Annex B: VIS 2018 candidates: cost, impact and case for investment

Cost and impact projections

The following tables provide a summary of the projected costs to Gavi and health impact for each VIS candidate in Gavi's 5.0 and 6.0 strategic periods. These projections assume all six VIS vaccines are supported and account for projected introductions of the current portfolio of supported vaccines.

Table 1: Total cost to Gavi, 2021-2025 and 2026-2030[1], in US$ millions

VIS candidate	2021-2025		2026-2030	
	Procurement costs	Operational costs	Procurement costs	Operational costs
Cholera	124	37	159	49
D, T, P - containing boosters	19	22	77	18
Hepatitis B birth dose	0	5	0	9
Multivalent meningococcal	82	38	81	0
Rabies PEP	10	2	26	12
RSV maternal vaccine	12	4	159	13
Total cost by cost type	248	111	504	103
TOTAL COST	360		608	

Table 2: Total deaths averted, 2021-2025 and 2026-2030[2], in thousands

VIS candidate	2021-2025		2026-2030		2021-2030	
	Low	High	Low	High	Low	High
Cholera	8.1	91.0	10.8	119.8	19.0	210.8
D, T, P - containing boosters	6.9	6.9	30.6	30.6	37.6	37.6
Hepatitis B birth dose	11.3	56.0	75.1	337.9	86.5	394.0
Multivalent meningococcal	6.0	20.5	8.7	28.3	14.8	48.8
Rabies PEP	1.4	5.8	19.7	58.9	21.1	64.7
RSV maternal vaccine	0.5	5.2	7.0	56.6	7.5	61.8
Total	**35**	**180**	**150**	**630**	**180**	**810**

Table 3: Total cases averted, 2021-2025 and 2026-2030, in thousands

VIS candidate	2021-2025		2026-2030		2021-2030	
	Low	High	Low	High	Low	High
Cholera	870	9,150	800	8,320	1,670	17,470
D, T, P - containing boosters	1,500	1,500	3,950	3,950	5,460	5,460
Hepatitis B birth dose	130	180	510	630	640	820
Multivalent meningococcal	170	560	130	440	310	1,000
Rabies PEP	-	-	-	-	-	-
RSV maternal vaccine	100	430	1,220	2,670	1,330	3,100
Total	**2,800**	**11,840**	**6,630**	**16,040**	**9,430**	**27,880**

[1] The projected costs for D, T & P-containing boosters assume that all Gavi-supported countries would elect to use the pentavalent vaccine for the 1st booster dose due to programmatic benefits. The use of the pentavalent vaccine for the 1st booster dose would result in increased cost to Gavi due to vaccine co-financing.

[2]The low and high values represent the lower and upper range of potential health impact outcomes of each VIS candidate. The range of potential health impact reflects both uncertainty in key parameters as advised by disease experts (e.g. vaccine efficacy, burden of disease) and the use of multiple disease impact models. Deaths averted will be in future years based on vaccination in this time period.

Description of VIS candidates

The proposed investment for **diphtheria-, tetanus- & pertussis-containing (D, T & P) boosters** would catalyse introductions through establishment or strengthening of the immunisation platform for the relevant D, T & P-containing booster vaccine.[3,4] From 2021-2035, support for D, T & P-containing boosters would cost ~US$ 2,070 – 5,900 per death averted[5]. This investment would help to complete the vaccination series for all three diseases to confer longer-term protection to address the waning immunity of the primary pentavalent series. These boosters would also support sustaining the elimination of maternal and neonatal tetanus, and help reduce diphtheria outbreaks. Despite long-standing WHO recommendations for the boosters, national uptake has been slow due to barriers related to establishing the timepoints. Investment in platform establishment could mitigate this risk and would be crucial for programmatic success.

The proposed investment for **hepatitis B birth dose** would accelerate introduction via funding to establish the immunisation platform.[6] From 2021-2035, support for the birth dose would cost ~US$ 70 – 400 per death averted. This vaccine closes the immunity gap between birth and the first dose of pentavalent vaccine, protecting newborns who are at higher risk of developing chronic hepatitis B virus infection. The birth dose also promotes integration of the maternal, neonatal and child health (MNCH) and Expanded Programme on Immunization (EPI) platforms to strengthen delivery of other interventions. To address the challenge of reaching newborns born outside health facilities, the VIS learning agenda could consider delivery technology innovations.

The proposed investment for **multivalent ACW-containing meningococcal conjugate vaccine** (e.g., ACWY or ACWYX) is in routine immunisation in high-risk areas of the meningitis belt in sub-Saharan Africa. A targeted, risk-based vaccination strategy was developed with input from partners and disease experts for the purposes of the investment case.[7] Given the lack of a licensed, prequalified multivalent conjugate vaccine that meets the price parameters (assumption of up to US$ 3/dose initially at low volumes), a decision to invest at this stage would be in-principle. From 2021-2035, support for multivalent meningococcal vaccine would cost ~US$ 6,350 – 13,350 per death averted.[8] This investment would enhance protection to address incidence of serogroups C, W and potentially other emerging serogroups, and would strengthen routine immunisation to reduce reliance on the stockpile to

[3] Funding would support activities intended for platform strengthening beyond just the introduction of the booster. This support would be further defined as through the update of the HSIS Support in 2019-2020.
[4] The WHO recommended strategy is a booster that includes tetanus, diphtheria & pertussis (DTwP or pentavalent vaccine) between 12-24 months of age, and two additional tetanus & diphtheria-containing boosters at between 4-7 years of age and 9-14 years of age.
[5] Cost includes procurement costs only, to Gavi and countries where cost-sharing applies.
[6] Funding would support activities for platform strengthening beyond introduction.
[7] There are currently 26 countries in the meningitis belt. 11 high and medium incidence countries were assumed to switch to multivalent conjugate vaccines in routine immunisation. These countries were further assumed to conduct subnational campaigns in high risk areas at introduction. The final programme will be developed following recommendation from the Strategic Advisory Group of Experts in Immunization (SAGE).
[8] This figure is inclusive of NmA impact.

manage costly and disruptive outbreaks. It would also provide Gavi an opportunity to shape the multivalent market towards improved supply and price.

