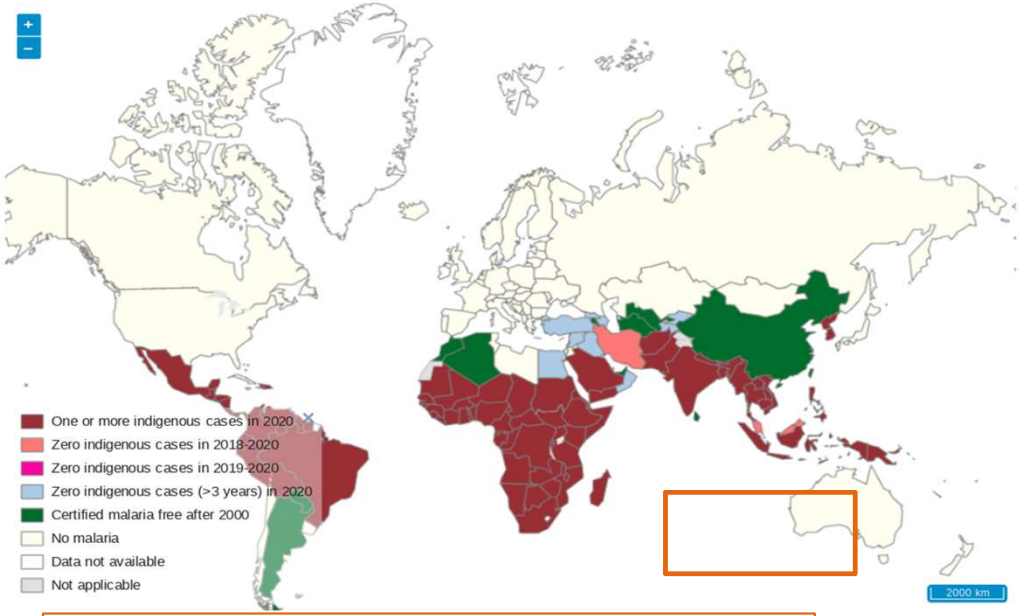
Update On Malaria Vaccine : R21/Matrix-M (R21)

Apt. Puspagita Wardhani
Manajemen Produk Nasional
PT Bio Farma (Persero)

Malaria Burden

WHO, 2023



Indigenous case kasus yang bukan dari wilayah lain

Worldwide, 2021

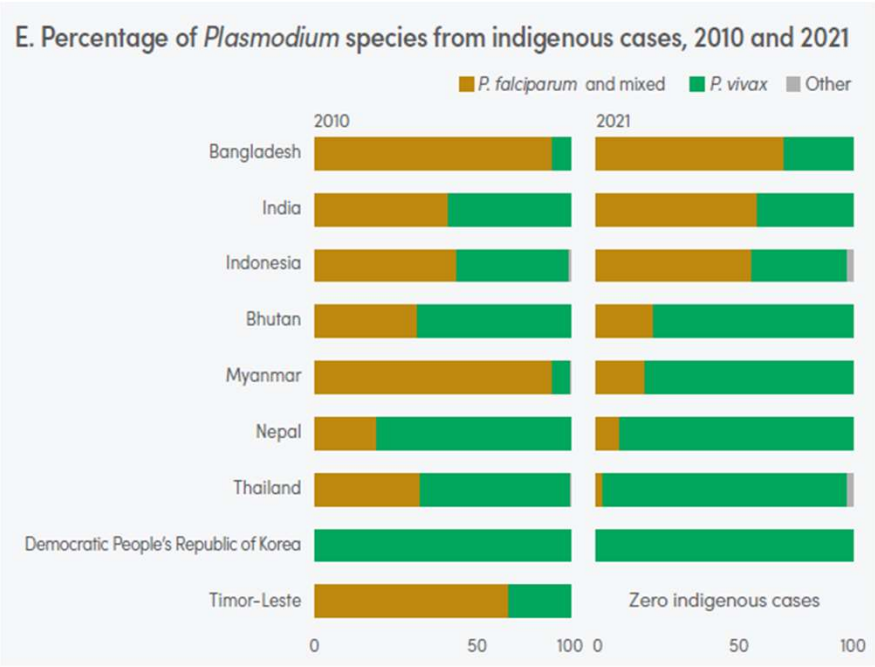
247 million cases
619.000 deaths

Indonesia, 2021

304.607 cases
48 deaths

Causative plasmodium in Indonesia:
P. falciparum and mixed (55%), P. vivax (44%), Other (1%)

