

Gavi Vaccine Investment Strategy (VIS) 2024

Marta Tufet

Head, Policy, Gavi

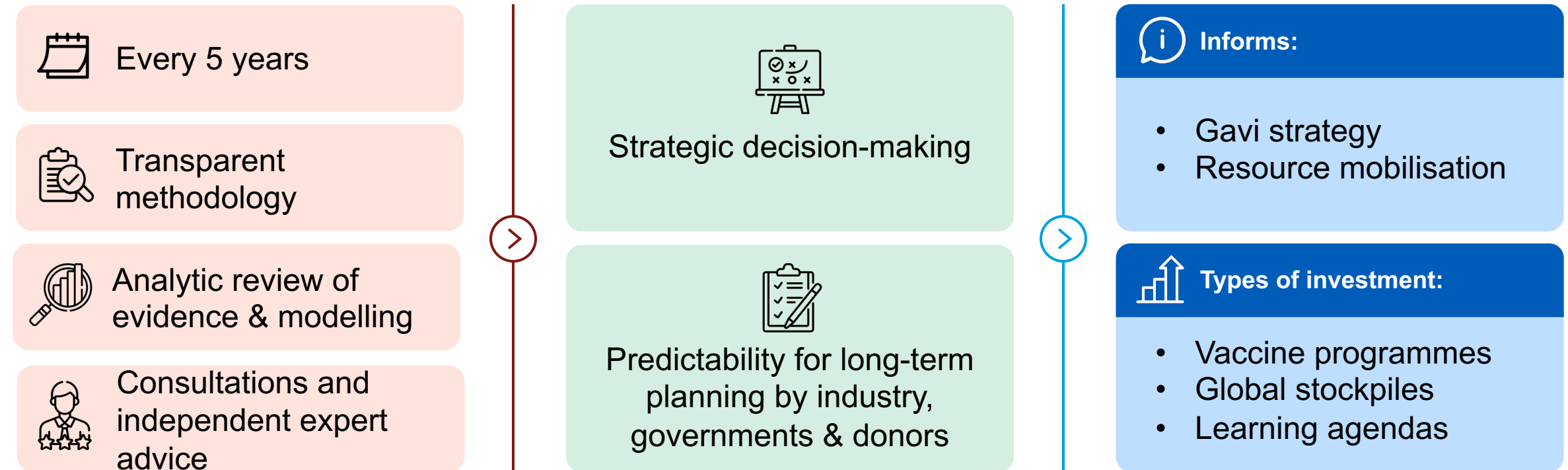
December 2023

gavi.org



Vaccine Investment Strategy informs Gavi 6.0 (2026–2030)

Evidence-based approach to identify immunisation investments for future strategic cycle(s), while sending valuable advance signals to vaccine developers and suppliers

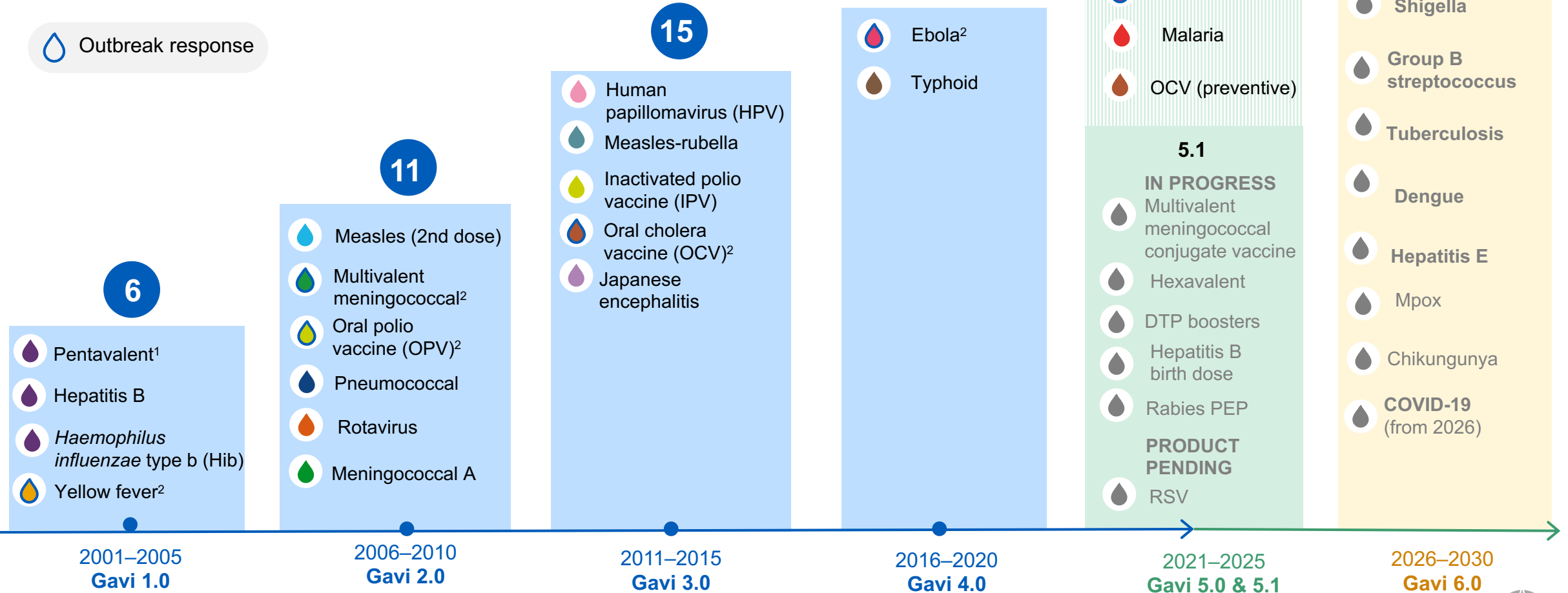


← In response to public health threat or a research and development (R&D) milestone for a priority pathogen, diseases of epidemic/pandemic potential can be evaluated in real time, outside five-year cycle, through VIS epidemics framework. →

