress review meeting.



**November:** DSMB quarterly progress review meeting.



**November-December:** Malawi MOH and evaluation partners conduct sub-national sensitization with regional and district health management teams to explain the purpose of the MVIP and obtain approval for the pilot evaluations.



**December:** PAG quarterly progress review meeting.



**December:** The MOH Ghana Health Service (GHS) completes IEC materials for communities, caregivers and health workers developed by the ACSM – a committee with broad public and private representation, including the GHS Health Promotion Division, GHS Office of the Director-General, Ghana Broadcasting Corporation, Red Cross Society, Daily Graphic (media outlet), Ministry of Education, Ministry of Information, local NGOs, Ministry of Women’s and Children’s Affairs, UNICEF, NMCP, PATH and the FDA. The community materials emphasize the reasons for the pilots, the 4-dose schedule, the partial protection provided by the vaccine, and need to continue to use other proven malaria control methods, and why only some communities are getting the vaccine now, among other things.

## 2019

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**January:** The Ghana protocol for the pilot evaluation is approved by the WHO Ethic Review Committee (ERC), and later in February 2019, by the GHS Ethical Review Committee (GHSREC). Annual continuing review is sought and approved.



**January:** RITAG receives an update on MVIP and the Framework for Policy Decision.



**January:** WHO registered the Malaria Vaccine Evaluation Programme (MVPE), the study conducted in the context of the MVIP, a programmatic activity, as an observational study on the ClinicalTrials.gov website. Although not a clinical trial, registration of the MVPE in this registry ensures transparency in research, and 20% of studies registered on the site are listed as observational. Registry was requested by the WHO ERC at the time of approval of the evaluation master and country protocols.



**January:** DSMB quarterly progress review meeting.



**January – April:** Senior MOH officials in Malawi and Ghana conduct in-country orientations and briefings with national and community organizations, civil society groups and government leaders.

- In Malawi, consultations are held with MOH partners from the Malawi-Liverpool Wellcome Trust, Malaria Alert Centre, Christian Health Association of Malawi (CHAM) and JSI.
- In Ghana, briefings are held with the Academy of Arts & Sciences, health professional groups, the Ghana Parliamentary Select Committee on Health and the full Parliament.



**February:** PAG quarterly progress review meeting.



**February:** An implementation agreement is signed between Ministry of Health & Population of the Republic of Malawi and the WHO. The agreement establishes the terms under which the parties will cooperate in, and contribute to, the malaria vaccine introduction and the pilot evaluations.



**February:** MOH Malawi convenes an event to randomly assign areas to receive the vaccine. The event is attended by four officials from each of the 11 MVIP districts (including a member of the District Health Management Team, the Malaria Coordinator, the EPI Coordinator and a representative of the District commissioner), and EPI staff, NMCP staff, MOH officials, evaluation partners, WHO and PATH.



**February:** The Kenya National Vaccines and Immunization Programme (NVIP) and the National Malaria Control Programme (NMCP) convene an event to randomly assign counties to receive the vaccine. The event is attended by the Executive Committee members for Health of the MVIP counties, county representatives from the County Health Management Team and Health Directors, and representatives of the Kenya NITAG, MOH, evaluation partners, PATH and WHO.



**February:** Kenya MOH pre-test and then adapt IEC messages and materials for health workers and caregivers in MVIP areas to identify any gaps in information or where clarifications would be helpful.



**February-April:** In Ghana and Malawi, following a training-of-trainers approach, health worker trainings are conducted for health staff at regional, district and facility levels. Training modules include: 1) rationale for implementation of the pilot project; 2) vaccination schedule and co-administration of RTS,S/AS01 with other EPI antigens; 3) injection site and technique with special focus on multiple injections at the same immunization session; 4) injection safety and waste management; 5) AEFI surveillance; 6) vaccine storage and management; 7) cold chain maintenance; 8) ACSM roles and communication plans aimed at health workers, communities and caregivers; and, 9) monitoring and supervision of implementation.



**February:** Kenya's National Vaccine Safety Advisory Committee (KNVSAC) inauguration is held. Training organized jointly by Kenya NVIP and the Pharmacy and Poison Board (PPB), supported by WHO and PATH on AEFI reporting, AEFI investigation and causality assessment.



**March:** The Kenya country-specific protocol for the pilot evaluation is approved by the WHO ERC and later in June, by the Scientific and Ethics Review Unit of the Kenya Medical Research Institute (KEMRI SERU). Annual continuing review is sought and approved.



**March:** The Malawi country-specific protocol for the pilot evaluation is approved by the College of Medicine Research Ethics Committee (COMREC) and later in April, by WHO ERC. Annual continuing review is sought and has been approved.



**March:** Kenya's MVIP communications plan is finalized, with audiences and activities aimed at community organizations and leaders (health, traditional, religious and other interested groups), health workers, caregivers and community members, and key stakeholders such as local and national media.