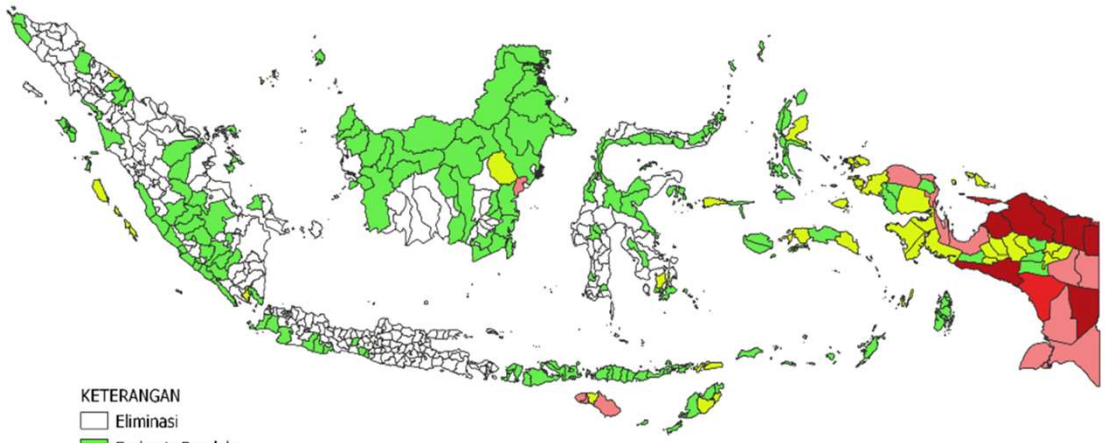
https://www.who.int/teams/global-malaria-programme/reports/world-malaria-report-2023



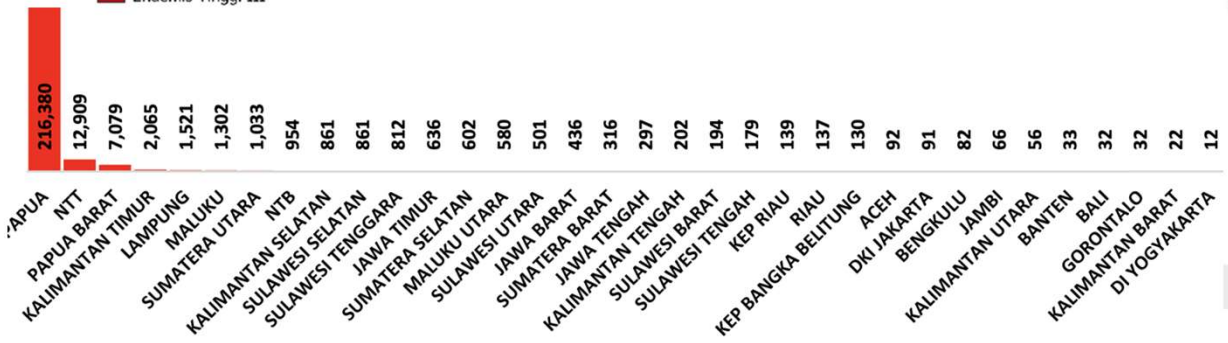
Global
*Plasmodium falciparum (the **deadliest malaria parasite** and the most prevalent on the African continent*
Indonesia
*P.falciparum, P. vivax (the **dominant malaria parasite** in most countries outside of sub-Saharan Africa) and P. knowlesi*