Gavi's portfolio: significant growth over time

Gavi now provides vaccines against **19 infectious diseases** through **46 product presentations**

 Outbreak response



¹ Diphtheria, tetanus, pertussis (DTP) boosters, hepatitis B, *Haemophilus influenzae* type b (Hib),

² Emergency stockpiles

³ Final shortlist to be approved by Gavi Board in December 2023

Analytical and consultative process with 3 decisions

Process for defining the long list of pipeline vaccines for Gavi VIS

33 Pathogens evaluated

Products expected to be licensed by 2030: endemic diseases relevant to

8 pathogens in VIS 2024 longlist based on WHO landscape analysis

Scope and inclusion criteria

- ✓ Vaccines and immunisation products of relevance to Gavi-eligible countries
- ✓ Licensed but not in Gavi's portfolio
- ✓ With expected impact by 2030

VIS 2024 longlist

- Mpox
- COVID-19

VIS 2024 Evaluation framework for vaccines for endemic disease

Ranking Criteria		Modulating Criteria	
Criteria	Indicators	Criteria	Indicators
Health impact	Total future deaths averted 2025-2040, and per 100,000 vaccinated	Global health security impact	Epidemic potential of disease
	Total future DALYs averted 2025-2040, and per 100,000 vaccinated		Impact on AMR
Value for money	Vaccine Price	Climate change risks and mitigation	
Equity and social protection impact	Vaccine Price		
Gavi comparative advantage	Disproportionate groups		
Economic impact	Vaccination gender-equality associated		
	Direct medical cost		
	Indirect cost		

Degnue Scorecard: Ranking criteria

Vaccination strategy presented: e.g. vaccination of 9 year olds in routine programme

VIS criteria	Indicator	Results	Evaluation ¹
Health impact	Total deaths averted	~300-720K future deaths averted, 2025-2040	
	Deaths averted per 100K vaccinated	~5,790-6,930 future deaths averted, 2025-2040, per 100K vaccinated population	
Value for money	Procurement cost averted	~5,790-6,930 future DALYs averted, 2025 - 2040, per 100K vaccinated population	
	Impact on value		
Equity & social protection impact	Addresses gender		
Gavi comparative advantage	Vaccine market		
Economic impact	Direct medical cost		
	Indirect cost		

Board predominantly favors health impact and value for money as the key indicators

Average weighting used for shortlisting

Median and ranges applied as sensitivity analysis

Shortlist options for PPC/Board consideration

	Option A	Option B	Option C	VIS assessment and SC guidance
Vaccine A	✓	✗	✓	• Benefits and special considerations
Vaccine B	✓			
Vaccine C	✓			
Vaccine D	✓			
Vaccine E	✓			
Vaccine F	✓			

TB Investment Options

Investment Options

- Min: Stockpile size 100k / year**
 - Based on minimum demand calculated from modelling and based on current Proof-of-Concept approach for 100k doses / year (after experience with need in Bentiu camp), multiplied by average # of outbreaks per year observed in last 10y (~5)
 - ~ \$485K per year
- Base: Stockpile size 220k / year**
 - Based on a maximum of ~44k doses total demand per outbreak from primary vaccination strategy (vaccination of >16y old and pregnant people) * average # of outbreaks per year (~5)
 - ~ \$38M per year

Learning Agenda

- Burden of disease estimation based on natural history approach
- Proof-of-Concept of stockpile sought by Gates Foundation, awaiting ICG review