**March/April:** Sub-national stakeholder engagement in Malawi and Ghana by the MOH and evaluation partners is rolled out in all MVIP-implementing areas. This includes communication orientations of district health management teams on key messages and components of the MVIP, including key information to deliver to caregivers and communities.





**March/April:** Orientations and community information briefings are held in Malawi with traditional leaders, religious leaders and other community opinion leaders. The aim is to provide key information on the new vaccine and the pilot, evaluation studies and what communities and caregivers should expect in vaccinating areas.



**March/April:** Ghana MOH and evaluation partners carry out briefings with the Regional Coordinating Councils of all MVIP regions in the country, including Regional Health Management Teams, all District Assemblies in both vaccinating and non-vaccinating districts, and all District Health Management Teams. At the community level, local chiefs, National House of Chiefs, religious leaders and other community opinion leaders are provided opportunities to hear about the pilot and ask questions.



**March-April:** IEC materials are widely circulated to communities and caregivers in Ghana and Malawi through community meetings, radio, television, print, and social media platforms at district, regional, and national levels prior to the start of vaccinations.



**April:** An implementation agreement is signed between MOH of Ghana and the WHO. The agreement establishes the terms under which the parties will cooperate in, and contribute to, the malaria vaccine introduction and the pilot evaluations.



**April:** In preparation for start of vaccinations, the Ghana and Malawi MOHs convene media sensitization events with local, national and internationally-based media, issue press releases and disseminate other materials for communities such as a [Ghana brochure](#) and a [Malawi brochure](#) about the pilots.



**April:** [SAGE](#) receives an update on the MVIP and endorses the proposed framework for policy decision on use of the RTS,S/AS01 vaccine.



**April:** [MPAC](#) receives an update on the MVIP and endorses the proposed framework for policy decision on use of the RTS,S/AS01 vaccine.



**April 23:** RTS,S/AS01 vaccine implementation starts in Malawi. There was no formal launch event as advised by the National Task Force, but key stakeholders and media witnessed and documented the vaccination of the first child at Mitundu Rural Hospital in Lilongwe. The initiation of the Malawi pilot, its purpose and the expected benefits to communities was declared by the MOH in national press and also in local feature stories about family experiences during first vaccination clinics. The pilot launch – of the world’s first malaria vaccine in childhood vaccination – was one of the top health news stories in 2019 and of high interest in Africa and globally.



**May 1:** RTS,S/AS01 vaccine implementation starts in Ghana. The themed launch event – “Malaria vaccine for additional protection” - on 30 April 2019 in Cape Coast was opened by remarks from the Hon. Regional Minister, the CEO of the Food and Drugs Authority (FDA), the Director-General of the Ghana Health Services, the Paramount Chief of Cape Coast, the Minister of Health, the Director of Health Services, and representatives from the Local Council of Churches and the Moslem Council. The community launch event drew hundreds of observers, including local community health volunteers, caregivers and children, traditional leaders, health partners and local and national media.





**May:** MVIP symposium at the Malaria Vaccines for the World scientific conference, hosted by the University of Oxford, UK, provided an overview of the pilot programme and included presentations by WHO, the Malawi EPI manager, and African-based lead evaluators.



**May:** PAG quarterly progress review meeting.



**May:** DSMB quarterly progress review meeting.



**June:** Kenya MOH convenes communications trainings at national and county levels, which include participants from the NMCP, EPI, NRA, pilot evaluation consortia, and other MOH units and in-country stakeholders. The training generated a pool of trainers to work with county, sub-county and facility-level teams to ensure correct messaging and community engagement regarding the MVIP – particularly aimed at engagement with community leaders and groups, traditional leaders, media, community health volunteers (in regular contact with caregivers) and others.



**June:** WHO hosts a pre-Gavi Board meeting event to update Board members and their delegations on the status of the MVIP.



**August:** An implementation agreement is signed between MOH of the Republic of Kenya and the WHO. The agreement establishes the terms under which the parties will cooperate in, and contribute to, the malaria vaccine introduction and the pilot evaluations.



**August:** MPAC issued a strong [statement of support](#) for RTS,S/AS01 and the MVIP.



**September:** Kenya MOH convenes a stakeholders' meeting to bring together malaria and immunization partners as well as county teams for a technical discussion on the malaria vaccine launch.



**September:** PAG quarterly progress review meeting.



**September:** DSMB quarterly progress review meeting.



**September 13:** RTS,S/AS01 vaccine implementation starts in Kenya with a major launch event in Homa Bay, western Kenya. The launch was led by the (then) Cabinet Secretary for Health, Sicily Kariuki, and other national and local health and elected officials, and attended by hundreds of community members, caregivers and children, traditional and local leaders and media. Subsequent county-level launch events for were held the other participating sub-counties.




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For more information, visit the WHO [MVIP website](#)

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