Malaria in Indonesia

Kemenkes, 2019

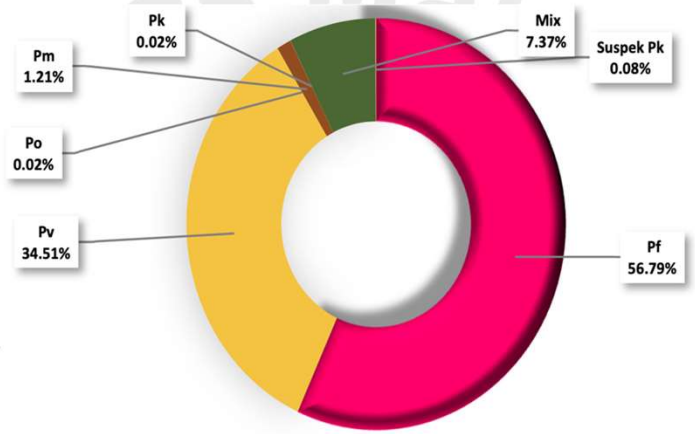


86% kasus malaria di Indonesia→ Papua



Tabel 1. Jumlah Kab/Kota dan Penduduk Berdasarkan Endemisitas Tahun 2019

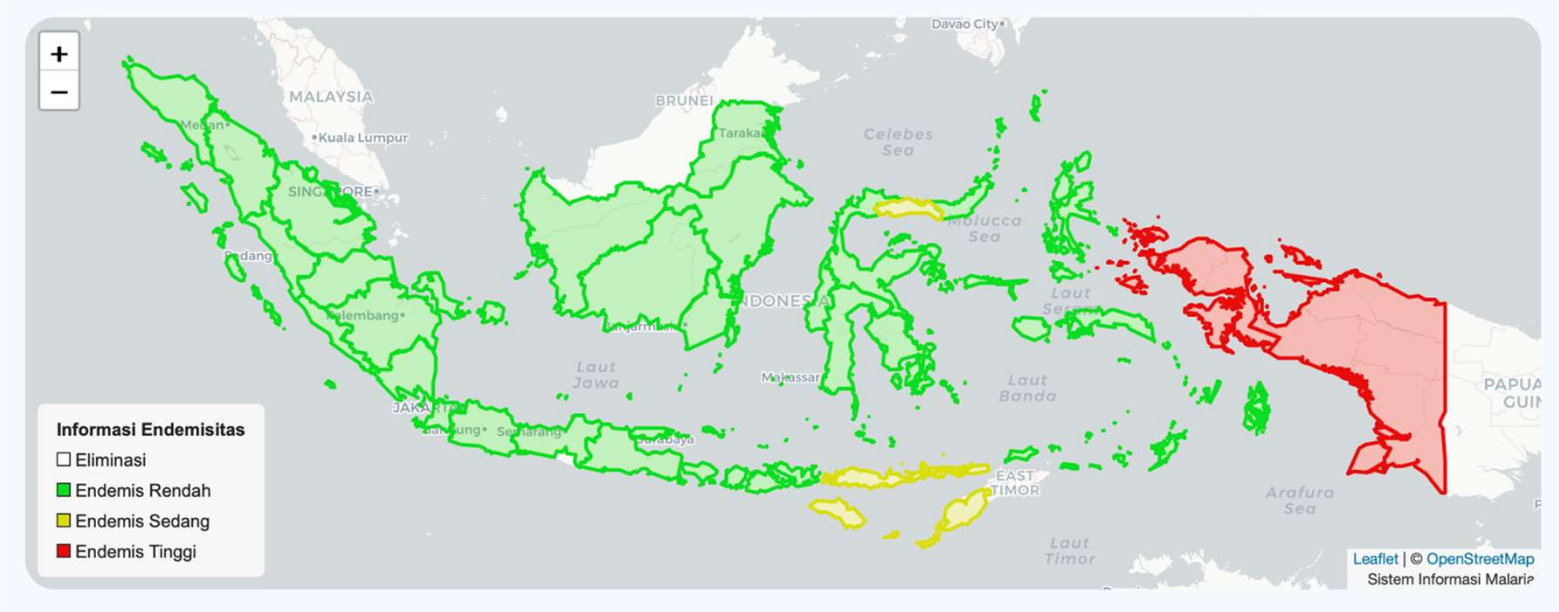
No	Endemisitas	Penduduk 2019		Kab/Kota 2019	
		#	%	#	%
1	Eliminasi (Bebas Malaria)	208,160,937	77.7%	300	58%
2	Endemis Rendah (API < 1)	52,474,602	19.6%	160	31%
3	Endemis Sedang (API 1-5)	4,478,911	1.7%	31	6%
4	Endemis Tinggi (API > 5)	2,960,115	1.1%	23	4%
	Total	**268,074,565**	**100%**	**514**	**100%**