1. WHO vaccine landscape analysis

2. VIS candidate longlist

3. Evaluation framework

4. Vaccine analyses

5. Prioritisation methodology

6. Vaccine shortlist

7. Refined analyses

8. Investment Cases

Extensive consultations

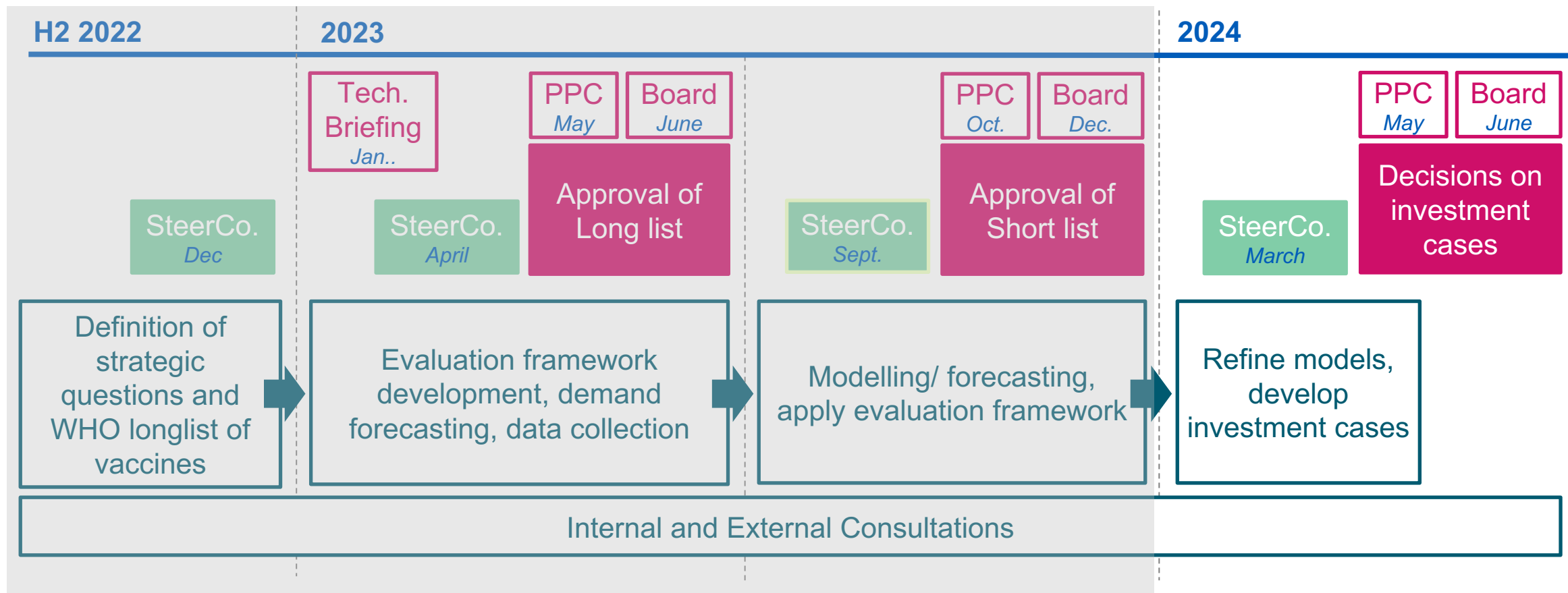
Longlist decision
June 2023

Shortlist decision
Dec 2023

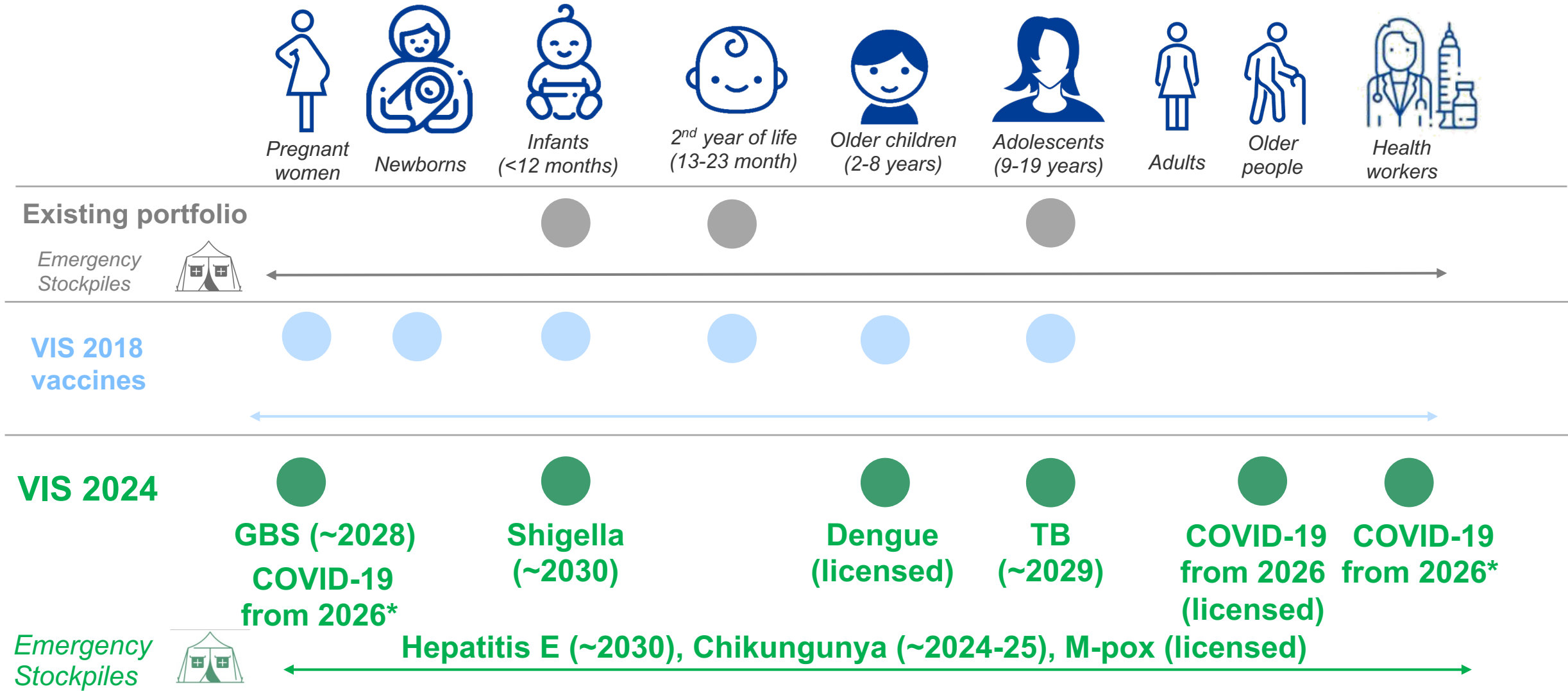
Investment decision
June 2024

Timelines for VIS 2024

The VIS 2024 includes three decision points which will take place from now until June 2024

