VACCINE INVESTMENT STRATEGY: Oral cholera vaccine

GTFCC Annual Meeting

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13-14 June 2018, Annecy, France

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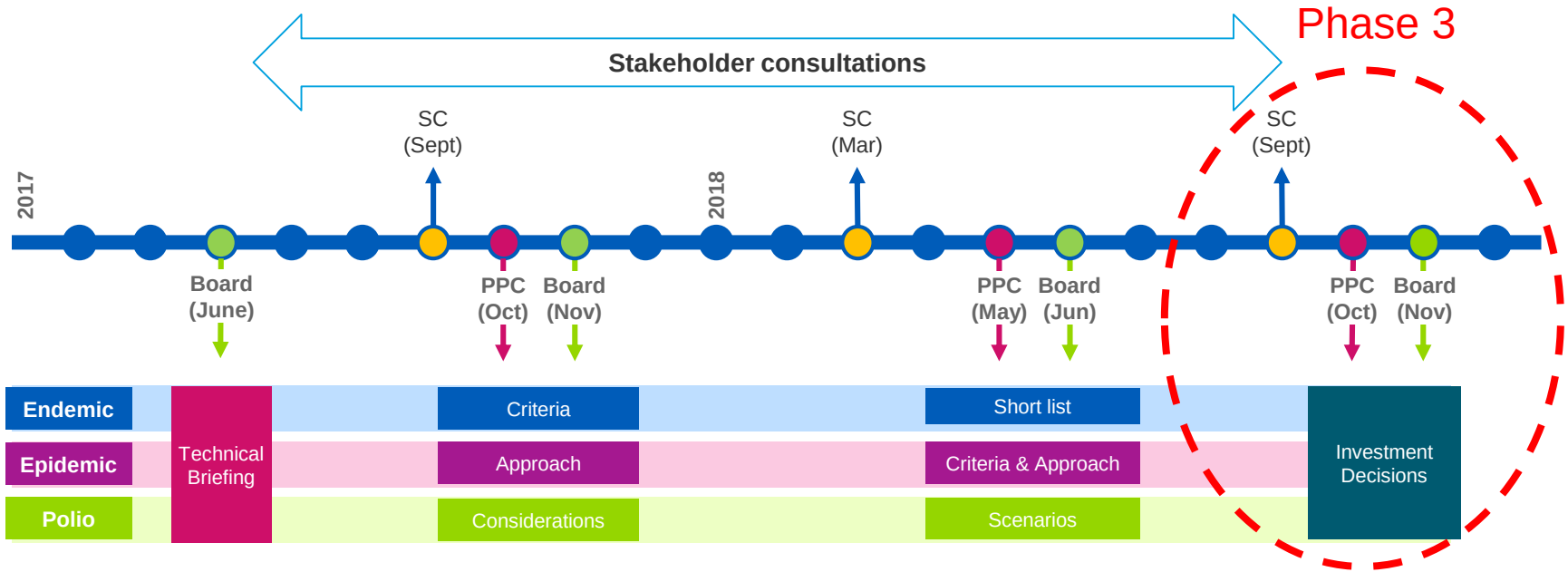
VIS 2018 timeline and process



Evaluation criteria and indicators for vaccines for endemic disease prevention

	Criteria	Indicators
Ranking criteria:	Health impact	Total future deaths averted 2020-2035, and per 100,000 vaccinated Total future cases averted 2020-2035, and per 100,000 vaccinated
	Value for money	Vaccine procurement cost per death averted Vaccine procurement cost per case averted
	Equity and social protection impact	Disproportionate impact of disease on vulnerable groups Special benefits of vaccination for women and girls
	Economic impact	Direct medical cost averted Indirect cost averted
	Global health security impact	Epidemic potential of disease Impact of vaccination on antimicrobial resistance (AMR)

	Criteria	Indicators
Secondary criteria:	Other impact	Total U5 deaths averted 2020-2035, and per 100,000 vaccinated Total DALYs averted 2020-2035, and per 100,000 vaccinated Vaccine procurement cost per DALY averted
	Gavi comparative advantage	Degree of vaccine market challenges Potential for Gavi support to catalyse additional investment
	Implementation feasibility	Ease of supply chain integration Need for health care worker behaviour change Feasibility of vaccination time point Acceptability in target population Long-term financial implications
	Alternate interventions	Optimal use of current and future alternative interventions (prevention and treatment)
	Broader health system benefits	*No specific indicator – evaluated case-by-case*
Financial implications:	Vaccine cost	Total procurement cost to Gavi and countries, 2020-2035
	Operational cost	Incremental in-country operational costs per vaccinated person
	Additional implementation costs	Additional costs for introduction