Gambar 15. Persentasi Kasus Malaria Berdasarkan Jenis Parasit

Malaria in Indonesia

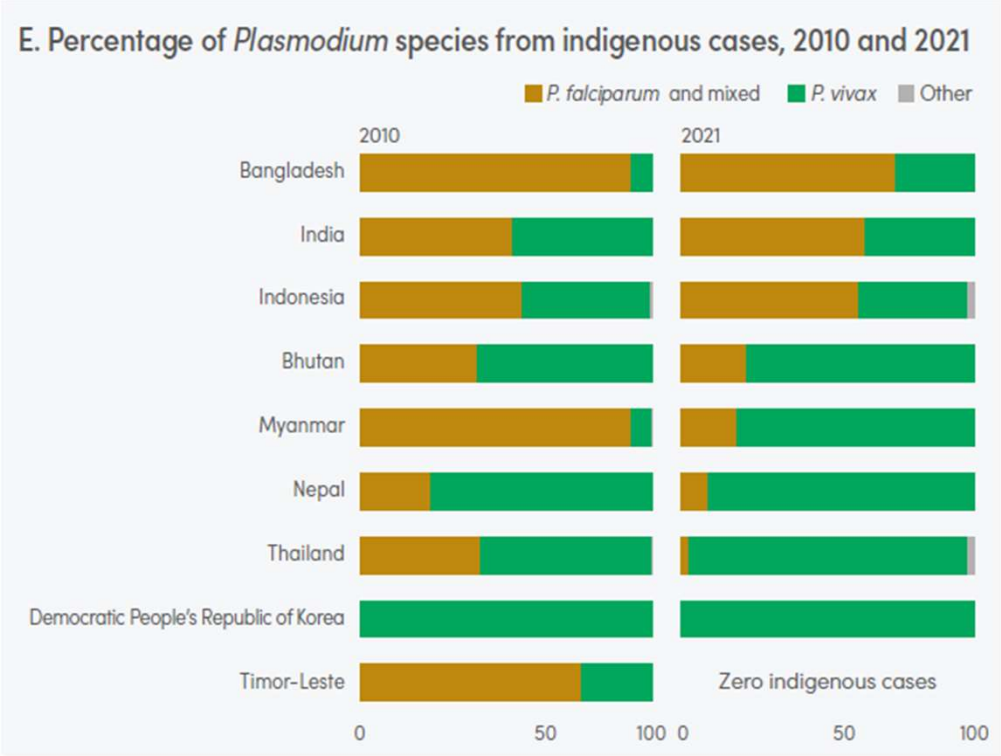
Kemenkes, 2022



Indonesia adalah salah satu negara endemis Malaria dengan jumlah kasus **443.530, sebanyak 89% kasus positif malaria dilaporkan dari Provinsi Papua** (Sumber: Situasi Malaria Terkini Indonesia 2022).

Epidemiologi

Plasmodium species in WHO South-East Asia region



Global

Plasmodium falciparum (the deadliest malaria parasite and the most prevalent on the African continent

Indonesia

P.falciparum, P. vivax (the dominant malaria parasite in most countries outside of sub-Saharan Africa) and P. knowlesi

Causative plasmodium in Indonesia:

P. falciparum and mixed (55%), *P. vivax* (44%), Other (1%)

WHO Strategies and Recommendations

Strategies:

- Reducing malaria case incidence by at least 90% by 2030
- Reducing malaria mortality rates by at least 90% by 2030
- Eliminating malaria in at least 35 countries by 2030
- Preventing a resurgence of malaria in all countries that are malaria-free.

WHO recommendation (June 2022):

- Case management
- Vector control
- **Vaccines**
- Malaria chemoprevention (SMC)
- Mass drug administration (MDA)
- Elimination

October 2021

WHO recommended the world's first malaria vaccine (RTS,S/AS01) be used for the prevention of *P. falciparum* malaria in children living in regions with moderate to high transmission

Pilot implementation programme 2017-2023 in Ghana, Kenya & Malawi

Roll-out

Progress

- https://www.cdc.gov/malaria/malaria_worldwide/impact.html
- World Malaria Report, WHO 2022

Malaria vaccine implementation programme

As of October 2023, **WHO recommends the programmatic use of malaria vaccines for the prevention of *P. falciparum* malaria in children living in malaria endemic areas, prioritizing areas of moderate and high transmission.** This applies to both RTS,S/AS01 and R21/Matrix-M vaccines.

- The malaria vaccine should be provided in a schedule of 4 doses in children from around 5 months of age. (Vaccination programmes may choose to give the first dose at a later or slightly earlier age based on operational considerations.)
- A 5th dose, given one year after dose 4, may be considered in areas where there is a significant malaria risk remaining in children a year after receiving dose 4.
- In areas with highly seasonal malaria or areas with perennial malaria transmission with seasonal peaks, countries may consider providing the vaccine using an age-based administration, seasonal administration, or a hybrid of these approaches.
- Countries should prioritize vaccination in areas of moderate and high transmission, but may also consider providing the vaccine in low transmission settings. Decisions on expanding to low transmission settings should be considered at a country level, based on the overall malaria control strategy, cost-effectiveness, affordability, and programmatic considerations.
- Vaccine introduction should be considered in the context of comprehensive national malaria control plans.