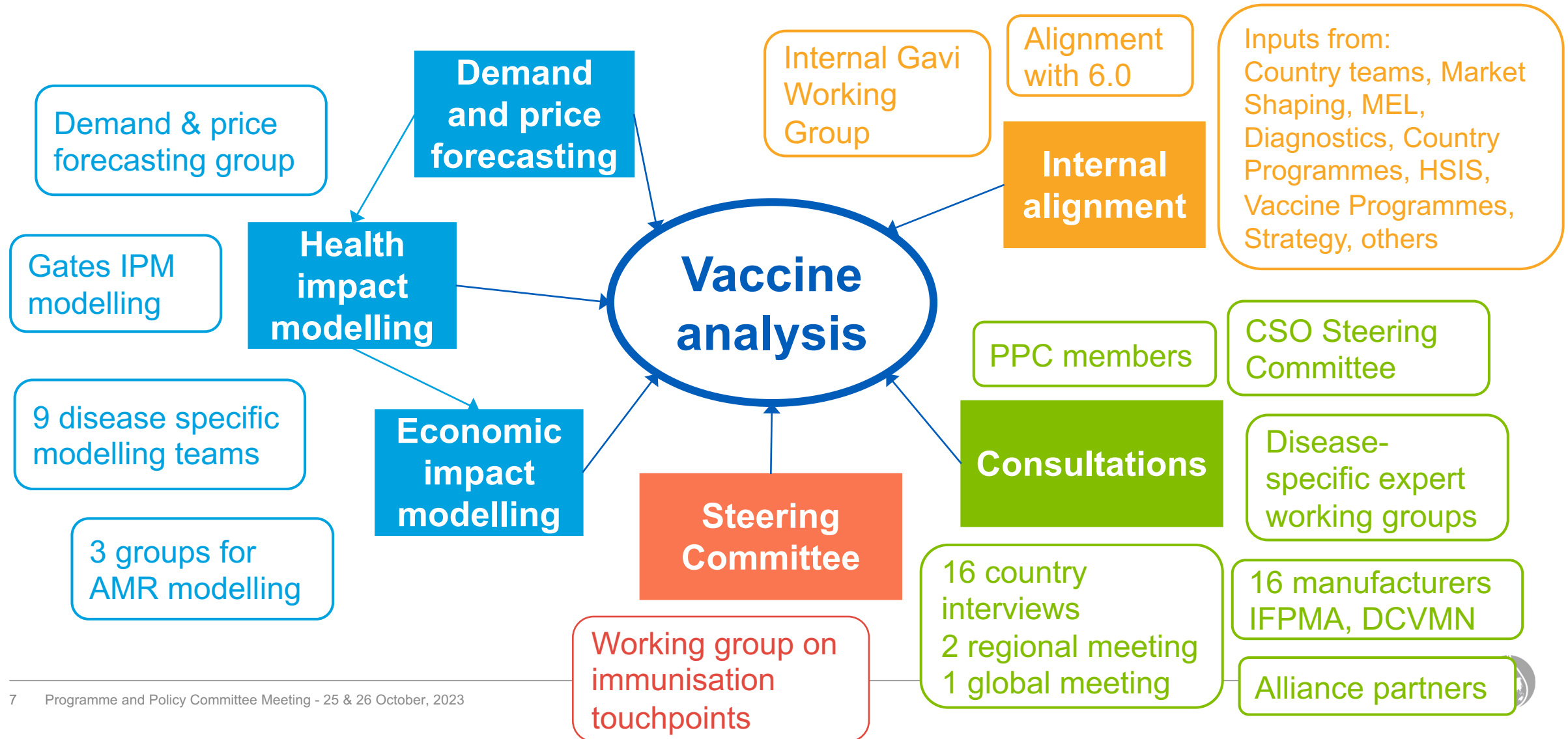


VIS 2024 longlisted vaccines



*Pending further review of WHO COVID-19 Vaccine Roadmap

Vaccine analyses have been possible thanks to collaboration and contributions from many stakeholders



VIS 2024 Evaluation framework for vaccines for endemic disease

Ranking Criteria

Criteria	Indicators
Health impact	Total future deaths averted 2026-2040, and per 100,000 vaccinated
	Total future DALYs averted 2026-2040, and per 100,000 vaccinated
Value for money	Vaccine Procurement cost per death averted
	Vaccine Procurement cost per DALY averted
Equity and social protection impact	Disproportionate impact of disease on vulnerable groups
	Vaccination contributes to addressing underlying gender-related barriers faced by caregivers, adolescents and health workers and/or gender associated differences in immunisation coverage
Gavi comparative advantage	Degree of vaccine market challenges
	Gavi role in addressing challenges
Economic impact	Direct medical cost averted
	Indirect cost averted

Modulating Criteria

Criteria	Indicators
Modulate up	
Global health security impact	Epidemic potential of disease
	Impact on AMR
	Climate change risks and mitigation
Other impact	Total U5 deaths averted 2026-2040, and per 100,000 vaccinated
Contribution to global agenda	Fit with global development (SDGs), immunization (IA2030) agendas and other relevant global targets
Broader health system benefits	No specific indicator – evaluated case-by-case
Contextual	
Implementation feasibility	Ease of supply chain integration
	Need for healthcare worker training/ behaviour change
	Requirements of vaccination timepoint
	Need for demand promotion (e.g., acceptability, understanding of disease burden)
	Availability of epidemiological data to inform programmes
Alternate interventions	Diagnostics availability/ needs
	Optimal use of current and future alternative interventions (prevention and treatment)



Framework for evaluating epidemic-prone diseases (1/2)