The proposed investment in **oral cholera vaccine (OCV)** is planned, periodic immunisation[9] in cholera endemic hotspots. This programme would build on Gavi's ongoing investment in a global OCV stockpile for both outbreak response and pre-emptive hotspot vaccination. From 2021-2035, support for OCV would cost ~US$ 2,050 – 20,600 per death averted.This investment would reduce cholera incidence among poor and vulnerable populations, closing a critical equity gap. A proactive immunisation approach would also provide greater demand predictability and improve supply. A Gavi investment would be most impactful as part of a multisectoral approach to cholera control, and vaccine cost-sharing and commitment to multisectoral plans would help ensure programmatic sustainability and ownership among countries.[10]

The proposed investment for **rabies post-exposure prophylaxis (PEP)** would be incremental support (in addition to existing domestic financing) for human rabies vaccine. As rabies is 100% fatal and disproportionately affects vulnerable people, a targeted programme would close a critical equity gap. From 2021-2035, support for rabies PEP would cost ~US$ 850 – 3,150 per death averted. This investment would help consolidate demand and improve access to rabies PEP by those who have previously been unable to obtain the vaccine. A demonstrated commitment to a multisectoral plan for rabies control and an assessment of financial and programmatic readiness would be required. Introductions would be phased over time to allow for continuous programme improvement. This would incentivise countries to strengthen the non-human rabies vaccine components of their broader plans.

The proposed investment for **respiratory syncytial virus (RSV)** is in-principle support for immunisation products (vaccine and monoclonal antibodies [mAb]) – contingent on regulatory approvals and WHO recommendation – and immediate support for introduction planning activities such as evidence and demand generation, in close collaboration with partners.[11] From 2021-2035, support for a maternal RSV vaccine would cost ~US$ 2,750 – 22,000 per death averted.[12] The primary benefit of this investment would be to avert significant global RSV burden in neonates and young infants who compromise the majority of deaths in children under 5, and is also an opportunity to accelerate the integration of EPI and MNCH services. In addition, Gavi could proactively shape the RSV market and ensure that lower-income countries can access RSV immunisation products simultaneous to high-income countries. Finally, the investment could also potentially reduce antibiotic use to treat lower respiratory infections and thereby reduce antimicrobial resistance.

[9] Given current evidence on the limited duration of protection of current vaccines, OCV would be delivered via preventive campaigns (e.g., every 3 years), although their size or frequency could reduce over time if longer-term cholera control interventions are effectively implemented.
[10] Appropriate cost-sharing would be determined in the review of Gavi's co-financing policy in 2019-2020.
[11] Suitable RSV immunisation products are not yet available, but a maternal vaccine may be available from 2020-2021 and an infant monoclonal antibody (mAb) from 2024. Gavi would engage with EPI and MNCH stakeholders to define its role in introduction planning activities in the context of the broader ongoing collaboration gaps in advance of RSV immunisation product availability.
[12] At current projected prices, the mAb does not match the value for money of the maternal vaccine.

VIS Learning Agenda

Given the different nature of the VIS vaccines (e.g., the establishment of new timepoints or need to integrate across sectors for broader disease control), a number of operational and programmatic questions remain. Answering some of these questions would close gaps in knowledge relevant for optimal programme design and enhance the impact of Gavi's investment. A VIS learning agenda across five of the six vaccines[13] would answer three main questions:

How can additional information regarding disease burden facilitate programme design and implementation as well as impact assessment? Key information would include:

- Adequate identification of cholera hotspots and the predictive value of these areas as sources of incidence and outbreaks;
- Trends in meningococcal strain/serogroup disease burden.

What is the optimal programme design or delivery strategy? Key information would include:

- Delivery innovation to reach out-of-facility births with hepatitis B birth dose;
- Effect of population characteristics (migrating, urban, fragile) on OCV preventive campaigns implementation;
- Appropriate partnership structure for complementarity between donor investments in human and animal rabies control, or country-level coordination of cholera control.

What lessons can be learned from roll-out of a Gavi programme to enhance feasibility and improve coverage? Key information would include:

- Lessons learned in establishing or strengthening the platforms for the second and third D, T, & P-containing boosters;
- Lessons learned in identifying relevant criteria for programmatic success in the roll-out of human rabies PEP within a broader integrated disease control programme.

Some aspects of this learning agenda (addressing the first two questions) could be implemented in 2019-2020 in advance of opening funding windows. Other components (addressing the third question) would span the first few years of the programme implementation beginning 2021 or beyond.

[13] RSV is excluded from the proposed learning agenda. The proposed RSV investment includes separate support towards introduction planning activities (e.g., evidence and demand generation) as part of a broader effort together with partners.