- Vaksinasi malaria dapat diberikan sebanyak 4 dosis mulai usia 5 bulan
- Pemberian vaksinasi diutamakan untuk daerah endemik
- Program vaksinasi malaria perlu dipertimbangkan untuk mendukung program elimisasi nasional malaria

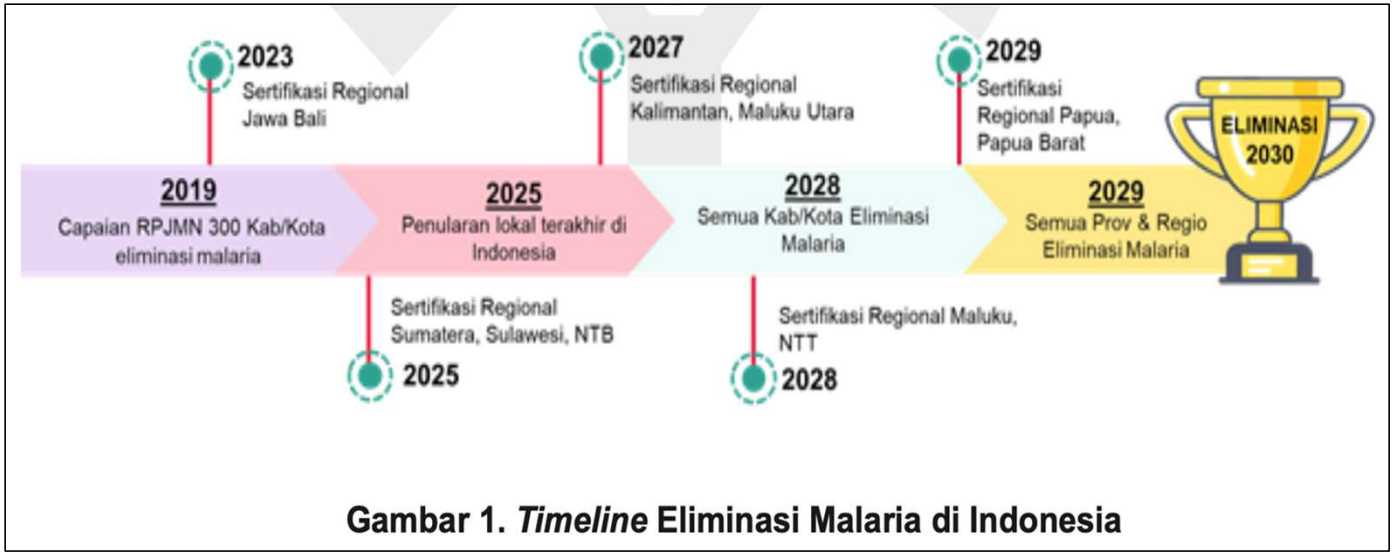
Malaria vaccine: https://www.who.int/teams/immunization-vaccines-and-biologicals/diseases/malaria

Indonesia Malaria Program

Elimination in 2030

Kementerian Kesehatan akan mengajukan penilaian sertifikasi eliminasi malaria di Indonesia kepada Badan Kesehatan Dunia (*World Health Organization* -WHO) pada Tahun 2030.

Rencana Aksi Percepatan Eliminasi Malaria Tahun 2020-2024



Gambar 1. *Timeline* Eliminasi Malaria di Indonesia

Indonesia dibagi menjadi 5 regional yaitu Regional Jawa dan Bali, Regional Sumatera, NTB dan Sulawesi, Regional Kalimantan dan Maluku Utara, Regional NTT dan Maluku serta Regional Papua Barat dan Papua.