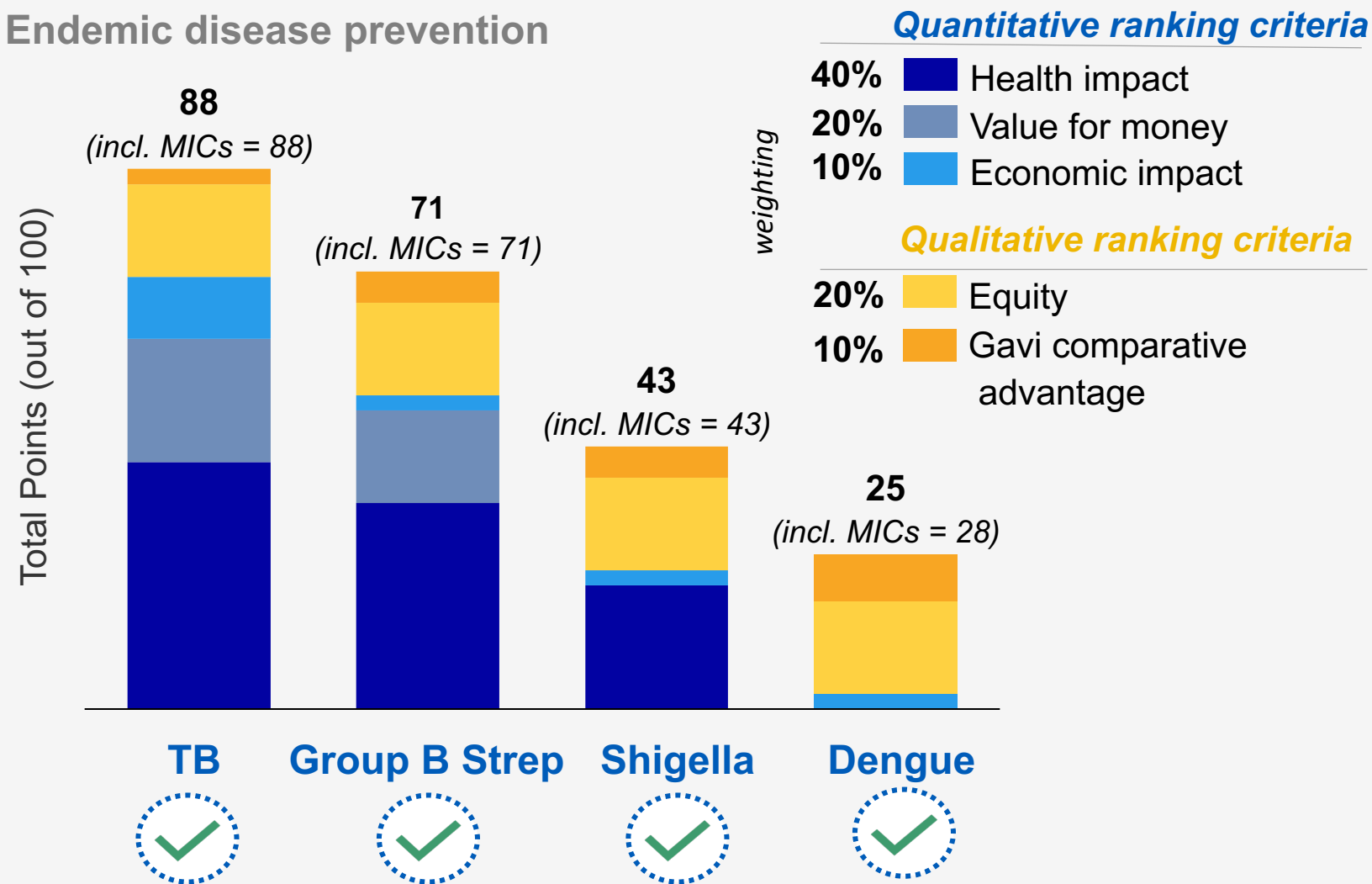
	Criteria	Indicators
Disease Risk & Burden	Epidemiology and risk	Frequency, geography and magnitude of outbreaks
		Global risk of outbreaks and epidemic/endemic potential
		Strain stability/adaptability
	Disease burden	Transmission routes, incubation period and disease manifestation
		Health impact (outbreaks, CFR, DALYs, YLLs)
	Economic and social burden	Direct and indirect costs of illness/outbreaks
		Disproportionate burden to women and vulnerable groups
Vaccine Impact and Feasibility	Epidemic risk reduction / mitigation	Vaccine impact and indirect effects (suitability to be used as part of outbreak response, herd immunity, cross strain protection)
		Health systems impact
		Efficacy of other available countermeasures
	Equity and social protection impact	Additional benefit to women and vulnerable groups
	Implementation feasibility	Storage requirements and shelf life
		Dosing schedule and cost of delivery
		Disease surveillance and seroprevalence to guide stockpile use
		Acceptability in target population

Framework for evaluating epidemic-prone diseases (2/2)

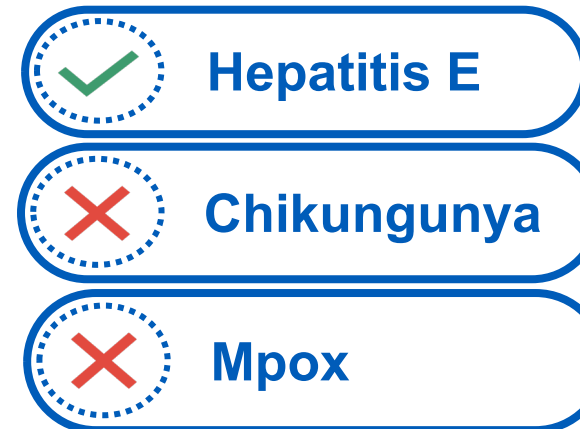
	Criteria	Indicators
Fit for Gavi & Partners	Relevance	Proportion of detected outbreaks in Gavi countries
		Alignment with Gavi's mission and strategy
	Comparative advantage	Role of GAVI market shaping and financing
		Contribution to access and equity
Financial implications	Risk	Alignment with activities of other donor organisations, Alliance partners, R&D, biosecurity
		Cost and consequences of inaction
	Vaccine costs	Major risks and potential mitigation strategies
		Procurement costs
	Stockpile / supply arrangement costs	Holding costs (storage and stockpile maintenance)
		Deployment costs
	Operational cost	Coordination and administration costs
		Incremental in-country operational costs
		Optional learning costs