Evaluation of vaccines conducted consultatively with technical partners and in-country stakeholders

Demand Forecasting

- Vaccine products
- Vaccination strategy
- Schedule/dosing
- Delivery strategy
- Target population
- Country introduction
- Coverage

Impact Modelling

- Burden of disease
- Case fatality rate
- Efficacy
- Duration of protection

Price Forecasting

- Products
- Supplier projections
- Price projections

Other quant. analyses

- Procurement cost
- Operational costs
- Value for money
- Economic impact: cost of illness
- Global burden of disease

Qualitative analyses

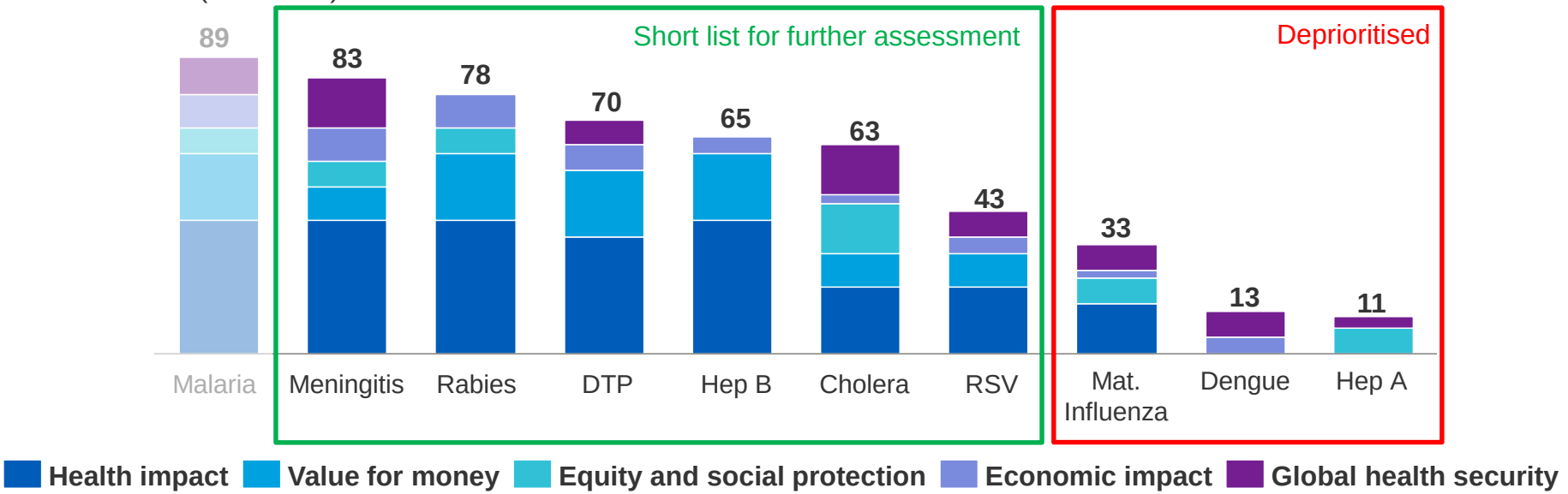
- Epidemic potential
- Impact on AMR
- Implementation feasibility
- Vaccination policy
- Other qualitative input

Bill & Melinda Gates foundation · Johns Hopkins University · London School of Hygiene & Tropical Medicine · Clinton Health Access Initiative · WHO · PATH · University of Glasgow · University of Cambridge · CDA Center for Disease Analysis · Imperial College London · University of Antwerp · Vaccine Impact Modelling Consortium · CDC Centers for Disease Control and Prevention · IHME Institute for Health Metrics and Evaluation · Swiss TPH

Note: Non exhaustive. Many other institutions and individuals were consulted as part of the VIS 2018

Final ranking of VIS candidates vaccines

Total Points (out of 100)[1]



1. Maximum 40pts for health impact (30pts for total deaths averted, 10pts for deaths averted per 100k), 20pts for value for money (cost per death averted), 15pts for equity and social protection impact, 10pts for economic impact and 15pts for global health security
Note: Malaria not up for investment decision. Used as comparator with Health impact and economic impact based on high-level estimates

Key findings from VIS 2018 analysis and recommendation for OCV

Gavi VIS 2018 key findings

Medium health impact, but contribution to equity, social protection, and global health security