Biofarma Presentation

Malaria Vaccines Roll Out

RTS,S/AS01 (*Mosquirix*)

- Developed by GSK
- Recommended by WHO for the prevention of P. falciparum malaria in children living in regions with moderate to high transmission (as defined by WHO) in October 2021
- **WHO-PQ approval in July 2022**
  - Indikasi Usia **6 minggu hingga 17 bulan**

R21/Matrix-M (R21)

- Developed by the University of Oxford and manufactured and scaled up by the Serum Institute of India (SII)
- **Recommended by WHO October 2023**
- **WHO-PQ approval in December 2023**
- Ghana is the first country to approve
- Targets the plasmodium 'sporozoite', which is the first form of the malaria parasite entering the human body.
- **On Process to be registered in Indonesia by Bio Farma**

Gavi, the Vaccine Alliance (Gavi) and WHO are supporting the rollout of the malaria vaccine. Following the WHO recommendation, in December 2021, the Gavi board approved an initial investment of almost US$ 160 million (2022–2025) to support broader rollout of the malaria vaccine in Gavi-eligible countries

- https://www.cdc.gov/malaria/malaria_worldwide/impact.html
- https://www.who.int/news-room/questions-and-answers/item/q-a-on-rts-s-malaria-vaccine#:~:text=The%20RTS%2CS%20malaria%20vaccine%20is%20the%20result%20of%2030,network%20of%20African%20research%20centres

R21/Matrix-M

Malaria Vaccine

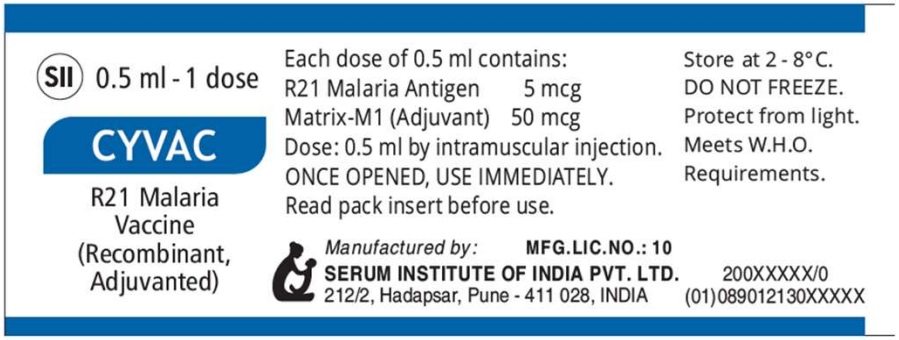
Komposisi :
Tiap 0.5 mL mengandung:
R21 Malaria Antigen 5 mcg
Matrix-M1 (Adjuvant) 50 mcg

Indikasi :
Imunisasi Aktif terhadap P. falciparum pada anak usia 5 bulan - 36 bulan

Dosis:
3 dosis @0.5 mL, interval 4 minggu
Dosis ke 4 diberikan 12 bulan setelah dosis ketiga

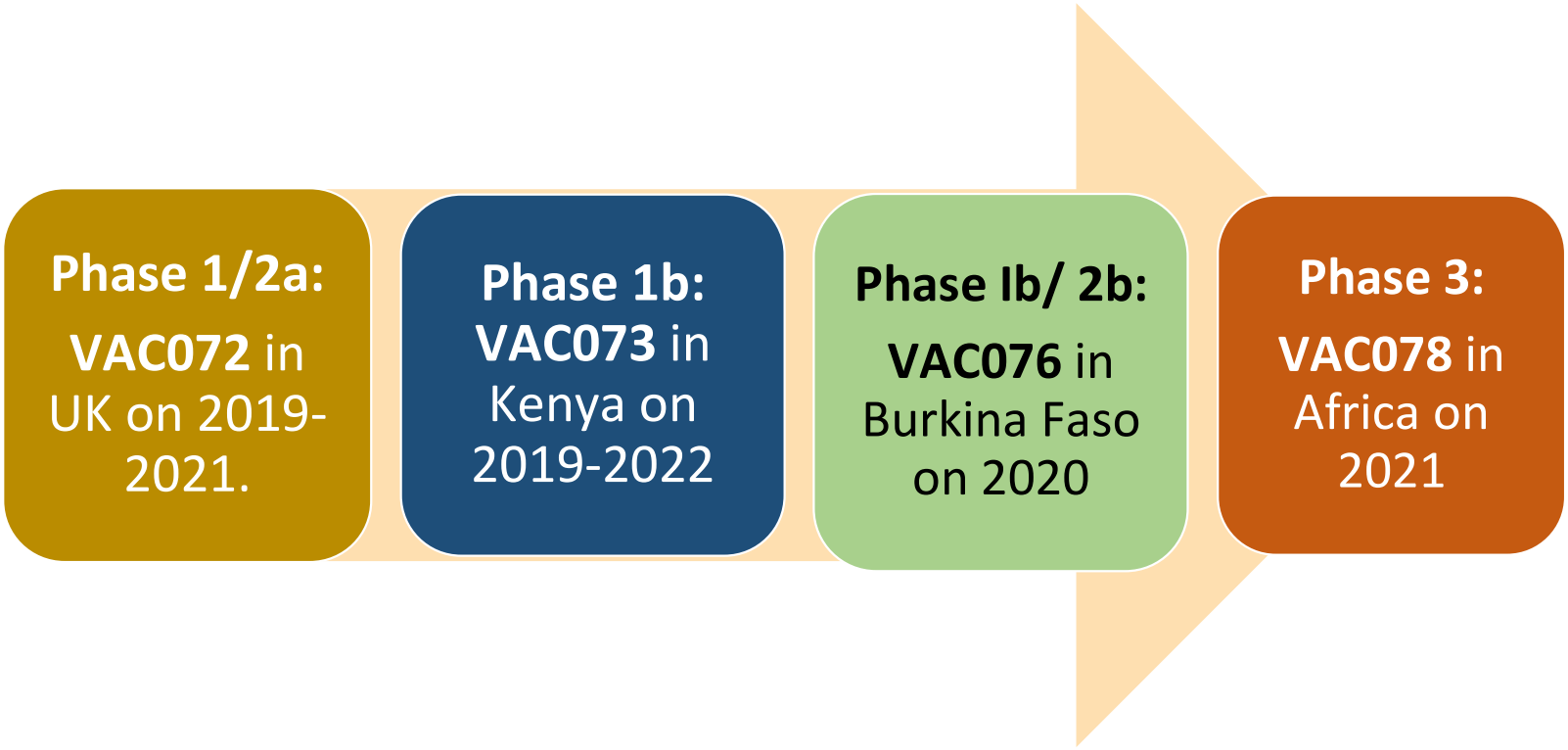
Penyimpanan dan Shelf Life:
2- 8 C, 24 bulan
Open vial policy : 6 jam