Proposed vaccine shortlist

Endemic disease prevention



Epidemic disease prevention

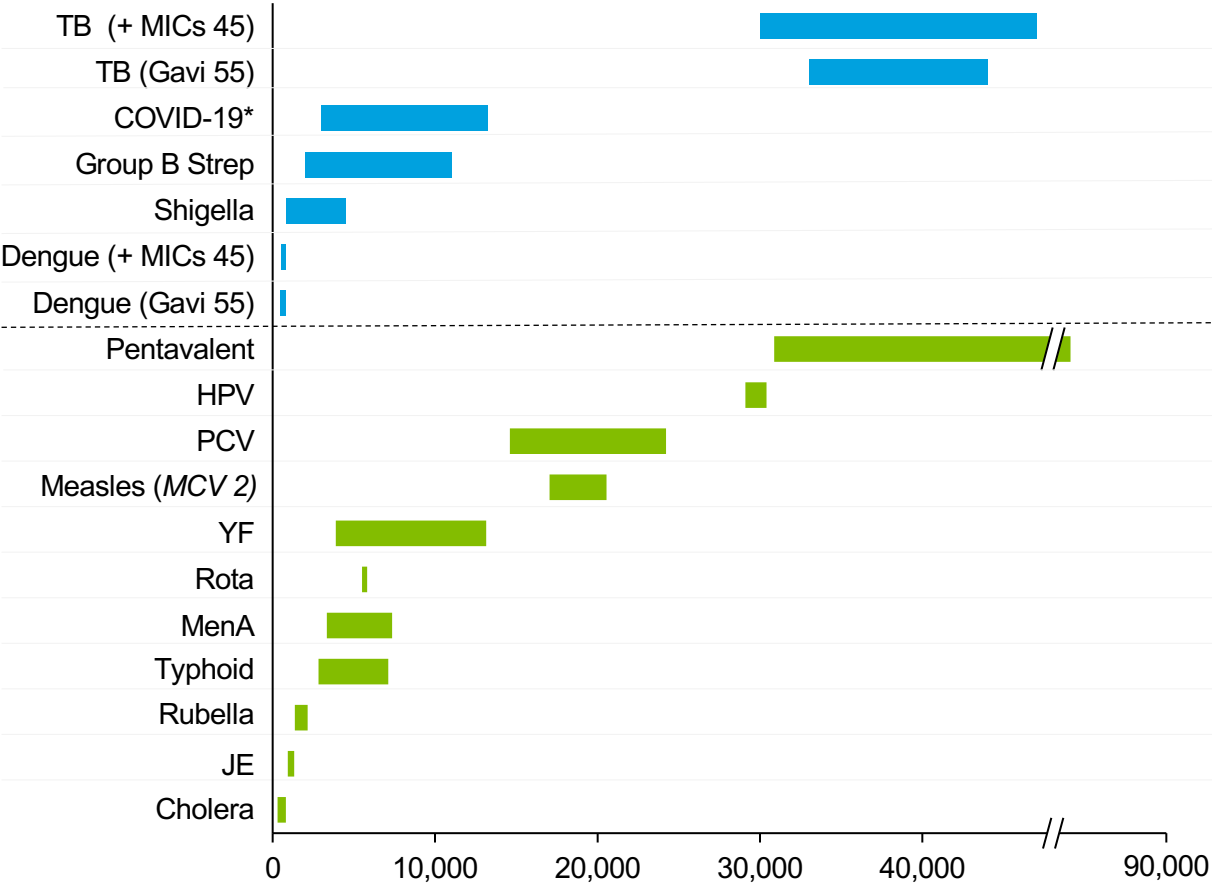


Covid-19

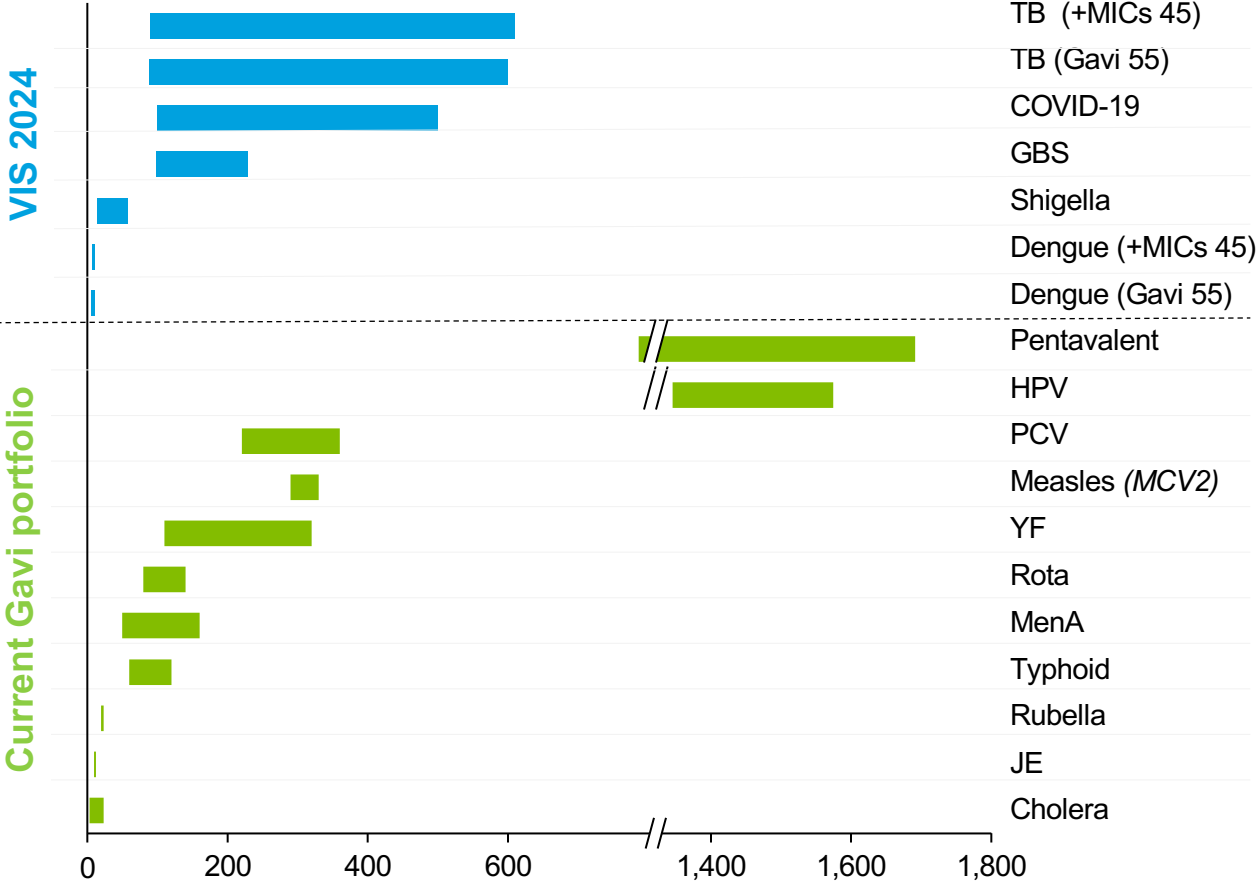


VIS 2024 impact comparable to current portfolio

DALYs averted per 100K vaccinated



Deaths averted per 100K vaccinated



¹²Upper end of the range represents YLL averted in the worst-case epi scenario (new variant with increased transmission and corresponding immune escape and severity comparable to the Delta variant; DALY estimates for COVID-19 are currently not available, in this instance YLL is being used for a comparator as evidence suggests YLLs account for >95% of DALYs for the majority of vaccine preventable diseases. Vaccine impact for current Gavi portfolio vaccines is based on Gavi operational forecasting version 20 (2022-2030). Vaccine impact for VIS candidate vaccines (2026-2040), COVID-19 (2026-2023). Source: External modellers, Gavi portfolio data