- Risk of large-scale socio-political and economic consequences from outbreaks
- Burden continues to be under-estimated

Importance of shifting to comprehensive immunisation and disease control strategy

- Include preventive vaccination in high risk areas and not just reactive
- Supplement WaSH scale-up

Continued market shaping role for Gavi

- Ensure supply can meet increasing demand, building on gains made through Gavi's initial stockpile investment in 2013

Recommendation

✓ **Prioritize for shortlist**

Address open programmatic questions:

- Evolution of stockpile with expanded preventive vaccine use
- Links between emergency and preventive vaccination programmes, and more broadly with multi-sectoral disease control strategy
- Components of continued learning agenda (e.g., interval between dosing)
- Country commitment to WaSH

Evaluate financial implications:

- Whether to include surveillance to identify hotspots in operational support for campaigns

Experts consulted in Phase 2 of VIS

Experts consulted	
Abdinasir Abubakar - WHO EMRO	Justin Lesser – JHU
Andrew Azman - JHU	Myron M. “Mike” Levine – U of MD
Hans Christiansen - UNICEF	Tina Lorenson – BMGF
Kashmira Date - CDC	Imran Mirza – UNICEF
Johanna Fihman – WHO HQ	Vittal Mogasale - IVI
Guillermo Gimeno – UNICEF	Francisco Luquero – Epicentre
Tracey Goodman – WHO HQ	Julia Lynch – IVI
Linda Omar Haj – WHO AFRO	Helen Matzger – WHO HQ
Alan Hinman – independent	Lorenzo Pezzoli – WHO HQ
Shannon Larsen - BMGF	David Sack – JHU
Dominique Legros – WHO HQ	

Note: Materials represent the view of the Gavi Secretariat based on expert input. Individual experts might not agree with all presented information

Cholera Scorecard

Modelled strategy: campaigns with 2 doses to at risk population ≥ 1 year old

VIS criteria	Indicator	Results	Evaluation[1]
Health impact	Total impact averted	~21-660K future deaths, ~2-26 million future cases averted, 2020-2035	
	Impact averted per 100K	~6-180 deaths, ~560-7140 cases averted, 2020-2035, per 100K vaccinated population	
Value for money	Procurement cost per event	~$ 1,490-47,600 procurement cost per death, ~$ 40-480 procurement cost per case averted	
Equity & social protection impact	Impact on vulnerable groups	Burden concentrated among lower socioeconomic groups and displaced populations	
	Benefits for women and girls	Some evidence for increased burden in women >5 yo and differences in access to treatment	
Economic impact	Direct medical cost averted	~1% of average consumption per capita averted in out-of-pocket medical costs	
	Indirect cost averted	~$2-47 productivity loss averted, 2020-2035, per vaccinated person	
Global health security impact	Epidemic potential	IHR notifiable; antigenic changes previously caused epidemics; outbreaks in areas of low sanitation and poor access to clean water	
	Impact on AMR	High impact of vaccination on AMR (4.1/10 points in expert consultation)	
Vaccine cost	Total procurement cost	~$ 1.0-1.8 billion total procurement cost to Gavi and countries, 2020-2035	
Relevant second. criteria	Vaccine market challenges / Catalytic investment	High potential for Gavi to manage demand and supply and catalyse add. investments, e.g., WaSH, data/surveillance, GTFCC	

Additional considerations

- Significant under-reporting of disease burden due to socio-political and economic disincentives, which may drive large incidence ranges and lower impact estimates in VIS 2018 analysis
- Strong stakeholder momentum and improved understanding of implementation feasibility since 2013
- In 2016, the Gavi Board confirmed future Gavi support for vaccine procurement and operational costs for emergencies
- Reduced impact of future propensity for illness following exposure to diarrheal diseases

1. Evaluation based on comparison with other VIS 2018 candidates. For Health impact and Value for money, evaluation based on deaths averted. Details on evaluation methodology can be found in Methodology appendix

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Some questions remain for the development of investment case

Key questions / issues

- Programme Design
  - How should preventive campaigns be designed and operationalised (e.g. dosing, frequency of campaigns, hotspot identification)?
  - How should Gavi structure its OCV support to ensure OCV reinforces the broader strategy of cholera control (e.g., approval of Gavi support for preventive campaign tied to commitment on WaSH scale-up)?
  - How can we ensure that OCV use does not displace WASH?
- Supply
  - What are the implications for future management and use of the OCV stockpile in context of expanded campaigns?
  - How should supply be prioritised between outbreak response and preventive campaigns?
- Monitoring
  - What are the challenges around surveillance and M&E requirements for hotspot identification?
  - How can we monitor and measure coverage and impact of OCV use? What type of investments do we need (e.g., burden, transmission, WASH coverage, etc)?