Kemasan:
Dus, 50 vial @ 1 dosis
Dus, 50 vial @ 2 dosis



Clinical Trial

R21 Malaria VACCINE In Children



Clinical Trial

R21 Malaria VACCINE In Children

Study Identification	Phase	Location	No. of partipants	Objectives	Results
VAC 072	I	England	76 Adults	Safey, Immonogenicty and efficacy (R21/Matrix-M), administred in different dose schedules in Malaria-naïve adults	No Safety concerns.
VAC 073[a]	Ib	Kenya	91 (Adults, 1-5 years old, 5-12 month olds)	Safety and Immonogenicty	Safety and Immonogenicty demonstrated
VAC 076[b]	Ib/2b	Burkina Faso	450 (5-17 months olds)	Safety, Immonogenicty and Efficacy	76 %, 77 % and 73 % efficacy over one, two and three years of follow-up resepctivly. Well tolarated safety profile
VAC 078[c]	III	Mali, Burkina Faso, Kenya, Tanzania	4878 (5-36 months old)	Safety and Effacy	Efficacy against clinical material (time to first episode) was 76 % (seasonal sites) and 70 % (standard sites). Well-tolerated safety profile.

Clinical Trial Phase III - R21 Malaria Vacine

Efficacy and Immunogenicity in Children

Study	VAC078
Design Study	A Phase III randomised controlled multi-center trial in Africa on **2021**
Schedule	4878 participants of children **aged 5-36 months old** **Group Malaria vaccine: 3252 participants** Three doses of vaccine were administered four-weeks apart followed by a planned booster dose of vaccine 12-months after the third dose of vaccine **Group Rabies vaccine: 1626 participants**
Result	Overall, 13 AESIs; 10 events of febrile convulsion, 2 events of meningitis bacterial and 1 event of cerebral malaria. **Efficacy:** ● Efficacy against clinical malaria at the seasonal sites was 76% (95% CI 72-79%) and 70% (61 – 78) at the standard sites. ● Efficacy against severe malaria across all sites was 74% (12 – 93, P = 0.03) in a time to event analysis.

Clinical Trial Phase III - R21 Malaria Vacine

Efficacy and Immunogenicity in Adult

Study	PHASE III IN THAILAND
Design Study	A Phase a phase 2, open-label computer-randomised, controlled safety in Thailand on 2023
Schedule	120 adults aged 18-55 years • **Group 1 (n = 50)**: 3 doses of R21/Matrix-M™ for three consecutive months concurrently with 3-days of daily dihydroartemisininpiperaquine and a single low dose of primaquine (SLDPQ). • **Group 2 (n = 50)**: 3-daily doses of R21/Matrix-M™ alone for three consecutive months. • **Group 3 (n = 20)**: 3-days of dihydroartemisinin-piperaquine and SLDPQ for three consecutive months.