Shigella assessment

Shigella Vaccine Scorecard: Ranking criteria

Vaccination strategy presented: vaccination of children at 9 and 12 months in routine programme

VIS criteria	Indicator	Evaluation ¹
Health impact	Total deaths averted	
	Deaths averted per 100K vaccinated	
	DALYs averted per 100K vaccinated	
Value for money	Procurement cost per death averted	
	Procurement cost per DALY averted	
Equity & social protection impact	Impact on vulnerable groups	
	Addresses gender-related barriers	
Gavi comparative advantage	Vaccine market challenges	
	Alliance role in addressing challenges	
Economic impact	Direct medical cost averted	
	Indirect cost averted	

¹⁴ ¹ Evaluation based on comparison with other VIS 2024 candidates. For Health impact and Value for money, evaluation based on deaths per x FVPs averted. Details on evaluation methodology can be found in Methodology appendix

Shigella Vaccine Scorecard: Modulating criteria

Vaccination strategy presented: vaccination of children at 9 and 12 months in routine programme

VIS criteria	Indicator	Results	Evaluation ¹
Global health security impact	Epidemic potential of disease	Rapidly changing epidemiology with evolution of pathogen (>40 serotypes), not IHR notifiable, <i>Shigella</i> associated to outbreaks and risk of cross-border transmission from travellers, Recent (2021) Shigellosis outbreak in the UK sexually-transmitted ²	
	Impact on AMR	Moderate impact of vaccine on AMR, high potential impact on AMR-related healthcare costs	
	Climate change risks and mitigation	Likely impact due to increased likelihood of flooding/ extreme weather, concentrated in poorest and most vulnerable	
Other impact	U5 deaths, per 100K	14 to 40 future deaths averted, 2026-2040, per 100K vaccinated population	
	U5 DALYs, per 100K	~1.7K to 3.7K future DALYs averted, 2026-2040, per 100K vaccinated population	
	Impact on Stunting and wasting	~7K-12K stunting deaths averted, ~0.9K-1.7K stunting DALYs averted, 2026-2040, per 100K vaccinated population, potential additional impact on wasting	n/a
Implementation feasibility	Ease of supply chain integration	Storage at 2-8°C; presentations suitable for LMIC context (MDV, easy handling)	
	Need for HCW behaviour change	n/a – needs as for set up of new routine program	
	Feasibility of vaccination time point	No vaccination time-point at 12 months, while 9 months timepoint already crowded	
	Acceptability in target population	Expected high acceptability as diarrhoea a common syndrome in Gavi countries, however need for education on <i>Shigella</i>	
	Availability of epi data to inform programmes	Etiology-agnostic diarrhoeal disease burden. <i>Shigella</i> attributable data inferred from regional estimates, Rapidly changing epidemiology	
Alternative interventions	Diagnostics availability/ needs	Insufficient data on disease burden and systematic surveillance not in place. Gavi impact would depend on development and scaling of new test (currently reliant on stool culture).	
	Alternative interventions	Supportive care (oral rehydration solution) and antimicrobials (fluoroquinolone, ciprofloxacin) – 75% of cases do not seek medical treatment	
Contribution to global agenda	Fit with SDGs, IA2030, other agendas, Regional manufacturing	<i>Shigella</i> vaccine a strategic priority for WHO	
Broader health system impact	Broader health system impact	- Potential to enhance surveillance of diarrheal diseases - Vaccination against <i>Shigella</i> can contribute to a broader set of interventions against malnutrition (stunting and potentially wasting)	

¹⁵¹ Evaluation based on comparison with other VIS 2024 candidates.

² Lancet Infect Dis.. 2022 Oct;22(10):1503-1510. doi: 10.1016/S1473-3099(22)00370-X.

Key outstanding learning questions for a *Shigella* Vaccine

- Suggestions how to work around unclear demand and unclear burden?
- Early development stage of vaccine pipeline: For broad implementation of a *Shigella* vaccine, including in children in low resource settings, a multi-site field efficacy study is needed to support a global policy decision
- Is there a pathway or mechanism to accelerate vaccine development, licensure and WHO policy recommendation based on efficacy/safety data generated from human challenge studies?
- Evidence on link between vaccination and impact on stunting and antimicrobial resistance¹
 - Prevention of long-term morbidity due to sequelae resulting from malnutrition and growth stunting is considered important to demonstrate effectiveness, and will likely be important for policy consideration
 - Vaccine impact on antibiotic use as a secondary endpoint
- How are country priorities considered given *Shigella* does not rank highly and will that affect if / how / when policy is developed?
- Is there a plan to develop an ECVP?
- **Provide signal for combination vaccine development...**

Combination vaccines are needed to optimise the effect of vaccination

Considerations

- Immunisation programmes are saturated with vaccines and the number of available vaccines is increasing – *at least six visits are required in the first two years of life to receive the 10 currently recommended vaccines*
- Significant implications for vaccine confidence, programme cost, injection supplies required, cold chain capacity and potential health impact
- Many new vaccines are likely to have moderate health impact or moderate market sizes due to regional deployment, casting doubts on eventual uptake and commercial viability
- Manufacturers are seeking signals on which combinations to prioritise

Need for global prioritisation of desirable combinations, clarity on policy pathway and regulatory policy