Stakeholder consultations will be crucial in answering these questions

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Next steps to develop investment cases

Programme design
- Programme / support options
- Implementation requirements and feasibility

Financial implications
- Procurement costs (Gavi and countries)
- Operational costs, including for new platforms
- Financial implications for countries

Consultations
- In-country, technical partners, experts, Board
- Vaccine preferences, programme design, implementation

Portfolio considerations
- Synergies and trade-offs across potential investments and with current portfolio
- Alignment / implications for Gavi's current model
- Continue linking with ongoing 5.0 development

June-July:
- Consultations
- Programme design
- Costing analyses
- Implementation feasibility

August:
- Investment case development
- Cross-portfolio analyses

September: VIS Steering Committee

October 18-19: PPC
November 28-29: Board

Thank you

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BACKUPS

VIS 2018 candidates

	Vaccines / products linked to current investment		*New vaccine / product*
Endemic Disease Prevention	• Diphtheria, Tetanus, Pertussis containing boosters • Hepatitis B (birth dose) • Cholera (preventive immunisation)	• Meningitis (multivalent conjugate) • Rabies vaccine and Ig/mAb • Malaria*	• Hepatitis A • Dengue • Influenza (maternal) • RSV maternal vaccine and mAb
Epidemic Preparedness and Response	• Ebola (2nd generation)		• Pandemic influenza • Hepatitis E • Chikungunya • Zika
Polio Eradication	• IPV (post-2020)		

* Not for investment decision in 2018 as Gavi-supported pilots are ongoing. Treated as comparator in VIS 2018.

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Does not include pandemic flu and IPV post-2020

Total procurement cost (M$), by strategic period[1]

Vaccine	2020	2021-2025	**2020-2035**
Cholera	~ 60 - 160	~ 500 - 830	**~ 980 - 1850**
DTP boosters	~ 6	~ 90	**~ 280**
Hepatitis B birth dose	~ 1	~ 20	**~ 100**
Meningitis (multivalent conj.)	-	~ 360 - 420	**~ 910 - 1930**
Rabies	-	~ 30 - 80	**~ 110 - 260**
RSV (maternal)	-	~ 5	**~ 385 - 485**
Total	**~ 67 - 167**	**~1,000 - 1,400**	**~2,800 - 4,900**

1. Total procurement costs specific to procurement of vaccine including freight, syringe, safety box. These figures do not distinguish between what costs would be borne by Gavi versus countries under current Gavi policies. This detailed analysis will be conducted in the next phase of the VIS.

Cholera Executive Summary

Cholera causes ~2.9M cases per year which result in ~95,000 deaths per year, mostly among poor and vulnerable populations in Sub-Saharan Africa, South Asia, and parts of the Americas

- Significant under-reporting of disease burden due to socio-political and economic disincentives
- Cholera has high epidemic potential with associated risks of large-scale societal disruption and political / economic consequences
- Vaccination can have broader impact (beyond health) given its ability to prevent spread of disease and control outbreaks

VIS 2013 decision to support the global cholera stockpile and strengthen evidence base for preventive campaigns has led to strong stakeholder and country momentum as well as:

- Improved supplier landscape with a new manufacturer (PQ 2015), decreases in vaccine price, and PQ of an innovative presentation (2017)
- Insights on questions identified in 2013 VIS regarding vaccine effectiveness and implementation feasibility
- Improved understanding of disease burden and OCV impact in endemic countries
- Increased use of oral cholera vaccine (OCV) stockpile for preventive vaccination

Strategy being considered in VIS 2018 consists of campaigns among high-risk populations in sub-national hotspots, which will complement the already Board approved OCV support for emergencies

- In 2016, the Gavi Board approved the use of existing funding to support operational costs and confirmed future Gavi support for emergencies, moving away from time-limited VIS 2013 decision
- Additionally supporting preventive campaigns would unlock stronger market-shaping potential by improving the predictability of demand and decreasing outbreak occurrence would reduce need for use of stockpile for emergency settings over time
- Modelled vaccination strategy would support a multi-sectoral disease control strategy that also involves WaSH

As currently modelled, cholera vaccination strategy could avert ~21,000 – 660,000 deaths and ~2-26M cases between 2020-2035 at a procurement cost of ~$1.0-1.8 billion (~$1-48K per death averted)