Clinical Trial Phase III - R21 Malaria Vacine

Efficacy and Immunogenicity in Adult

Study	PHASE III IN THAILAND
Result	**Safety :** 1 kejadian CAP (community-acquired pneumonia)pada group 1 1 kejadian neuromyelitis optica relapse pada group 3 **Immunogenicity:** ● The geometric mean IgG concentrations were similar when the vaccines were administered with or without antimalarial drugs. ● No difference in immunogenicity was observed between male and female participants.
Conclusion	R21/Matrix-M™ combined with and without antimalarial drugs, was safe, well-tolerated and immunogenic.

Malaria Vaccine Product Comparison

Malaria VACCINE COMPARISON

	RTS,S/AS01 vaccine-MOSQUIRIX (GSK)	R21/Matrix-M vaccine-SII
SPONSOR	**GSK (GlaxoSmithKline Biologicals S.A.)**	**SII (Serum Institute India)**
Indikasi Usia	Usia **6 minggu hingga 17 bulan**	**Usia 5 bulan hingga 36 bulan**
Komposisi	Setelah dilarutkan, tiap 0.5 ml mengandung **25 mcg** of RTS,S[1,2] (adjuvant : AS01E3[3])	Tiap 0.5 mL mengandung : R21MalariaAntigen **5mcg** Matrix-M1 (Adjuvant) **50 mcg**
Indikasi	Imunisasi aktif terhadap ***Plasmodium falciparum*** dan hepatitis B pada anak usia **6 minggu hingga 17 bulan**	Imunisasi aktif terhadap ***Plasmodium falciparum*** pada anak usia **5 bulan hingga 36 bulan**
Kontraindikasi	Hipersensitifitas terhadap Mosquirix dosis sebelumnya atau hepatitis B vaccines.	Hipersensitivitas terhadap dosis R21 Malaria Vaccine (Recombinant, Adjuvanted) sebelumnya
Bentuk Sediaan	serbuk dan suspensi untuk injeksi	larutan injeksi
Posologi	• **3 dosis @0.5 mL, interval 4 minggu** • Dosis ke 4 diberikan **18 bulan setelah dosis ketiga** *WHO recommends that the first dose of vaccine be administered from 5 months of age.*	• **3 dosis @0.5 mL, interval 4 mniggu** • Dosis ke 4 direkomendasikan untuk diberikan **12 bulan setelah dosis ketiga**
Rute Pemberian	IM	IM

Malaria VACCINE COMPARISON

CRITERIA	RTS,S/AS01 vaccine-MOSQUIRIX (GSK)	R21/Matrix-M vaccine-SII
EFFICACY	• Vaccine efficacy in the **first 6 months following completion of the initial 3 doses was 68%;** efficacy waned over time. Six months after the fourth dose, vaccine efficacy was 43%; • Over the entire **7-year period,** vaccine efficacy against clinical malaria was **24%** (95% CI 16–31, *P*<0.0001) for the 3-dose group and **19%** (95% CI 11–27; *P*<0.0001) for the 4-dose group.	**Efficacy:** • Efficacy against clinical malaria at the seasonal sites was 76% (95% CI 72-79%) and 70% (61 – 78) at the standard sites. • Efficacy against all clinical malaria episodes was similar: 75% (71 - 78) at seasonal sites and 72% (63-79) at standard sites. • Efficacy against severe malaria across all sites was 74% (12 – 93, P = 0.03) in a time to event analysis.
SAFETY	The most commonly reported adverse reactions were **fever (27%), irritability (14%) and injection site reactions such as pain (16%) and swelling (7%).**	Overall, 13 AESIs; 1**0 events of febrile convulsion, 2 events of meningitis bacterial and 1 event of cerebral malaria.**
Co-Administration	Mosquirix can be given concomitantly with any of the following monovalent or combination vaccines including diphtheria (D), tetanus (T), whole cell pertussis (Pw), acellular pertussis (Pa), **hepatitis B (HepB),** *Haemophilus influenzae* type b (Hib), oral polio (OPV), measles, rubella, yellow fever, rotavirus and pneumococcal conjugate vaccines (PCV)	The co-administration of R21 Malaria Vaccine (Recombinant, Adjuvanted) with other vaccines is not currently recommended as **no clinical data are yet available.**

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