Chikungunya assessment

Chikungunya vaccine: Summary

Case for investment: ■ Weak ■ Moderate ■ Strong

Vaccination strategy presented: stockpile investment

VIS Criteria	Key Results	Assessment
Disease risk and burden - is the epidemic potential sufficient to prioritise a stockpile or stockpile-like investment?		
Epidemiology and risk	- The virus is transmitted through mosquito vectors, giving rise to broad geographic spread across all continents. - Global climate change allows mosquito vectors to thrive in new altitudes and latitudes and increase global CHIKV burden. - Outbreak size ranges from 500-600,000 cases. Outbreaks are explosive and cases grow quickly in affected areas.	Disease associated with low mortality but high-morbidity. Broad and increasing geographic spread of disease. Investment in diagnostics and learning agenda would address data gaps around disease burden.
Disease burden	- CFR ~0.1, increases with age and co-morbidities. Average yearly loss of 106,000 DALYs estimated globally 2010-2019. - Common symptoms are fever and joint pain for <1 week but 42.5% develop persistent neurologic or rheumatic symptoms. - Surveillance is challenged in LMICs, with misdiagnosis and under-reporting of cases and outbreaks, particularly in Africa.	
Economic and social burden	- Increased risk of severe disease among newborn babies, the elderly, and those with underlying medical conditions - CHIKV can significantly impact the health system and economy of countries, with indirect consequences for other diseases - Estimates in Colombia show cost of US\$258 for children and US\$67 for adults with CHIKV; Productivity loss of US\$81 per adult with CHIKV; Long-term morbidity (especially debilitating joint pain) results in even higher direct and indirect costs.	
Vaccine impact and feasibility - would the vaccine be feasible to use and impactful as part of epidemic preparedness and response?		
Epidemic risk reduction / mitigation	- Poor surveillance in LMICs and lack of available diagnostics limit ability for timely intervention and mitigation of threat - Apart from vector control (+ related community sensitisation), no other countermeasures available to combat spread of CHIKV	Vaccination would be impactful but challenged implementation due to poor surveillance and timely response to explosive outbreaks. In tandem with diagnostics investment, could significantly enhance impact.
Equity and social protection impact	- Female sex is a risk factor for chronic disease, especially for chronic arthritis and arthralgia. - Elderly individuals (particularly with pre-existing conditions e.g. diabetes or hypertension) at higher risk of severe disease. - CFR for at-risk subpopulations: 2.8% for neonatal infections, 0.6% for maternal-neonatal infections, 1.5% in elderly people.	
Implementation feasibility	- Implementation not easy as surveillance is weak in LMICs - Efforts under the WHO Arbovirus Initiative seek to bolster surveillance efforts for these diseases, including Chikungunya	
Fit for Gavi & Partners - what is Gavi's comparative advantage and how can Gavi's expertise contribute to the funding and delivery of this vaccine?		
Relevance	- Aligned with pandemic preparedness and equity goals; alignment with partners, e.g. CEPI priority pathogen - Gavi could be well placed to ensure that LMIC demand is better understood, e.g. via diagnostics work and learning agenda	Low risk of investment at low price for Gavi, though with potentially low demand in endemic regions due to poor disease surveillance.
Comparative advantage	LMIC demand uncertainty complicates the estimate of an appropriate size of stockpile for LMIC and market sustainability may depend on MIC/HIC demand.	
Risk	Increasing risk of epidemics as climate change broadens geographic scope; low supply of vaccine to LMICs without Gavi	

Key data gaps (draft to be reviewed with experts)

Disease-related

- Burden of disease data is very limited
- Limited available data on economic impact of outbreaks (both direct and indirect healthcare costs)
- Limited routine surveillance to guide stockpile use due to widespread underreporting of cases and misdiagnosis for dengue or other arboviruses
- Demand uncertainty, relating to uncertain country scope

Vaccine-related

- Direct data on vaccine efficacy; clinical trials for the most advanced candidates used immunogenicity as a primary endpoint
- Duration of protection; follow up studies ongoing
- Studies on individuals that are pregnant, immunocompromised, and <12y
- Demonstrate feasibility of vaccine deployment (in outbreak setting if possible)
- Research on how to implement chikungunya diagnostic tools in Gavi countries (including potential impact of supporting PQ of existing diagnostics)

Draft Investment Options

Stockpile (annual)*

Low: Stockpile size 8.3M

- Based on model, adjusted to 33% as approximation of % outbreaks reported
- Outbreak response ≥ 18 yo in at-risk populations
- ~ \$14M per year (\$2M-61M)

Base: Stockpile size 9.9M

- Based on model, adjusted to 33% as approximation of % outbreaks reported
- Outbreak response ≥ 12 yo in at-risk populations
- ~ \$17M per year (\$3M-71M)

High: Stockpile size 30M (55M with MICs)

- Based on model, assuming diagnostics implemented to guide outbreak response
- Outbreak response ≥ 12 yo in at-risk populations
- ~ \$51M per year (\$95M with MICs)

Learning Agenda

- Address key data gaps in health and economic burden of disease
- Demonstrate feasibility of vaccine deployment (in outbreak setting if possible)
- Research on how to implement chikungunya diagnostic tools in Gavi countries (including potential impact of supporting PQ of existing diagnostics)

Routine vaccination / preventive campaigns in endemic settings

- Several Gavi countries identified as having endemic transmission year on year¹
- Higher health impact than outbreak response in these settings
- Higher impact on preparedness; preempts issues around vaccine deployment being too slow to control explosive outbreaks
- Cost-effectiveness depends on endemicity (need for more seroprevalence studies)
- Strong incentives for manufacturers and opportunities for market shaping

Deprioritised due to lack of risk appetite

Next steps

Last phase is focusing on refining models, developing cost estimates and assessing implementation feasibility

Analyses

- Refined demand forecasting
- Updated health impact modelling
- Costs of programme implementation to Gavi and countries
- Assess feasibility of vaccine introduction

Develop proposals

- Develop learning agenda proposals
- Develop investment cases including risks of investment/ no investment
- Present analyses to the Steering Committee in early March

Alignment and approval

- Align to Gavi 6.0 Strategy development
- Present to PPC (May) and Board (June) for approval