- Medium procurement cost per deaths averted relative to other VIS vaccines

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VIS 2013 outcomes and key changes to vaccine context

VIS 2013 decision and key findings

Gavi Board approved $115M from 2014-18 to procure vaccines for the global OCV stockpile with three objectives

- Breaking the current cycle of low demand-low supply of oral cholera vaccine;
- Reducing outbreaks in Gavi-supported countries; and
- Strengthening the evidence base for periodic, pre-emptive campaigns

Evidence gaps included:

- Lack of vaccine efficacy / effectiveness data, uncertainty of demand and impact, uncertainty of programmatic feasibility

Changes to context since VIS 2013

Increased demand and associated supply constraints

- 100x increase in demand from 0.2M doses in 2013 to 20M doses in 2017 regardless of severe supply constraints
- One new manufacturer with an innovative presentation, which is easier to administer, lighter and smaller (PQ 2017)
- Decrease in weighted average vaccine price of ~28%

Improved understanding of burden, impact and effectiveness, and implementation feasibility even in high-risk settings

- Feasibility to achieve high coverage in conflict and humanitarian settings was confirmed and alternative delivery strategies to decrease operational costs were explored
- SAGE updated its recommendations to clarify vaccination strategy based on improved understanding of effectiveness and impact

2016: Gavi Board approved the use of existing funding to support operational costs and confirmed future Gavi support for vaccine procurement and operational costs for emergencies

Cholera key assumptions

xx: included in model uncertainty range
xx: not included

Models	IPM direct	JHU
Vaccination strategies	2 doses to at risk population ≥ 1 yo Every 3 years; Crisis countries vaccinate every 2 years[1]	2 doses to at risk population ≥ 1 yo Every 5 years
Uncertainty analysis driving ranges	Effectiveness (62%, 76%, 85%) Burden estimated (Low[2], Base, High) Duration of protection (3yr, 5yr)	
Other key assumptions	Fully vaccinated persons: Gavi Strategic Demand Scenarios (S2, S3 and S5) Estimated at risk population decreasing over time based on Ending Cholera Roadmap assumptions	

1. Applies to base and high scenario; three crisis countries currently included in model; 2. Low burden estimates not included for JHU model, as overall cholera burden likely underestimated

Secondary criteria and financial implications

Modelled strategy: campaigns with 2 doses to at risk population ≥ 1 year old

VIS criteria	Indicator	Results	Evaluation[1]
Other impact	U5 deaths averted, total	~1-80K U5 deaths averted, 2020 – 2035	
	U5 deaths averted, per 100K	~0-22 U5 deaths averted, 2020 – 2035, per 100K vaccinated population	
	DALYs averted (cost per DALY)	~0.7-20 million DALYs averted, 2020 – 2035, ~$ 50-1370 cost per DALY	
	DALYs averted, per 100K	~190-5,420 DALYs averted, 2020 – 2035, per 100K vaccinated population	
Gavi comp. advantage	Vaccine market challenges	High potential to influence the market (e.g., stabilize supply by increasing supplier base, further decreases in price)	
	Catalytic investment	High potential to catalyse investments in complementary investments (e.g.,WASH, data/surveillance, GTFCC)	
Implementation feasibility	Ease of supply chain integration	Packed volume of 3-17cc; 24-30 months shelf life at 2-8°C; VVM = 14-30	
	Need for HCW behaviour change	Some need for HCW behaviour change: Campaign with outreach requiring some training	
	Feasibility of vaccination time point	Campaigns outside routine vaccination schedule	
	Acceptability in target population	Ranked 5/9 in country stakeholder survey, but likely need for high-level advocacy	
	Long-term financial implications	Falls within the category of price per course $ 2-5	
Alt. interventions	Alternative interventions	No alternative interventions but complementary prevention measures include improvements in water and sanitation (e.g.,WaSH), effective ORS treatment, antibiotics and case management	
Broader health system impact[2]	Broader health system impact	Opportunity to promote WaSH interventions	
Operational cost[3]	Incremental costs per vac. person	High incremental cost of ~$ 1.80: Already used in ~20 Gavi countries; costs mostly due to technical assistance, micro-planning, and data-related costs	
Implementation costs	Additional costs for introduction	Medium: already used in ~20 Gavi countries; costs mostly due to technical assistance, micro-planning, and data-related costs	

1. Evaluation based on comparison with other VIS 2018 candidates 2. Contextual information, not evaluated 3. Generic methodology based on routine campaigns. Details on evaluation methodology can be found in Methodology appendix